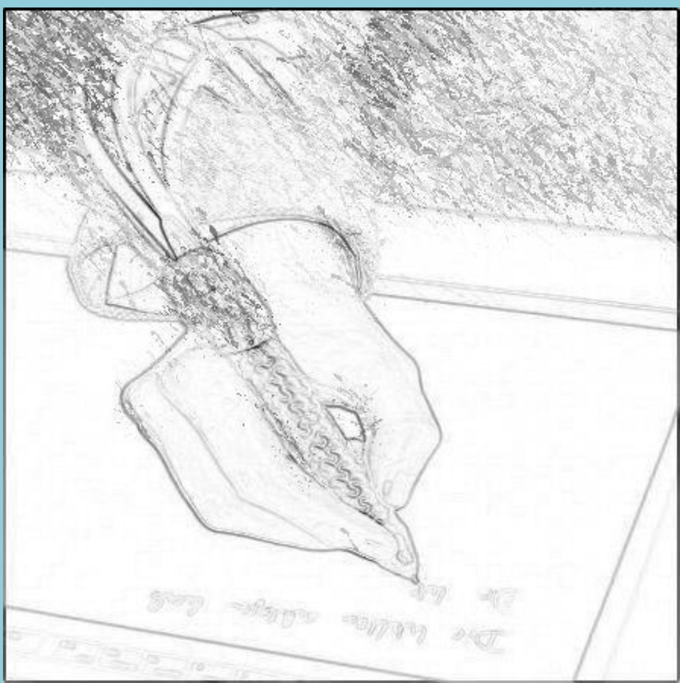
Kinematische und Kinetische Charakteristika des Schreibkrampfes

Kinematic and Kinetic Characteristics of Writer´s Cramp



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Kinematic and Kinetic Characteristics of Writer´s Cramp

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Content

List of abbreviations

WC: Writer´s Cramp

sWC: simple Writer´s Cramp

dWC: dystonic Writer´s Cramp

cWC: complex Writer´s Cramp (same condition as dystonic Writer´s Cramp)

pWC: progressive Writer´s Cramp

Ctr: Control

NIV: Number of Inversions in Velocity per stroke:

SEP: Somato Sensory Evoked Potential

PET: Positron Emission Tomography

VBM: Voxel Based Morphometry

fMRI: functional Magnetic Resonance Imaging

EMG: Electromyography

TMS: Transcranial Magnetic Stimulation

PAS: Paired Associative Stimulation

TENS: Transcutaneous electrical stimulation

Preface

Since 4.000 before Christus- when oral transmission was replaced by the development of written script - handwriting played an essential role for transfer of knowledge and traditions. Even the progression of electronic media could not reduce the importance of handwritten notes. Notes can be written everywhere and anytime. Furthermore handwriting in letters, notifications and cards is sign of personal note. Since handwriting is an essential and granted basic, people with deficits in handwriting are hit even harder. Normal events like filling in a form or signing a contract can constitute insurmountable hurdles. Many patients are also impaired by the execution of their jobs. The level of suffering depends both on the type and degree of the deficits in Writer´s Cramp and individual living conditions.

1. Introduction

1.1 Dystonia

In our days the term dystonia is used to refer to a heterogeneous group of clinical and genetic movement disorders. Dystonia is characterized by sustained muscle contractions frequently leading to repetitive abnormal postures or twisting movements (Fahn et al., 1987; Fahn, 1998; Burbaud, 2012).

The prevalence of dystonia is estimated to be 15 to 30 per 100 000 and is third most common movement disorder after essential tremor and Parkinson´s disease. (Defazio, 2010; ESDE, 2000; Nutt et al., 1988).

Dystonia can be classified depending on aetiology, age of onset and affected body regions (Albanese et al. ,2011) (see Table 1). Depending on epidemiological studies the cause of primary dystonias seems to be a combination of genetic background and exogenious causes (Defazio, 2010).

Primary or idiopathic dystonia is definied as a condition where dystonic movements and a possible coexistent tremor are the only clinical symptoms. Further no pathology of the central nervous system or other apparent cause are present (Breakfield et al., 2008; Cassidy, 2010). Focal dystonia or task-specific dystonia is the most common form of primary dystonia (Burbaud, 2012). Focal dystonias are categorized by the body part affected or impaired task. Among them are: Writer´s and Musician´s Cramp (hand), Blepharospasm and Oromandibular Dystonia (facial musculature), Spasmodic Torticollis (neck) and Laryngeal Dystonia (vocal cords) (Cassidy, 2010; Burbaud, 2012).

Table 1: Classification of dystonia

Classification of dystonia	
1. Classification by cause	
a) Primary (or idiopathic):	dystonia is the only clinical sign, apart from tremor; no identifiable exogenous cause or other inherited or degenerative disease. Example: DYT1 and DYT6 dystonias
b) Dystonia plus:	dystonia is a prominent sign, but associated with another movement disorder; no evidence of neurodegeneration. Example: Myoclonusdystonia (DYT11)
c) Heredodegenerative:	dystonia as a prominent sign, among other neurological features of a heredodegenerative disorder. Example: Wilson's disease.
d) Secondary:	dystonia as a symptom of an identified neurological condition, such as a focal brain lesion, exposure to drugs or chemicals. Examples: dystonia due to a brain tumour, off-period dystonia in Parkinson's disease.
2. Classification by age of onset	
a) Early onset:	usually starts in a leg or arm and frequently progresses to involve other limbs and the trunk
b) Late onset (> 21 years):	usually starts in the neck (including the vocal folds), the cranial muscles or one arm; tends to remain localised with restricted progression to adjacent muscles.
3. Classification by affected body region	
a) Focal:	single body region (e. g., writer's cramp, blepharospasm)
b) Segmental:	contiguous body regions (e. g., cranial and cervical, cervical and upper limb)
c) Multifocal:	non-contiguous body regions (e. g., upper and lower limb, cranial and upper limb)
d) Generalised:	both legs and at least one other body region (usually one or both arms)

Table 1 adopted from Albanese 2003; Albanese et al. 2011

1.2 Writer´s Cramp

Writer´s Cramp (WC) is a specific form of focal hand dystonia or task specific dystonia (Sheehy und Marsden 1982; Hallett 2006). The prevalence of Writer´s Cramp is estimated to be about 1.1 to 1.7 per million persons, as shown in a study conducted in eight European countries (Warner et al., 2000). A study in Munich 2002 estimated a prevalence of 0.2 per 100.000 (Castelon Konkiewitz et al., 2002). Exact numbers are however not available and number of unknown cases may be high.

Writer´s Cramp is classified by uncontrollable muscle co-contraction and hyperactivity, muscle spasms and dystonic postures of the writing limb when attempting to write. This is clinically expressed by pain, loss of control of the writing stylus and use of exaggerated forces on the stylus and against the surface (1st study). Script production is slowed, strenuous and akward (Sheehy & Marsden, 1982; Mai & Marquardt, 1994; 1st study). Most of the time the script is still legible but this often goes to the expense of abnormal posturing of fingers, hand, wrist, elbow and shoulder (Sheehy & Marsden, 1982; Mai & Marquardt, 1994, 1st study; 2nd study).

Risk factors can be long periods of skilled repetitive movements in writing combined with genetic predisposition and environmental modifiers (Frucht, 2004; Hallett, 2006; Torres-Russotto & Perlmutter, 2008; Hallett, 2011). Former studies showed that the development of Writer´s Cramp is related to activities with intense and precise writing (Lin & Hallett, 2009, Jedynak et al., 2001; Hallett, 2006, Quartarone et al., 2005).

The precise **pathophysiology and aetiology of WC** is still unclear and multifactorial, but there are several hypothesizes identified by neurophysiological and neuroimaging studies: decreased inhibition at different levels of the nervous system, impaired sensorimotor processing, maladaptive plasticity and abnormalities within the basal ganglia, overuse dedifferentiation or cortical reorganisation (Hallett, 2006; Torres-Russotto & Perlmutter, 2008; Lin & Hallett, 2009; Cassidy, 2010).

Abnormal somatosensory processing is not obvious on a clinical level, but spatial and temporal discrimination testing, testing of Somatosensory Evoked Potential (SEP), Positron Emission Tomography (PET) and Voxel Based Morphometry (VBM) can uncover subtle derogations in both affected and unaffected hands (Bara-Jimenez et al., 1998; Murase et al., 2000; Molloy et al., 2003; Sanger et al., 2001; Lerner et al., 2004; Garraux et al., 2004; Tinazzi et al., 2009). Peller et al. (2006) showed an increase in BOLD (blood oxygen level-dependent) signals for WC patients compared to healthy controls in fMRI (functional Magnet Resonance Tomography) in thalamus and basal ganglia structures by performing a simple spatial discrimination task, although patients were able to perform the task without impairments.

A lack in inhibition at different levels of the nervous system is one of the suggested mechanisms to describe the underlying pathophysiology in focal hand dystonia (Hallett, 2006; Torres-Russotto & Perlmutter, 2008; Hallett, 2011). The nervous system needs an equilibrium between excitation and inhibition (Lin & Hallett, 2009). Loss of inhibition is likely amenable for the excessive motor activity in writer´s cramp leading to pathological long bursts of EMG activity, reduced level of reciprocal inhibition in forearm muscles, subfunction of cortical inhibitory circuits in TMS protocols, co-contraction in antagonist muscles with voluntary movement, overflow of muscle interaction not needed for the writing movement and dystonic symptoms in the affected joint (Nakashima et al., 1989; Panizza et al., 1990; Chen et al., 1997; Sohn & Hallett, 2004; Hallett, 2006, 2011; Torres-Russotto & Perlmutter, 2008).

The mechanism of homeostatic plasticity has been found abnormal in patients with focal hand dystonia (Byl et al., 1996; Blake et al., 2002; Quartarone et al., 2003, 2005, 2008). Plasticity is needed to integrate new motor skills in a dynamic environment and to ease learning and memorization (Lin & Hallett, 2009). It seems that increased plasticity is triggered by repetitive activity over long periods and so the threshold for activation of special circuits is decreased (Torres-Russotto & Perlmutter, 2008). Applying of paired associative stimulation (PAS) with TMS revealed exaggerated facilitation and loss of spatial specificity (Quartarone et al., 2003).

Cortical reorganisation: Uncommon repetitive fine motor tasks seem to enlarge repetitive fields and map onto neurones of the motor system and in this way initiate dystonic movements (Byl, 2007). This idea derived from experiments with owl monkeys, conducted by Byl et al. (1996, 1997). The primates were trained to perform a new motor task by maintaining grasp on a manipulandum that opened and closed (Byl et al., 1996, Byl et al., 1997). Excessive repetition of that task led to signs of a dystonia-like phenotype in the investigated primates.

The study group around Mai and colleagues (Mai & Marquardt, 1994; Mai, 1995) hypothesized that symptoms and impairment in Writer´s Cramp are a **combination of initial perturbation and the following compensative strategies as well as a result of an inadequate motor learning process.** Handwriting is a highly skilled and automated movement. A speculation is that dyskinesia induces a control strategy with deceleration of movement, stabilisation of joints by the use of co-contractions and intensification of conscious control. Similar mechanisms are used to learn new motor skills, but already automated movements can be disturbed by such mechanisms (Mai, 1995).

Current therapeutic approaches for writer´s cramp include pharmacological and non-pharmacological treatments (Zeuner et al., 2009).

The most important current pharmacological treatment is the injection of **botulinum toxin type A** into affected muscles of hand and forearm resulting in chemodenervation (Kruisdijk et al., 2007; Djebbari et al., 2004; Wissel et al., 1996; Cole, 1995; Tsui et al., 1993). Besides the significant benefit, the therapeutical success is weakened by a loss of effect after three month past injection and a need of long-term treatment. Further there is a risk of a lasting weakness of the hand and/or forearm and a lack of response in subgroups of patients (Delnooz & van de Warrenburg, 2012; Zeuner & Baur, 2009; Djebbari et al., 2004; Wissel et al., 1996).

Non-pharmacological approaches include occupational therapy, immobilization, neurostimulation, sensory and motor training programs. These attempts are mainly based on pathophysiological findings (Lin & Hallett, 2009).

Patients showing mild symptoms are advised to reduce handwriting and/or consult an occupational therapist (Zeuner & Baur, 2009).

Immobilization as a form of therapy relies on the mechanism of neuronal plasticity and retuning. This paradigm was tested in patients with musician and writer´s cramp by limb immobilization for one month (Priori et al., 2001; Pesenti et al., 2004). The therapeutic effect after removal of splints remained for at least 12 months.

The effect of **neurostimulation** in the treatment of Writer´s Cramp relies on the improvement of loss of reciprocal inhibition in hand and forearm muscles (Tinazzi et al., 2005a; 2006; Hallett, 2006). Transcutaneous electrical stimulation (TENS) in simple WC of the forearm muscles for two weeks showed a significant effect that remained for three weeks (Tinazzi et al., 2005b).

Transcranial magnetic stimulation (TMS) to primary motor cortex contralateral to the affected arm showed no significant effect but a transient improvement of handwriting in some of the patients (Siebner et al., 1999a,b). Murase et al. (2005) applied TMS to the dorsal premotor cortex contralateral to the affected arm and showed a significant effect on handwriting. Likewise Borich et al. (2009) observed an improved performance of handwriting lasting for at least ten days after the application of repetitive TMS to the premotor cortex.

A sensory training program was tested in the form of Braille reading by Zeuner et al. (2002). Improvement of handwriting and dystonic symptoms correlated with improvement of sensory perception. (Zeuner et al., 2002; Zeuner & Hallett, 2003).

Training procedures which aim to retrain sensorimotor skills include tailored programs based on individual patterns of preserved and pathological writing aspects (Mai & Marquardt, 1999; Schenk et al., 2004), the usage of a modified pen grip (Baur et al., 2006; 2009), the usage of auditory grip force feedback (Baur et al., 2009b) and a single finger training program in combination with splinting of the non-trained fingers (Zeuner et al., 2005). The behavioural treatment of Mai and Colleagues using handwriting movements to improve symptoms in WC and reduce inappropriate handwriting strategies was proven efficient by Schenk et al. (2004) and Baur et al. (2009).

1.3 Subtype and task specificity in Writer´s Cramp

An important clinical feature of WC is the task specifity (Lin & Hallett, 2009). Typically symptoms first only occur during writing but can progress to proximal and distal muscles or even involve other fine motor tasks (Sheehy & Marsden, 1982; Torres-Russotto & Perlmutter, 2008). Consequently Writer´s Cramp can be classified into three different subgroups. In 1888 Gowers was the first to distinguish the entity according to the co-occurence of deficits. Sheehy and Marsden (1982) retained this classification and classified three subgroups: simple, dystonic/complex and progressive WC. In simple Writer´s Cramp(sWC) symptoms are only present during performing writing or drawing movements, while other manual tasks are performed normally. Conversely, patients with dystonic/complex Writer´s Cramp (dWC) develop muscle hyperactivity in non-writing tasks such as activities like drinking, eating, shaving / makeup or computer work. Patients with progressive Writer´s Cramp (pWC) initially only had symptoms while writing and drawing (like sWC) and subsequently evolved difficulties in performing other fine motor tasks (like dWC).

Only a few studies investigated whether this clinical differentiation also indicates an underlying different aggravation in handwriting. Schenk & Mai (2001) compared the handwriting performance in all three subgroups and the only significant difference was that dWC patients had less movement automation (NIV) than sWC patients. Also Das et al. (2007) investigated the difference between simple and dystonic (complex) WC and found out that patients with dWC had a longer disease duration and a higher severity score on the BFM scale. On the contrary Jedynak et al. (2001) reported similar age of onset, legibility, pain, handicap, similar mean scores of handicap and similar mean numbers of written words on the writing test. Like in the latter study our findings also yielded that there were no significant differences between sWC and dWC patients.

Hence one aim of our first study was to shed more light onto the performance differences in handwriting itself between subtypes of WC (simple and dystonic/complex WC) as well as between controls and WC patients. As our sample was mainly based on self-reports we only differentiated between simple (sWC) and dystonic/complex WC patients (dWC/cWC).

1.4 Grip force

As uncontrollable muscle co-contraction and hyperactivity are cardinal symptoms of WC, forces produced during handwriting, pen-tip force and grip force play a pivotal role. Elevated pen tip forces were found in studies among WC patients in comparison to healthy controls (Marquardt et al., 1996; Zeuner et al., 2005; Chakarov et al., 2006; Baur et al., 2006; Zeuner et al., 2007; Baur et al., 2009 a, b). Conversely grip force during handwriting has not yet been intensely investigated. This may be due to the fact that it is difficult to measure grip force without interfering the writing process and individual positioning of the fingers on the barrel. A solution was the usage of flexible and flat pressure sensitive matrices that can be wrapped around the writing stylus. With that technique applied forces can be measured at multiple sites and the distribution of different types of grips can be recorded. Chau et al. (2006) used such a technique to investigate children with cerebral palsy, and a control group and stated that this was a feasible method. We used a similar method with a pen equipped with a fine grain force sensor matrix and a digitizing tablet. We expected a high diversity of grip force in patients ranging from normal values up to manifold increases. As Herrick and Otto (1961) found a correlation of pen tip force and grip force in healthy objects we expected to confirm this finding and in addition to that to find a similar correlation in patients. Therefore we measured both forces as well as kinematic parameters in a set of 27 WC patients (14 sWC; 13 dWC) and 14 controls during writing the sentence “Die Wellen schlagen hoch”.

Besides, little is known on the generalisation of excessive forces in patients. In particular individual characteristics of force control in patients across different fine motor tasks are of interest. Studies on sensorimotor and cognitive control strategies used tasks like grasping, lifting or moving hand-held objects. Analysis in healthy subjects showed that they adjust their grip force to the weight of the object and surface friction (Johansson & Westling, 1984; Flanagan & Johansson, 2002). Previous studies found increased grip force levels in WC patients compared to healthy controls while grasping, lifting and moving hand-held objects (Odergren et al., 1996; Serrien et al., 2000; Schenk & Mai, 2001; Nowak et al., 2005). However information on the correlation and generalisation of grip forces is rare. Especially information on the comparison of individual grip force levels in handwriting and in other manipulative tasks is missing as former investigations weren´t able to correlate grip forces in different fine motor tasks, especially the comparison of grip forces during handwriting and other fine motor tasks. The above-mentioned studies compared either severity of WC or pen pressure in handwriting with grip force levels in hand-held tasks. Thus we designed this study in order to get more information on grip force control, finger force regulation and progression of force deficits in handwriting and two other fine motor tasks (lifting and vertically moving of hand-held objects). Our aim was to answer questions on generalisation of impairment of forces in WC patients.

1.5 Procedures: Kinematic and Kinetic Characteristics

1.5.1 Handwriting

Handwriting of WC patients is frequently abnormal in aspects of writing speed and fluency, abnormal letter forms and the usage of excessive forces on writing stylus and surface.

The evaluation of handwriting was done with the help of movement and kinetic analysis. We used a digitizing tablet (Wacon IV, sampling rate 200Hz, spatial resolution 0.05mm), a special writing stylus with integrated force sensor and a matrix of force sensors wrapped around the writing stylus (Pliance-system, Novel, Munich).

The position of the tip of the writing barrel was registered with the digitizing tablet. The pen pressure vertically exerted onto the tablet was extrapolated from the axial force measurement inside the pen. The grip force was measured by a matrix consisting of 88 force sensors distributed across the whole pen surface with a spatial resolution of 5 x 10 mm (Pliance-system, Novel, Munich). Nonparametric regression methods were used to calculate and smooth movement trajectories and corresponding velocity curves (Mai & Marquardt 1994). Data analysis was done with the software CSWin 2007 (Medcom, Munich). A set of different handwriting tasks was performed. For the first study (Schneider et al. 2010) the spectrum consisted of repetitive writing of simple symbols and letters to copy a given text. The other two studies analysed the test sentence ("Die Wellen schlagen hoch"). In particular the set of tasks were:

- Superimposed circles within 3 s
- Pairs of lower case lls in cursive writing style within 10 s
- The German sentence: "Die Wellen schlagen hoch". The time needed to complete the sentence was measured.
- Copying of a given text (weather forcecast) that was new to all subjects. Tested was prolonged writing. 5 min were recorded. The first 40 s were erased, the next 40 s as well as the last 40 s were analysed separately. The exclusion of the first 40 s was meant to avoid possible uncertainties at the beginning.

Three trials for each of the tasks (tasks 1. to 3.) were recorded and the results were averaged across the trials.

The following parameters were analysed:

- **Frequency (Hz):** Parameter of movement speed. Average number of strokes per second.
- **NIV (Number of inversions in velocity per stroke):** Parameter of movement automation. Average number of local peaks in the vertical velocity profile within each segment. The greater the value, the less automated is the writing process. In skilled writers each stroke is associated with a smooth velocity profile, which has only one peak (NIV=1, Mai & Marquardt 1994).
- **Amplitude (mm):** Parameter of script size. The average vertical amplitude of strokes with stroke length in the vertical direction.
- **Coefficient of variation (CV) of stroke duration (%):** Parameter of temporal variability.
- **Pen tip force = Pen pressure (N):** Parameter of vertical pressure
- **Grip force (N):** Parameter of integral grip force. Calculated for the periods when the pen was in contact with the paper.
- **Relaxation:** Parameter calculated by dividing grip force during periods without pen contact with the tablet by grip force during contact periods. Parameter of fatigue und economic motor strategy
- **Duration of the test sentence (s):** Parameter of handwriting speed. Time needed to complete the sentence "Die Wellen schlagen hoch".
- **Number of written characteristics** in the copying task.

1.5.2 Object manipulation

In their seminal study of 1984 Johansson and Westling introduced their sensitive paradigm for studies of grip force control under natural conditions with usage of object manipulation, more precisely the grasping and lifting of objects (Hermsdörfer, 2009). Studies using this paradigm revealed that healthy persons precisely adjust the amount of grip force to the object´s weight and other characteristics of the object (Johannson & Westling, 1984, Johannson, 1996; Flanagan & Johannson, 2002) whereas patients with central nervous disorders showed abnormal patterns in grip force control(Fellows et al., 1998; Nowak & Hermsdörfer, 2005; Hermsdörfer et al., 2003; Rhaghavan et al., 2006; Fellows et al., 2001; Brandauer et al., 2008). Studies that measured the grip force used to grasp and lift an object (box lifting) in WC revealed that grip forces were increased in WC patients compared to healthy controls (Odergren et al., 1996; Serrien et al., 2000; Schenk & Mai, 2001; Nowak et al., 2005b).

Appearing time-varying inertial load forces during vertical up and down movements (cyclic movements) of an object have to be adjusted by simultaneous and sufficient grip force adjustments to prevent the object from falling (Flanagan & Wing, 1995; Nowak & Hermsdörfer, 2005, Nowak & Hermsdörfer, 2009). Compared to healthy subjects patients with central nervous disorders showed an impaired coordination of grip force and load force (Hermsdörfer et al., 2008; Brandauer et al., 2010). While previous studies in WC patients only used the lifting paradigm to investigate grip force behaviour in WC patients, we were the first ones to test grip force behaviour in a cyclic movement task. We hypothesised that the cyclic task may match the demands during handwriting closer since the patient´s grip force has to be continuously modulated due to varying dynamic loads.

1.5.2.1 Box lifting

Box lifting was done with a plastic box (depth x width x height: 9 x 9 x 7 cm) with a vertical disk-like handle covered with fine grain sandpaper (see fig. 1 A).

The measurement of grip force by a force sensor incorporated in the handle (model BKS, Rieger, Rheinmünster, Germany) with a range of 0 to 100 N and an accuracy of ± 0.2 N. The weight of the object was measured with the platform on which the box was placed (model PW, HBM, Darmstadt, Germany) with a range of 0 to 100 N and an accuracy of ± 0.1 N. Data were analysed with a custom-made PC program (GFWIN).

The box had to be lifted to a height of 5 cm above the table surface, had to be held stationary for 5 s and finally had to be replaced on the table. Altogether 16 trials were performed with two different weights (300 and 600 g, handle included). The performance always started with the heavier weight for the first eight trials and then continued with the lighter object.

The following parameters were recorded and analysed for each lifting trial. Values were averaged across the 16 trials (cf Hermsdörfer et al. 2003):

- **Load force Lift (N)**: Sum of gravitational and inertial load of the object
- **Peak grip force Lift (N)**: Maximum grip force during lifting
- **Static grip force Lift (N)**: Grip force during stationary holding of the object
- **Lifting time (ms)**: Interval between contact with the handle and lift-off of the object

1.5.2.2 Cyclic movements

For the purpose of the cyclic moving task a manipulandum was grasped with the dominant right hand and repeatedly vertically moved up and down without tilting.

The manipulandum used was disc-shaped with diameter of 9 cm, width of 4 cm, a mass of 372 and both sides covered with fine grain sandpaper (see fig. 1B)

Movement amplitude was approximately 30 cm. Three types of frequency were used (slow, moderate, fast). Three trials were performed with 10 times slow, 10 times moderate and 10 times fast frequency.

The following parameters were used and determined for each selected epoch, later on averaged across these epochs (cf Hermsdörfer et al. 2003):

- **Average Grip Force Cycl. (N)**: Grip forces during cyclic movement, averaged across epochs
- **Grip Force/ Load Force Cycl. :** Ratio of grip and load forces
- **Cross-Correlation Coefficient Cycl.** : Max. coefficient of cross correlation between grip force and load force signal. Parameter expresses precision of coupling between forces
- **Time Lag Cycl.**: Time lag of cross correlation analysis. Parameter expresses temporal relationship between grip and load force.

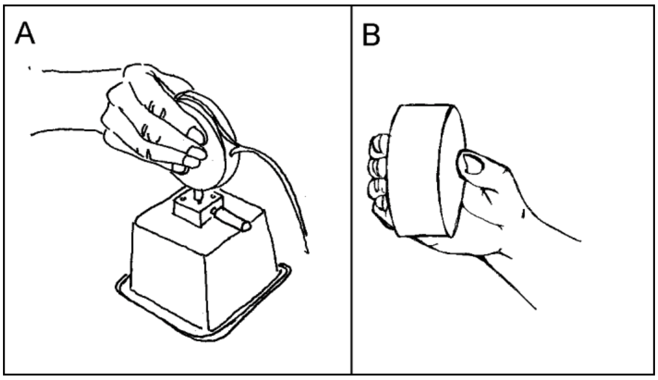

Fig. 1: Schematic drawings of the box for the lifting task (A) and the manipulandum for cyclic movements (B).

2. Summary

2.1 Summary in German

Schreibkrampf wird als fokale tätigkeitsspezifische Dystonie klassifiziert. Leitsymptome sind muskuläre Ko-Kontraktionen und Hyperaktivität während des Schreibens. Dies äußert sich klinisch häufig in einer bizarren Schreibhaltung, verlangsamtem und mühsamem Schreibvorgang und erhöhtem Schreibdruck.

Die zugrundeliegende Pathophysiologie und -genese ist noch nicht gänzlich geklärt und multifaktoriell. Zu den Theorien zählen: eine gestörte sensomotorische Integration, gestörte Regulation von Inhibition und Exzitation auf verschiedenen Ebenen des Zentralen Nervensystems, maladaptive Plastizität, Störung im Bereich der Basalganglien oder erworbene motorische Fehlstrategien (Hallett, 2006; Torres-Russotto & Perlmutter, 2008; Lin & Hallett, 2009; Cassidy, 2010). Basierend auf der Klassifizierung von Sheehy und Marsden (1982) werden die Subtypen des Schreibkrampfes in simpel, komplex/dyston und progressiv (fortschreitend) unterteilt.

In der vorliegenden Doktorarbeit und den drei integrierten Studien wurde ein System zur computerunterstützten Analyse von Schreibbewegungen und Objektmanipulation verwendet, um einen Vergleich zwischen dem Schreib- und Griffkraftverhalten von Patienten und Gesunden zu ziehen. Zur Analyse des Bewegungsverhaltens während des Schreibens und der Objektmanipulation wurden verschiedene kinematische und kinetische Variablen verwendet. Insbesondere interessierten wir uns für die Frage der Aufgabenspezifität der Entität Schreibkrampf und die Generalisierung der vorhandenen Defizite auf schreibfremde Aufgaben.

Die erste Studie befasste sich mit dem Einfluss verschiedener Schreibaufgaben mit variierender Komplexität von „o“-ähnlichen Kringeln, dem Schreiben eines Buchstabenpaares (lls) und eines Satzes sowie dem Kopieren eines Wetterberichtes. Besonderes Augenmerk wurde hierbei auf die Unterschiede der beiden untersuchten

Patientengruppen (simpler und dystoner Schreibkrampf) und auf den Unterschied der Patientengruppen zu den gesunden Schreibern gelegt.

In der zweiten Studie ging es um die Erfassung der Griffkraft während des Schreibvorgangs. Bis dato war die Datenlage hierzu limitiert, da es nicht möglich war, die Griffkraft während des Schreibens zu messen, ohne den Schreibvorgang zu behindern. Wir lösten dieses Problem durch den Einsatz einer neuen Technik, einer speziellen Kraftsensormatrix, die um den Stift gewickelt werden kann (Pliance, Firma Novel).

Ziel der dritten Studie war es, das Griffkraftverhalten und die Griffkraftkontrolle während des Schreibens und während zwei weiterer feinmotorischer Aufgaben in Patienten und Kontrollen zu vergleichen. Die beiden feinmotorischen Aufgaben beinhalteten das 1.) Heben eines Objektes und 2.) zyklische vertikale Armbewegungen eines Manipulandums.

Bei der ersten Studie zeigten die beiden Patientengruppen im Vergleich zur Kontrollgruppe eine deutlich schlechtere Leistung über alle Schreibaufgaben hinweg. Es zeigten sich signifikante Gruppenunterschiede für Schreibfrequenz, Schreibflüssigkeit (NIV), Griffkraft und axialen Schreibdruck. Es ergaben sich keine signifikanten Gruppenunterschiede im Vergleich zwischen den beiden Patientengruppen. Die Komplexität der verschiedenen Schreibaufgaben zeigte ähnliche Bewegungsalterationen in Patienten und Kontrollen. Allerdings zeigten alle Patienten im Vergleich zu den Kontrollen ähnlich erhöhte kinetische und kinematische Effekte über alle untersuchten Aufgaben hinweg. Auch nach Reduzierung der Komplexität auf einfachere Schreibaufgaben konnte keine Verbesserung der Defizite in Patienten im Vergleich zu den Kontrollen erreicht werden.

Die Ergebnisse der zweiten Studie zeigten beim Schreiben des Satzes eine signifikant schlechtere Schreibleistung der Patienten. Die angewendeten Schreibkräfte zeigten hierbei häufiger abnorme Werte als die Parameter der Schreibkinematik. Es konnten weder Korrelationen zwischen den Kräften und den kinematischen Parametern, noch zwischen dem axialen Schreibdruck und der Griffkraft gefunden werden.

In der dritten Studie produzierten die Patienten erhöhte Griffkraftwerte während des Schreibvorgangs im Vergleich zu den Kontrollen. Hingegen konnte dies nicht bei den beiden anderen Aufgaben „Heben“ und „zyklische vertikale Armbewegungen“ beobachtet werden. Interessanterweise zeigte die Kontrollgruppe eine Generalisierung des Griffkraftverhaltens über die getesteten manuellen Aufgaben hinweg. Ein signifikanter Zusammenhang konnte hierbei aber nur für die Griffkraftwerte der Schreibaufgabe und der Hebeaufgabe bewiesen werden.

Zusammenfassend konnten wir zeigen, dass die untersuchten Schreibkrampfpatienten Defizite in allen gemessenen kinetischen und kinematischen Parametern des Schreibens besitzen. Beide Subtypen (simpel, komplex/dyston) zeigten ähnliche Beeinträchtigungen während der untersuchten feinmotorischen Aufgaben. Dies unterstützt somit nicht die Vermutung einer einheitlichen Progression von Defiziten, die einen Wechsel von simplem zu dystonem Schreibkrampf verursachen könnten.
Bestehende Symptome in den dystonen Schreibkrampfpatienten scheinen sich unabhängig von der Schwere der Beeinträchtigung des Schreibvorganges auszubreiten und zu verschlimmern. Die Komplexität der Schreibaufgaben zeigte offensichtlich keinen Einfluss, was sich durch ein Defizit in den elementaren Komponenten des Schreibens in den Patienten erklären ließe. Die Entität Schreibkrampf zeigte ein heterogenes Muster an Schreibleistungen aufgrund der Variabilität an dystonen Symptomen und den verschiedenen sowie individuellen Kompensationsstrategien der Patienten.

2.2 Summary in English

Writer´s Cramp is classified as a task-specific form of dystonia. Cardinal symptoms are muscle co-contractions and hyperactivity during writing. This is clinically often expressed in a bizarre writing posture, slow and strenuous script production and elevated writing forces.

The underlying pathophysiology and genesis is still unclear and multifactorial. Possible hypotheses are: disturbed sensorimotor integration, impaired regulation of inhibition and exhibition at different levels of the central nervous system, maladaptive plasticity, malfunction within the system of basal ganglia or erroneously adopted movements (Hallett, 2006; Torres-Russotto & Perlmutter, 2008; Lin & Hallett, 2009; Cassidy, 2010). Based on the classification of Sheehy and Marsden (1982) subtypes of Writer´s Cramp are distinguished in simple, complex/dyston and progressive.

In this thesis and the three integrated studies a system of computer-assisted analysis of writing movements and object manipulation was used to make a comparison between writing and grip force behavior of patients and healthy objects. For the analysis of the persons´movements during writing and object manipulation different kinematic and kinetic variables were used. We were particularly interested in the question of task specificity, the entity of Writer´s Cramp and the generalization of existing deficits throughout non-writing tasks.

The first study dealt with the influence of different writing tasks of varying complexity from “o”-like circles, writing of a pair of letters (lls) and a sentence as well as copying the words of a weather forecast. Particular attention was paid to differences of the two investigated patient groups (suffering simple and dystonic Writer´s Cramp) and the difference of patient groups to healthy writers.

In the second study the issue was the registration of grip force during the writing process. Before the beginning of the study the scientific knowledge for this purpose was limited, as it had not been possible to measure grip force during writing without hampering the writing process. We solved this problem by using a new technique, a special force sensor matrix that can be wrapped around the writing stylus (Pliance, Novel).

The aim of the third study was to compare grip force behavior and grip force control during writing and two other fine motor tasks in patients and controls. The two fine motor tasks consisted of 1.) grasping and lifting of an object and 2.) cyclic vertical movements of a manipulandum.

In the first study both patient groups showed a significantly worse performance throughout all writing tasks - compared to healthy controls. Significant group effects were visible at writing frequency, writing fluency (NIV), grip force and pen tip force. There were no significant group differences between both patient groups. Complexity of the different writing tasks showed similar alterations in the persons' movements. However, patients showed similar increased kinetic and kinematic effects throughout all investigated tasks in comparison with controls. Reducing the complexity to simple writing tasks did not enhance deficits in patients – compared to controls.

The results of the second study showed a significantly worse writing performance of the patients when writing the test sentence. The applied writing forces were more frequently abnormal than parameters of writing kinematics. There was neither any correlation to be found between force and kinematic measure, nor between pen tip force (= pen pressure) and grip force.

In the third study patients generated exaggerated grip force values during handwriting compared to healthy controls. Whereas this could not be observed for the tasks "lifting" and "cyclic vertical movements". Here, the control group revealed a generalisation of grip forces across the tested manual tasks. A significant correlation however could only be proved for grip force values of the writing and lifting task.

In summary we were able to show that the investigated patients with Writer´s Cramp had deficits in all measured kinetic and kinematic parameters of handwriting. Both subtypes (simple, complex/dystonic) demonstrated similar impairments in all investigated fine motor tasks. This does not support the assumption of a unitary progression of deficits causing an alteration from simple to complex/dystonic Writer´s

Cramp.
Existing symptoms in patients with dystonic Writer´s Cramp seem to spread and aggravate independent of severity of impairment in handwriting. Complexity of writing tasks did not seem to have any influence which could be explained by deficits in elementary aspects of hand writing in patients.
The entity Writer´s Cramp presented a heterogeneous pattern of writing performance due to the variability of dystonic symptoms and both different and individual compensatory strategies of patients.

3. Research Articles

In detail this thesis emphasizes on the following questions:

1.) Effects of different handwriting tasks und differences in clinical subtypes (1st study). For the first study the spectrum consisted of repetitive writing of simple symbols and letters to copying a given text. Procedures were kinematic and kinetic handwriting analyses.

2.) Analysis of the new parameter pen grip force and the correlation to other kinetic and kinematic parameters (2^{nd} study). In this study the test sentence was used.

3.) Analysis of grip forces in three different fine motor tasks: handwriting, lifting and vertical arm movement (3^{rd} study).

3.1 Writing kinematics and pen forces in Writer´s Cramp: Effects of task and clinical subtype (1st study)

This is a pre-copy-editing, author-produced PDF of an article accepted for publication in Clinical Neurophysiology following peer review. The original publisher-authenticated version is available at: Schneider AS et al. Writing kinematics and pen forces in Writer´s Cramp: effects of task and clinical subtype. Clin Neurophysiol (2010), 121:1898–1907.
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Writing kinematics and pen forces in Writer´s Cramp:

Effects of task and clinical subtype

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Abstract

Objective: Writer´s Cramp (WC) is defined as a task specific form of focal-hand-dystonia generating hypertonic muscle co-contractions resulting in impaired handwriting. Little is known about kinematic and dynamic characteristics in handwriting in the different subtypes of WC.

Methods: In this study, kinematic and force analyses were used to compare handwriting capacity of 14 simple, 13 dystonic WC patients and 14 healthy subjects. The effect of task complexity was investigated using a simple repetitive writing-task, writing pairs of letters, a sentence and copying a text.

Results: In general, patients showed significant deficits in kinematic and force parameters, but no consistent differences between the two subtypes of WC were found. The complexity of writing material modulated writing parameters but not affect the deteriorating effect of WC.

Conclusion: The similarity of deficits in patients with simple and dystonic WC does not support the concept of a unitary progression of deficits causing a switch from simple to dystonic WC. Dystonic WC seems to be characterized by a spread of symptoms independent of severity. Obviously, the deficits concern elementary aspects of writing and are not modulated by more complex aspects.

Significance: Quantification of writing deficits by simple and short phrases with kinematic and force parameters can substantially improve the characterization of WC.

Key Words: Handwriting, Writer´s Cramp, focal dystonia, kinematic analysis, force analysis, grip force, pen tip force, pen pressure.

1. Introduction

Writer´s Cramp (WC) is considered a task-specific form of focal hand dystonia, which affects the dominant hand involved in handwriting. A cardinal symptom of Writer´s Cramp is uncontrollable muscle co-contraction and hyperactivity in agonist and antagonist muscles when attempting to write. This frequently results in pain, loss of control of the pen and the exertion of excessive pressure on the pen and against the writing surface. Most patients with Writer´s Cramp are still able to produce legible handwriting, often at the expense of peculiar and abnormal postures of fingers, wrist, elbow and shoulder. The handwriting of WC patients is jerky and often slow. The resulting script is often characterized by non-ergonomic, squashed and tremulous letter forms (Sheehy & Marsden, 1982, Mai & Marquardt, 1994).

Gowers (1888) was the first who differentiated between simple and dystonic Writer´s Cramp. This differentiation was retained in the seminal study of Sheehy and Marsden (1982). In simple Writer´s Cramp (sWC) symptoms only occur while holding a pen and performing writing or drawing movements, while other manual tasks are carried out normally. By contrast, patients with dystonic Writer´s Cramp (dWC) also develop muscle hyperactivity during other manual tasks such as handling a knife and fork or similar mechanical implements.

Methods of movement analysis allow objective and exact evaluation of the quality, automation and accuracy of handwriting movements. Using digitizing tablets and kinematic analyses, investigations of motor abnormalities in writer's cramp patients revealed less automation of writing movements and reduced frequency of strokes (Marquardt et al., 1996; Siebner et al., 1999; Schenk & Mai, 2001; Schenk et al., 2004; Baur et al., 2006; Zeuner et al., 2007). Further, patients with Writer´s Cramp needed more time than healthy controls to copy a prescribed text (Siebner et al., 1999; Baur et al., 2006).

Little is known, however, about the influence of different text materials on writing kinematics. In healthy subjects an effect of task complexity was demonstrated by Mergl et al. (1999). Previous studies on treatment approaches (Baur et al., 2006; Zeuner et al., 2002, Zeuner et al., 2005) used various writing tasks of different complexity to describe outcome, ranging from different test sentences to a simple repetitive writing task (superimposed circles). Zeuner et al. (2007) suggested that the sensitivity in detecting Writer´s Cramp may be higher in the kinematic analysis of producing superimposed circles than of the test sentence. With regard to writing pressure, the test sentence was more sensitive in detecting abnormalities in WC patients.

A major aim of the present study was therefore to analyse and compare writing performance in patients with WC and in control subjects across a larger set of different handwriting tasks. The tasks exhibited increasing complexity in length, semantic content, and spatio-temporal demands, ranging from stereotyped producing of superimposed "o"-like circles to copying a longer text. We expected a decrease in writing speed and automation with increasing complexity for all participants. In patients with Writer´s Cramp we expected impairments that may be further exacerbated with increasing task complexity. If however the writer's cramp deficit is triggered by handwriting per se, irrespective of content, identical task effects in patients and controls would be expected.

In addition to impaired writing kinematics, several studies have found elevated pen tip force exerted by the pen tip onto the writing surface in patients with WC compared to healthy controls (Marquard et al., 1996; Siebner et al., 1999; Baur et al., 2006; Chakarov et al., 2006; Zeuner et al., 2005; Zeuner et al., 2007). By contrast, there is limited information about grip force that is exerted by the fingers against the barrel of the writing stylus during handwriting. This is due to the difficulty to measure pen grip force without hampering the writing process and without restrictions of individual finger positions on the pen. We used a flexible force-sensor matrix wrapped around a writing stylus to measure grip force in patients with Writer's Cramp (see also Chau et al., 2006) to further characterise the disorder by investigating the effects of different writing tasks on pen-tip force and grip force.

As noted above, patients with simple versus dystonic WC are usually distinguished according to the co-occurrence of deficits in fine motor activities not related to handwriting (Sheehy & Marsden, 1982). The severity of handwriting deficits has not been used for differential diagnosis.

Schenk & Mai (2001) found a significantly reduced degree of movement automation in patients with dystonic WC compared to simple WC patients, but the sample of dystonic patients comprised only three patients. It was therefore a final aim of the present study to shed more light on possible differences in performance between simple and dystonic WC. According to Sheehy and Marsden (1982), simple WC can evolve into dystonic WC, given that patients with Writer´s Cramp show a general increase of dystonic symptoms which lead to disturbances in other fine motor tasks. Thus we hypothesise that dystonic WC patients will show a higher degree of disturbance in kinematic and force parameters than will simple WC patients.

2. METHODS

2.1. Subjects

We studied 27 right handed patients with writer's cramp (20 females, 7 males, age: 43.9 ± 11.6 years; see Table 1). The diagnosis was based on examination by a scientist experienced in the study of writer's cramp (Fürholzer, Baur) usually confirming earlier diagnosis by a neurologist. None of the patients had evidence of other neurological deficits as revealed by neurological examination. They were divided into two subgroups according to whether the impairment was restricted to writing (simple WC) or also involved other fine motor tasks (dystonic WC), according to Sheehy and Marsden (1982). The group of patients with simple WC (sWC) consisted of 14 patients; 11 females and 3 males (age: 45.6 ± 10.7 years). The sample of patients with dystonic Writer´s Cramp (dWC) consisted of 13 patients, 9 females and 4 males (age: 41.9 ± 12.7 years) [see Table 1].

Non-writing tasks in which patients in the dystonic group (N=13) reported impairments included activities like drinking (38.5%), eating (46.2%), shaving/make-up (46.2%), computer work (53.8%) and others (84.6%). The majority of all patients (85.2 %) reported pain (**sWC**: 85.7 %; **dWC** : 84.6 %) and 40.7 % had an additional action-related tremor during writing (**sWC**: 35.7 % / **dWC**: 46.2 %).

Two patients from the simple WC group and three patients from the dystonic WC group were previously treated with botulinum toxin. In all cases the treatment was more than three months ago. The simple and dystonic WC patient groups did not differ in age or symptom duration (t-test: $p > 0.1$), nor for pain or tremor (Mann Whitney test: $p > 0.1$).

The control group (Ctr) consisted of 14 healthy right-handed age-matched participants (11 female, 3 male, age: 42.1 ± 13.1 years. Both samples (patients and controls) were of similar age (t-test < 1; $p > 0.1$).

Informed consent was obtained from all participants. The experimental protocol was conducted according to the declaration of Helsinki and was approved by the ethical committee of the Bavarian Medical Association.

Table 1: Patients characteristics

Pat.	Age (years)	Gender	Profession	Subtype of Writer's Cramp	Symptom duration (years)	Age of onset (years)	Pain	Tremor	ADDS
1	49	f	Educator	Simple	11	38	Yes	Yes	60
2	44	f	Business economist	Simple	1	43	No	No	70
3	33	f	Interior designer	Simple	9	24	Yes	No	60
4	50	f	Nurse	Simple	5	45	Yes	No	60
5	32	f	Nurse	Simple	2	30	Yes	No	75
6	37	f	Merchant	Simple	9	28	Yes	No	65
7	42	f	Accoucheuse	Simple	36	7	Yes	Yes	64
8	34	m	Accountant	Simple	3	31	Yes	No	60
9	44	f	Employee	Simple	1	44	Yes	No	75
10	40	f	Speech therapist	Simple	12	29	Yes	No	73
11	64	f	House wife	Simple	48	17	No	Yes	75
12	51	m	Employee	Simple	15	36	Yes	Yes	70
13	67	m	Musicologist	Simple	20	48	Yes	No	64
14	52	f	Teacher	Simple	3	49	Yes	Yes	75
15	30	m	Employee	Dyston	3	27	Yes	No	25
16	22	f	Student	Dyston	1	21	Yes	Yes	50
17	42	f	Teacher	Dyston	27	15	Yes	No	60
18	27	f	Industrial clerk	Dyston	1	27	Yes	Yes	70
19	50	f	Medical secretary	Dyston	9	41	Yes	Yes	60
20	57	f	Nurse	Dyston	7	50	Yes	Yes	55
21	39	f	Secretary	Dyston	11	28	Yes	No	50
22	57	m	EDV-controller	Dyston	20	37	No	Yes	25
23	25	f	Student	Dyston	8	18	Yes	No	50
24	59	f	Teacher	Dyston	12	47	Yes	No	56
25	43	f	Banker	Dyston	8	35	Yes	No	55
26	48	m	Merchant	Dyston	20	29	No	No	55
27	46	m	Doctor	Dyston	9	37	Yes	Yes	56

2.2 Procedure

Subjects wrote with their dominant right hand on a blank A4 sheet of paper that was fixed on top of a digitizing tablet. They were instructed to write in their normal everyday writing style. They performed a set of handwriting tasks ranging from repetitive writing of simple symbols and letters to copying a given text, as follows:

Subjects drew superimposed circles within 3 seconds. In addition, subjects wrote as many pairs of lower case ll´s in cursive writing as possible within 10 seconds, and the German sentence, "Die Wellen schlagen hoch" (Engl.: "The waves are surging high"). Three trials were recorded for each of the tasks and results were averaged across trials.

In the most complex test subjects had to copy a given text that was new to each subject (weather forecast). To investigate prolonged writing, continuous copying of this text for 5 minutes was recorded. Accordingly a 40 s interval starting forty seconds after commencement and the last 40 s were analysed separately. The initial interval was excluded to avoid possible hesitations at the beginning.

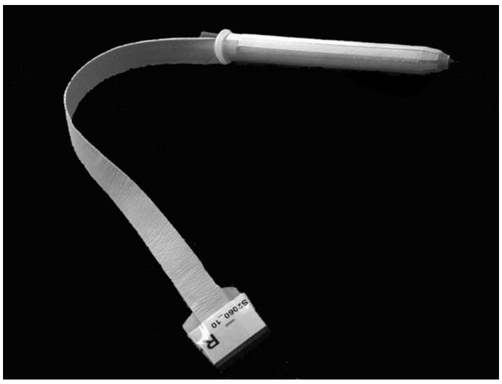

Fig.1: Writing stylus with force sensor matrix wrapped around the surface

2.3 Clinical rating of severity of dystonia

Severity of dystonia was rated with the Arm-Dystonia-Disability-Scale (ADDS), developed by Fahn (1989). The resulting score represents the percentage of normal activity. Thus the lower the total score, the more severe the functional impairment.

2.4 Data registration

Assessment of kinematic handwriting parameters and pen tip force

A digitizing tablet (Wacon IV, sampling rate 200 Hz, spatial resolution 0.05 mm) registered the position of the tip of the writing stylus. A pressure sensitive stylus was used that measured the pen tip force exerted onto the tablet (0-2.5 N, sampling rate 200 Hz; resolution 0.01 N). Recording started as soon as the subjects touched the digitizing tablet with the pen. The positional data were transmitted to a personal computer and analysed with the software CSWin 2007 (MedCom, Munich, see Mai and Marquardt, 1994). The movement trajectories and corresponding velocity curves were calculated and smoothed by nonparametric regression methods (Mai & Marquardt, 1994).

2.5 Assessment of grip force

A force sensor matrix that was wrapped around the pen (see Fig. 1) was used to measure the force exerted by the fingers against the pen barrel during writing (Pliance-system, Novel, Munich). Eighty-eight force sensors were distributed across the whole surface of the pen with a spatial resolution of 5x10 mm . In an area of one square centimetre, forces between 0.5 and 20 N could be measured. The total error including hysteresis was less than 10%. The sampling rate of the whole matrix was 50 Hz. This technique allowed the registration of grip force for any individual grip type and without restricting the finger positions.

2.6 Data analysis

For quantitative analyses the written trace was automatically segmented into subsequent up- and down- strokes. The algorithm calculated strokes in the spatial domain. Kinematic and force measures were averaged across trials. The following parameters were calculated:

- *Frequency (Hz):* Average number of strokes per second. This parameter is a measure of movement speed.

- *NIV (number of inversions in velocity per stroke):* Average number of local peaks in the vertical velocity profile within each segment. In skilled writers each stroke is associated with a smooth velocity profile, which has only one peak (NIV = 1, Mai and Marquardt 1994). This parameter reflects the automation in handwriting. The greater the value, the less automated is the writing process.

- *Amplitude (mm)*: The average vertical amplitude of strokes (stroke length in the vertical direction) indicates script size.

- *CV of stroke duration (%)*: The coefficient of variation (CV) of stroke duration.

This parameter expresses temporal variability.

-*Pen tip force (= "pen pressure") (N)*: Vertical pressure exerted onto the tablet by the tip of the writing stylus.

- *Grip force (N)*: Integral grip force exerted by the fingers against the pen, during the periods when the pen was in contact with the paper.

- *Duration of the test sentence(s)*: the time needed to complete the sentence is a measure of handwriting speed.

- *Number of written characters* in the copying task.

2.7 Statistical analysis

We used the software SPSS for all statistical analyses. Analyses of variance (ANOVAs) between repeated measurements relating to the three levels of subject group (healthy controls vs. simple Writer's Cramp vs. dystonic Writer´s Cramp) and within these groups relating to the four levels of task (circles vs. lower case ll´s vs. sentence vs. text) were performed. Post hoc tests (Games Howell (group effect) and Greenhouse Geisser (task effect)) were used to detect differences between different groups and tasks. The level of significance was set at $p< 0.05$.

For the analysis of effects of writing duration in the text copy task, t-tests were used to compare the first part (40-80 s) with the last part (last 40 s).

The range of normal performance was set at mean performance in healthy controls ± 2 standard deviations (SD). To elucidate the relationship between kinematic and force parameters as well as correlations with clinical scores, Spearman rank correlation were applied and corrected for multiple comparisons using the Bonferroni method.

3. RESULTS

3.1 Individual examples

Fig. 2 illustrates the handwriting performance of a healthy control subject and a patient with WC when writing the test sentence (A), cursive ll´s (B) and superimposed circles (C). There are a number of differences in the handwriting characteristics. Both specimens are legible, but the patient´s writing was less regular and slower. The patient needed 10.4 s and the control 6.8 s to complete the sentence.

Velocity profiles of both participants clearly differed: the patients' profiles were characterized by multiple peaks per stroke (NIV) over all tasks (sentence: 1.6; ll's: 1.7; circles: 1.1) whereas the healthy control subject showed smooth single-peaked velocity curves (sentence: 1.1; ll's: 1.1; circles: 1.1)

Both force profiles, pen tip force and grip force, showed elevated levels in the patients' writing performance throughout all three tasks. Pen tip force of the healthy control was between 0.8 N and 1.1 N, whereas the patient showed a pen tip force between 2.1 N to 2.2 N. A similar picture emerged for grip force used for identical writing tasks: between 5.5 N and 10.2 N for healthy subjects; between 34.7 N and 46.8 N for Writer´s Cramp patients. It should be noted however, that the trace of the pen tip force revealed a limitation of the measurement technique. Since the sensor is not designed to measure pathologically increased forces, signals of the patient group were at the upper measurement limit for most of the time. Despite this artificial limitation of the signal range, the average force of the patient is clearly increased compared to the control subject.

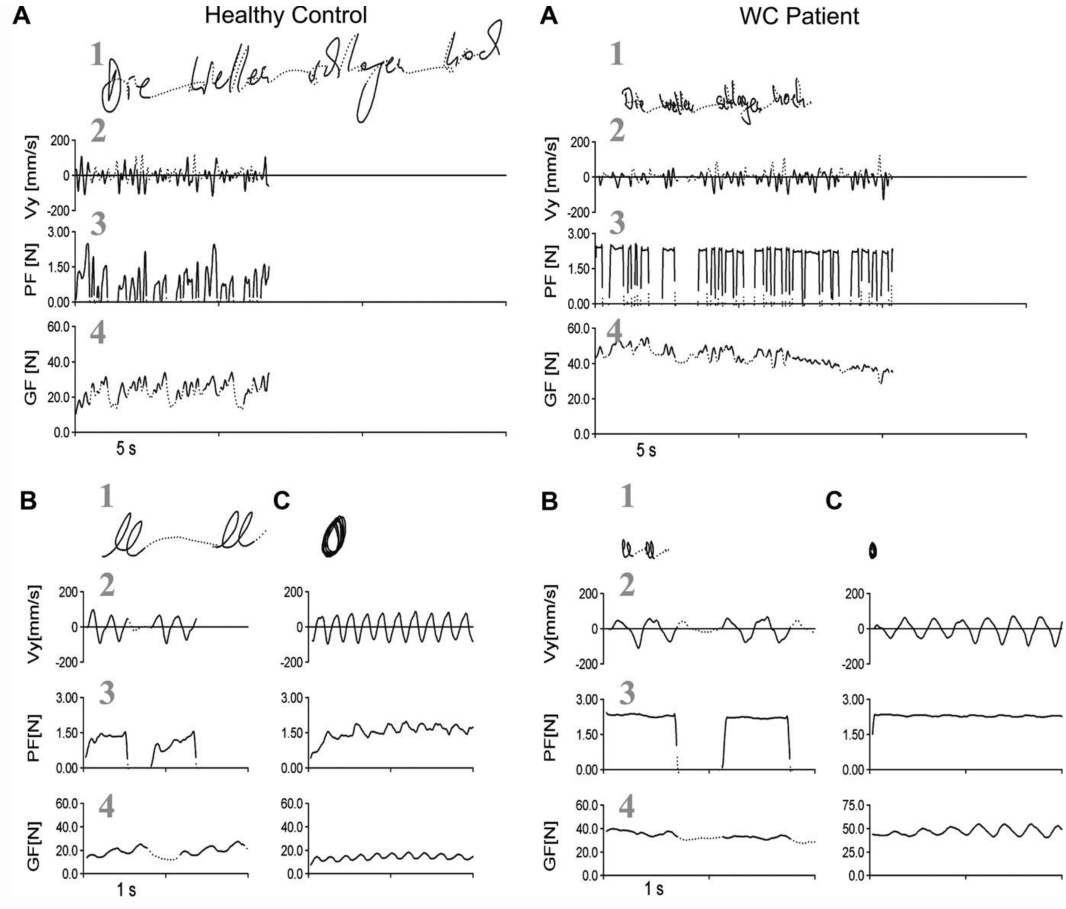

Fig. 2 Writing profiles: **examples of handwriting of a healthy control (left) and of a patient with Writer´s Cramp (right).** **A)** Sentence; **B)** Lower case ll´s ; **C)** superimposed circles. **1)** Trace of the handwriting performance (solid line: trace on paper; dotted line: trace in the air); **2)** Vertical velocity (mm/s) as a function of time; **3)** Pen pressure = Pen tip force (N) as a function of time; **4)** Grip force (N) as a function of time.

3.2 Group effects

Fig. 3 shows selected writing parameters of the different tasks for the subtype groups of patients with Writer´s Cramp and healthy controls. The corresponding results of statistical analyses (ANOVASs testing group and task effects) are given in table 2.

ANOVAs revealed significant group effects for writing frequency, fluency (NIV), grip force and pen tip force. Both patient groups showed a significantly lower writing frequency than healthy controls (Ctr: 4.45 ± 0.57 Hz; sWC: 3.64 ± 0.63 Hz; dWC: 3.54 ± 0.96 Hz; $p < 0.01$).

NIV was increased in both patient groups compared to healthy controls (Ctr: 1.19 ± 0.12; sWC: 1.43 ± 0.29; dWC: 1.75 ± 0.75; $p = 0.01$). Only for the subgroup of sWC did post hoc analysis reveal a significant increase compared to Ctr ($p = 0.027$) whereas the increased NIV in dWC was only a trend ($p = 0.055$).

Grip force in patients was also elevated compared to healthy controls (Ctr: 11.39 ± 4.21 N; sWC: 21.19 ± 13.59 N; dWC: 23.11 ± 12.16 N). We found a significant increase in dWC patients ($p = 0.01$) and a trend for increase in the sWC group ($p = 0.065$).

Pen tip force was clearly increased during writing in both WC patient groups compared with healthy subjects (Ctr: 1.19 ± 0.43 N; dWC: 1.85 ± 0.45 N; sWC: 1.57 ± 0.46 N; $p < 0.02$).

In contrast, no significant variations between groups were found for the coefficient of variation of segment duration (a measure of temporal variability ($p = 0.4$)) or amplitude of strokes (a measure of script size ($p = 0.15$). Duration, a parameter that was only computed for the sentence task, showed increased completion time for the sentence in both patient groups compared with healthy subjects (Ctr: 8.5 ± 1.5 s ; sWC: 11.2 ± 2.6 s ; dWC: 12.7 ± 3.7 s; $p = 0.001$). Analysis of variance and post hoc comparisons between groups revealed no statistically significant differences in any kinematic or force parameter for the clinical subgroups (sWC, dWC) of Writer´s Cramp.

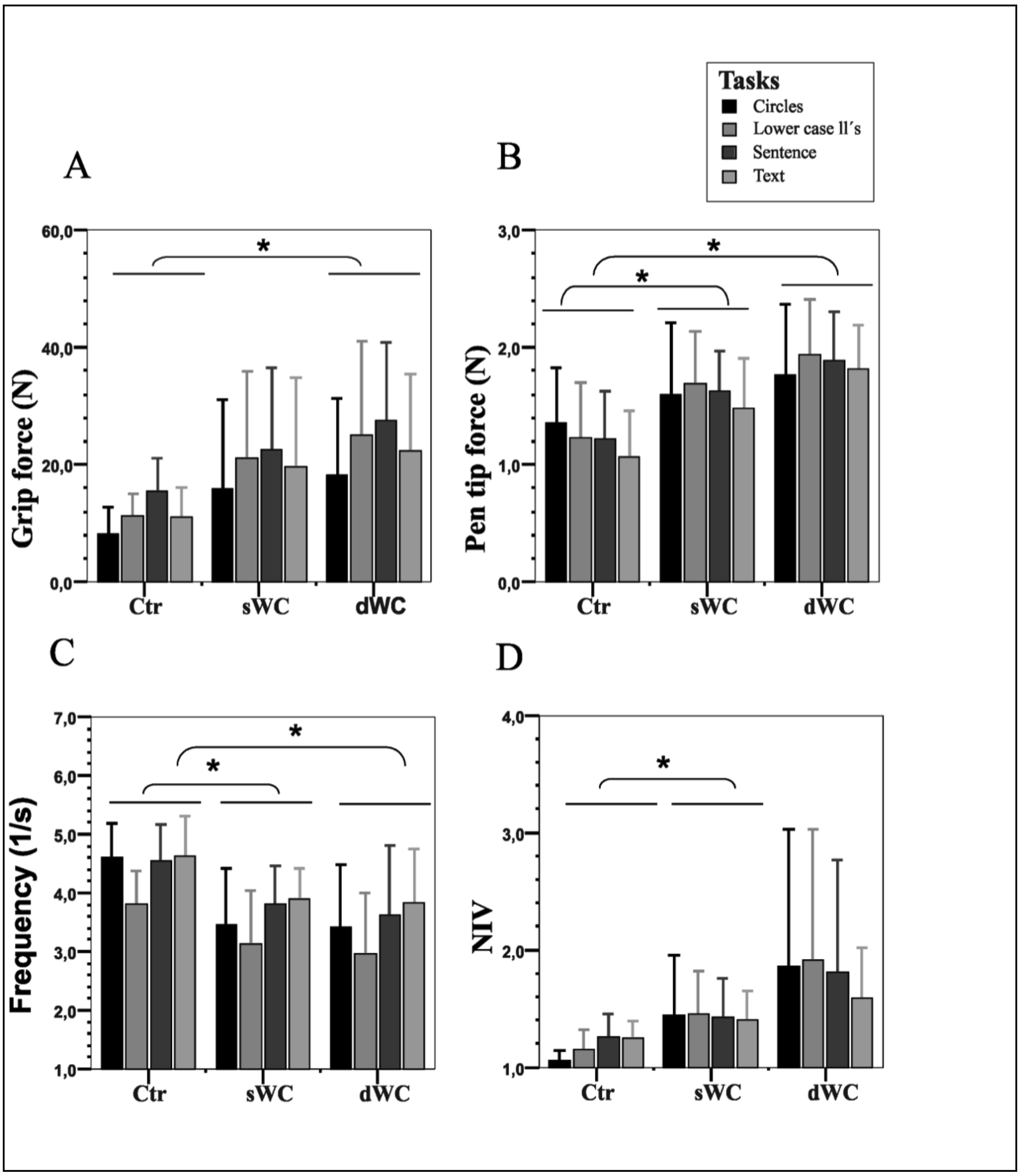

Fig. 3. Writing parameters of different tasks in patients with simple Writer´s Cramp (sWC; n= 14), dystonic writer´s cramp (dWC; n= 13) and control subjects (CTR; n=14). A) Grip force; B) Pen pressure; C) Frequency; D) NIV (defined as the number of inversions in velocity, parameter of automation). Bars show means, error bars indicate one standard deviation, brackets and stars indicate significant group effects (post hoc).

3.3 Task effects

3.3.1 Text copy task (weather forecast)

Participants received a given text and copied as much as possible within 5 minutes. We compared two time intervals, one at the start (first 40 - 80 s) and the other at the end (last 40 s). This task was chosen to explore the handwriting of different and novel letters and word combinations as well as to analyse the effort of writing for a period of 5 min.

The number of characters written within 5 min was significantly lower in patients (460 (± 95) characters) than in controls (581 ± 129 (t-test; $p = 0.005$). Comparison of the three groups showed a significant difference between controls and sWC as well as controls and dWC, but no difference between sWC and dWC (Ctr > sWC, $p= 0.021$; Ctr > dWC, $p= 0.004$).

The kinematics of writing movements, NIV and frequency showed no significant change across time periods (NIV: $p = 1.0$; frequency: $p = 0.56$). Pen tip force also showed no statistically significant difference between start and end of the copy task ($p = 0.18$). The only difference for the two time periods was a decreased level of grip force in the second time interval for all subject groups in the study ($F(1) = 15.7$; $p < 0.001$). The grip force level difference between start and end of the task was 3.01 N in controls, 5.2 N in sWC and 5.7 N in dWC. Since grip force was the only parameter that changed with time, we averaged parameters across the two time points for the task analyses described below.

3.3.2 Comparison across tasks

Significant task effects were found for frequency ($p < 0.001$), CV of segment duration ($p < 0.001$), amplitude ($p< 0.001$) and grip force ($p< 0.001$). No task effect was found for the parameter pen tip force and NIV (Fig. 3 and table 2). Writing frequency was lowest for writing lower case ll´s and circles, whereas highest values were shown for the more complex sentence and text-copying tasks. Similarly CV of segment duration was lowest for the simpler task and higher for the more complex tasks.

Grip force was highest in the task “sentence”. No difference could be found between the other three tasks. The largest script size (amplitude of stroke) was found in the stereotyped movements (ll´s and circles), the smallest script size during the prolonged writing task.

In general handwriting performance of the three groups did not significantly differ for the four handwriting tasks. Only for the amplitude parameter was a significant variation group by task interaction found ($F = 2.59$, $p = 0.04$, table 2). This interaction was due to the behavior of simple WC patients who produced bigger circles than the other groups. The underlying cause for that effect remains unclear.

Table 2: Results of ANOVAS.

Results of ANOVAs with between-subject factor "group" (three levels: healthy controls vs. simple vs. dystonic WC) and within-subject factor "task" (four levels, superimposed circles(1) vs. lower case ll`s (2) vs. sentence (3) vs. text (4)). ANOVA and post hoc results: Games Howell and Greenhouse Geisser (GG).

Table 2

Results of ANOVAs with between-subject factor "group" (three levels; healthy controls vs. simple WC vs. dystonic WC) and within-subject factor "task" (four levels; superimposed circles (1) vs. lower case ll's (2) vs. sentence (3) vs. text (4)).ANOVA and post hoc results: Games Howell and Greenhouse Geisser (GG).

Parameter	Group effect	Post hoc (Games Howell)	Task effect (GG)	Post hoc	Interactions (group task*) (GG)
Frequency (Hz)	$F(2) = 6.4$; $p = 0.004$	Ctr > sWC; $p = 0.004$ Ctr > dWC; $p = 0.018$ sWC–dWC ($p = 0.94$)	$F(3) = 33.7$; $p < 0.001$	2 < 1 < 4 2 < 3	n.s. ($p = 0.31$)
NIV	$F(2) = 5.09$; $p = 0.01$	Ctr < sWC; $p = 0.027$ Ctr – dWC; $p = 0.055$ sWC–dWC ($p = 0.33$)	n.s. (p = 0.53)		n.s.($p = 0.17$)
CV of segment duration (%)	n.s. ($p = 0.35$)		$F(3) = 159.8$; $p < 0.001$	1 < 2 < 3,4	n.s. ($p = 0.34$)
Amplitude (mm)	n.s. ($p = 0.15$)		$F(2) = 113.9$; $p < 0.001$	4 < 3 < 1,2	F(4) = 2,60; ($p = 0.04$)
Grip force (N)	$F(2) = 4.13$; $p = 0.02$	Ctr < dWC ($p = 0.01$) Ctr – sWC ($p = 0.065$) sWC–dWC ($p = 0.91$)	$F(2) = 17{,}1$; $p < 0.001$	1 < 2 < 3 4 < 3	n.s. ($p = 0.52$)
Pen tip force (N)	$F(2) = 9.2$; $p = 0.001$	Ctr < sWC ($p = 0.02$) Ctr < dWC ($p = 0.001$) sWC–dWC ($p = 0.27$)	n.s. ($p = 0.09$)		n.s. ($p = 0.35$)
Time duration (s)*	$F(2) = 8.6$; $p = 0.001$	Ctr < sWC ($p = 0.006$) Ctr < dWC ($p = 0.004$) sWC–dWC ($p = 0.45$)			

Groups: ctr = controls ($n = 14$); sWC = simple Writer's Cramp ($n = 14$); dWC = dystonic Writer's Cramp ($n = 13$).
Tasks: 1 = circles; 2 = lower case ll's; 3 = sentence; 4 = text.
* Only computed for the task "sentence".

3.4 Pathologic performance in Writer´s Cramp patients

Performance measures were defined as pathologic (abnormal) if the mean across all tasks exceeded the range of ± 2 standard deviations away from the mean performance of healthy controls ("+" or "–" depending on the parameter).

In the dystonic WC group 7 of 13 patients (54%) showed abnormal grip force and 9 of 13 patients (69%) showed elevated pen tip force. Thus abnormal forces were more often abnormal in the dystonic WC group than in the simple WC group (grip force: 6/14 (43%); pen tip force: 4/14 (29%)).

NIV was abnormal in 8 of 13 cases (61%) in the dystonic WC group and in 5 of 14 cases (36%) in the simple WC group.

In contrast, the occurrence of abnormalities in frequency did not differ that much between simple and dystonic Writer´s Cramp patients. (sWC: 6 / 14 (43%); dWC: 4/13 (31%)). (see Fig. 4)

3.5 Correlations

3.5.1 Correlation between writing parameters

There was no significant correlation between force parameters (pen tip force and grip force) within the control group, the group of sWC patients or the group of dWC patients. In the whole WC patient sample (sWC and dWC together) there was a low but significant positive correlation between pen tip force and grip force ($r = 0.40$; $p = 0.038$; see Fig. 4A).

We found a clear negative correlation between NIV and frequency in all three groups (Ctr: $r = -0.66$; $p = 0.001$; sWC: $r = -0.92$; $p < 0.001$, dWC: $r = -0.59$; $p = 0.027$) (see Fig. 4B), indicating that movement fluency and movement speed of all participants were closely related.

There was no significant correlation between force parameters (grip force and pen tip force) and kinematic parameters (frequency and NIV) in any of the groups (Ctr, sWC, dWC). (see Fig. 4 C,D).

In the combined patient group (sWC and dWC) we found a negative correlation for grip force and NIV ($p = 0.03$; $r = -0.43$). Some patients seem to have preserved automation mechanisms (NIV) although producing high grip forces.

3.5.2 Correlations between writing parameters and clinical scores

The correlation of symptom duration and kinematic parameters (NIV, frequency) revealed a positive correlation in the sWC group but not in the dWC group (sWC: symptom duration correlated with NIV; $r = 0.62$; $p = 0.018$). In the combined patient group (sWC and dWC) we found a negative correlation with frequency ($r = -0.39$; $p = 0.043$). Both correlations indicate that longer lasting disease was associated with less fluent writing movements.

These two correlations have to be considered carefully due to multiple testing. No other parameters (duration of the test sentence, pen tip force, grip force) were significantly correlated with symptom duration.

Furthermore no correlations were found between age, age of onset or ADDS score and force or kinematic parameters.

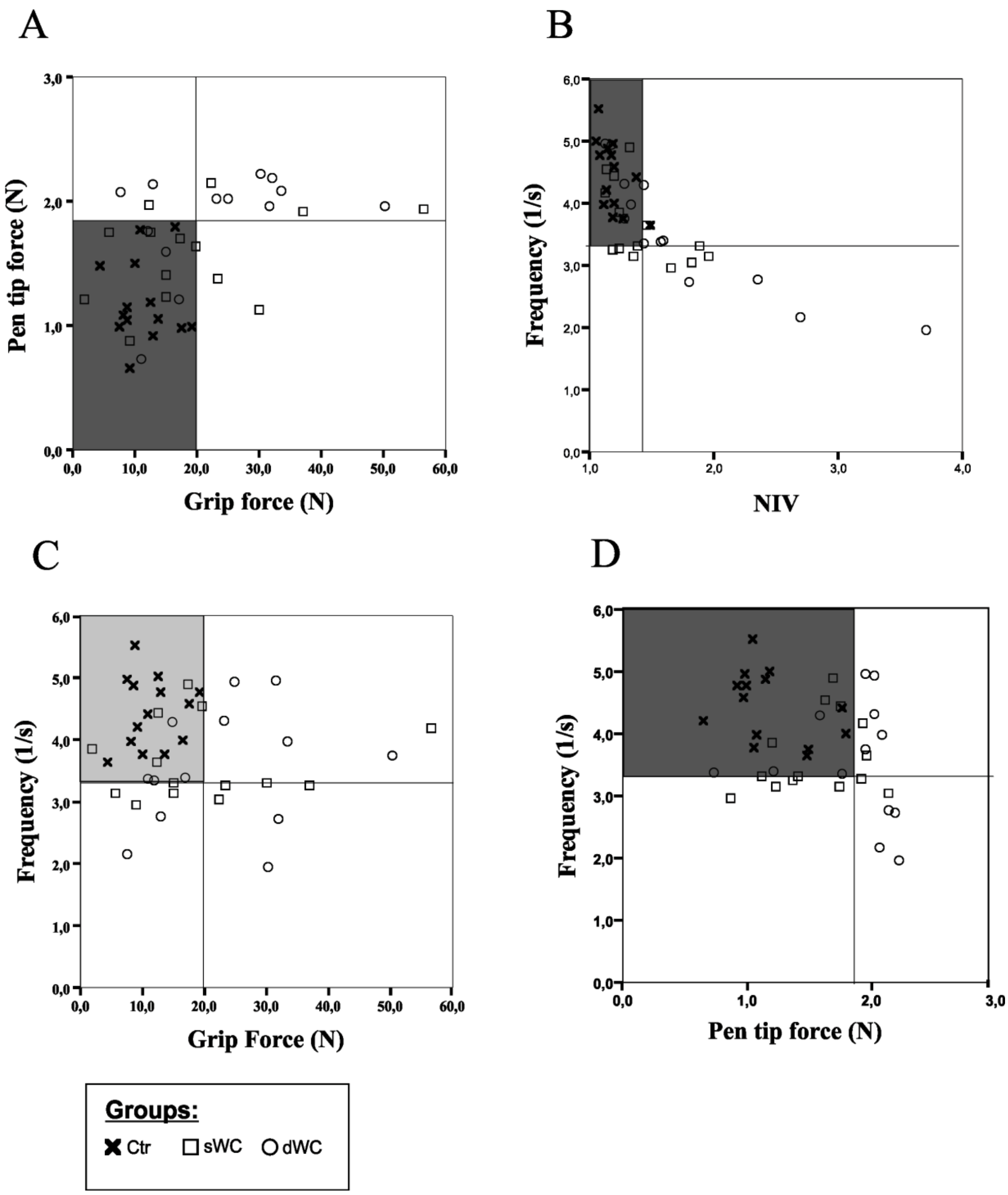

Fig. 4. Correlations: relationship between force and kinematic parameters. (A) Relation between grip force and pen tip force; (B) relation between frequency and NIV; (C) relation between grip force and frequency; (D) relation between pen tip force and frequency. Grey areas indicate normal performance (mean ± 2 SD).

4. Discussion

4.1 Group differentiation

In this study we investigated the handwriting movements of simple and dystonic Writer´s Cramp patients and healthy subjects. Although the script was mostly legible, both patient groups showed significant impairment in writing movements compared to healthy controls. Patients with Writer´s Cramp showed elevated grip force and pen tip force as well as reduced automation and writing frequency.

Analysis of variance and post hoc comparisons revealed no statistically significant differences in any kinematic or force parameters for the clinical subgroups of Writer Cramp defined according to the criteria of Sheehy and Marsden (1982). However, some indication for a difference between the two patient groups were suggested by a significant elevation of grip force compared with normal writers that could be detected only in the dystonic WC group ($p = 0{,}01$), whereas a significant loss of automation was found only in the simple WC group ($p = 0.027$). In addition, more dystonic than simple WC patients were impaired in grip force and pen tip force if pathological performance was defined according to a threshold (2 SD) provided by the controls' sample.

However, in general we did not find differences between the subgroups of Writer´s Cramp, which confirms the findings of Jedynak et al. (2001), who reported similar legibility and writing deficits in patients with simple and dystonic writer's cramp. In agreement with the former authors we conclude that dystonic Writer´s Cramp is usually not a more severe form of simple Writer´s Cramp. We therefore cannot confirm the findings of Das et al. (2007) that dystonic WC patients compared to simple WC patients had worse scores. The discrepancy could be related to the fact that the dystonic patients of Das et al. (2007) were older and had longer disease duration, while our patient groups did not differ in age or symptom duration. However, there was no correlation between performance measures and symptom duration or age in our patients.

We would conclude that for dystonic Writer´s Cramp an aggravation in dystonic symptoms other than writing does not inevitably lead to an aggravation in performance aspects of writing movements. Impairment in other fine motor tasks than writing does not necessarily affect writing. Also within the group of patients with dystonic WC, handwriting deficits were not related to severity of dystonia assessed by the ADDS score.

Furthermore, Sheehy and Marsden (1982) described a third form of WC called "progressive WC". Those patients initially had only problems while writing (simple WC) and then later developed difficulties in other fine motor tasks (dystonic WC). The underlying mechanism seems to be a conversion from simple to dystonic WC and therefore an aggravation of performance and symptoms as well as a generalisation of dystonic symptoms involving new tasks. Fahn et al. (1998) described that primary adult-onset dystonia often is focal at onset and has a limited tendency to spread to adjacent body regions. Spread of primary focal dystonia to other body regions is now clinically well established and was found in 38% of patients with primary focal hand dystonia (Abbruzzese et al. 2009).

In our patient sample the case history was in most cases based on self report, and therefore classification into dystonic and progressive WC would have been very insecure. Otherwise if our group of so called "dystonic" patients is considered as a mixture of dystonic and progressive WC patients, the difference in performance and clinical parameters between our dystonic and simple WC patients should be significant. But in general we found no significant differences. Thus, if a progressive form of Writer´sCramp exists, spreading and aggravation does not inevitably lead to an aggravation in all qualities of fine motor tasks, e.g. writing.

The mechanisms of spreading in dystonia are unknown but it is likely that an impairment of surround inhibition may play a role (Sohn and Hallett 2004; Hallett 2006, Richardson & Hallett 2009). The suppression of excitability in an area surrounding an activated neural network is a physiological mechanism to focus neural activity and to select appropriate neuronal responses. Impairment in this mechanism could disturb the selective execution of the desired movement and foster the development of co-contraction and spreading dystonia. Such a spread may cause dystonia in previously non-affected body regions and motor activities without necessarily deteriorating existing symptoms. Our results support such a mechanism.

It should be kept in mind that we found some indirect hints for more severe deficits in patients with dystonic Writer's Cramp in force data, such as somewhat more increased pen grip force in dystonic WC patients (see Section 3). In our opinion this does not justify a hypothesis of progression from simple to dystonic Writer's cramp by an aggravation of symptoms, but this finding may indicate differences between groups in dystonic symptoms and/or compensatory mechanisms specifically for aspects of force control.

4.2 Correlation between aspects of writing performance

A cardinal symptom of Writer´s Cramp is uncontrollable muscle co-contraction and hyperactivity when attempting to write. This condition is expressed by increased pen tip force and grip force. Our finding of increased forces reflects the findings of increased pen tip force in former studies (Baur et al. 2006; Schenk & Mai 2001; Siebner et al. 1999; Zeuner et al. 2007; Chakarov et al. 2006).

Both parameters were abnormal for the patients in our study, but the correlation between these parameters was unexpectedly low in both the healthy controls and in the patients. This may be due to two reasons. Firstly, measurement of pen tip force was limited by a "ceiling effect" which was not sensitive to pathologically high pen tip forces, whereas the measurement of grip force was not restricted by such technical deficits. This ceiling effect was a limit of measurement to normal values around the level of 2.5 N, and most of our patients showed pen tip force levels at this upper limit. Secondly, high grip forces must not necessarily result in high pen tip forces due to biomechanical effects such as individual pen grasp, and abnormal posturing of finger and joints while writing.

Further, kinematic and force parameters show no significant correlation in the subgroups. Only a low negative correlation between grip force and NIV was found in the combined patient group (sWC and dWC). This indicates that some patients can preserve automation mechanisms although producing high forces.

Slowed and reluctant handwriting was not associated with increased force parameters, and conversely, increased force did not inevitably lead to a slowing down of handwriting movements. Therefore a link between dystonic symptoms and hyperactivity in muscles and co-contraction and reduced speed as well as less automation was missing (Hermsdörfer et al. 2009; Mai & Marquardt 1994).

From our data three patient groups with pathological values could be identified. The three groups were: (1) patients with either isolated increase in forces (8/27); (2) disturbances in kinematics (11/27); (3) disturbances in both aspects (8/27). The reasons for these varied patterns of deficits remain speculative. One explanation could be compensatory strategies such as decreasing writing speed to better control forces or vice versa or a combination.

4.3 Task effects

Kinematic parameters of writing such as frequency, size of the script and temporal variability clearly differed between tasks. In particular the high frequency during text writing emphasizes the degree of automation despite complex writing material. Interestingly, also the grip force varied with writing content. Grip force increase seems to reflect the complexity of the material with the exception of the 5-min text. Lower grip force during the later task may however be due to longer breaks during reading the words to be copied. Interestingly all patients could write continuously for five min without high aggravation in kinetic parameters but with indication of pain. In this context, the patients in our sample seemed to suffer mild to medium Writer´s Cramp with preserved performances in writing.

Importantly, the pattern of performance for the different writing tasks was equal across groups. All patients showed equally increased levels of pen tip force and grip force, and equally compromised levels of kinematics (frequency, NIV) across all tasks.

Thus, deficits in different aspects of writing performance do not appear to depend on task complexity (ranging from stereotyped producing of superimposed “o”- like circles to copying a longer text). It seems that neither length nor semantic content nor spatio-temporal demands have a specific deteriorating effect on WC. Therefore the basic deficit may concern elementary script production independent of content.

In some discrepancy with our findings Zeuner et al. (2007) reported worse performance during writing a sentence if compared to producing superimposed circles. Interestingly, the performance in kinematics greatly improved if patients were requested to draw the circles with reduced force exerted against the surface (Zeuner et al. 2007, see also Mai & Marquardt 1994). Thus, instruction-induced changes of the task can obviously induce massive alterations of performance in patients with writer's cramp. Instructed and trained alterations of hand writing tasks can actually be used as a basis for therapy in writer's cramp (Baur et al. 2006; Mai & Marquardt, 1994; Zeuner et al. 2002; Zeuner et al. 2005; Zeuner et al. 2007; Byl et al. 2009).

In our experiment, however, we examined a repertoire of various writing specimen that were spontaneously produced and probably all associated with typical script production by the subjects. In this situation patients exhibit similar impairments in all tasks.

5. Conclusion

Analysis of kinematic and force parameters should be considered to supplement the clinical diagnosis of WC. Our results suggest that the writing of different text materials does not provide specific information. As it is useful to look at script generation and written output we would propose the writing of the sentence as a sensitive and sufficient tool. Additionally the instruction of writing a test sentence is very clear and simple. Consequently the level of interference can be kept low. The length of time needed to write the sentence differed very significantly for healthy controls and patients. Furthermore patients' grip force was increased and frequency was clearly reduced while writing the sentence. The method is sensitive. About 85% of patients in our study could be diagnosed by writing the sentence and by measuring pen grip force and kinematics of handwriting.

Therefore, the registration of writing movements with a digitizing tablet and the analysis of kinematic and force parameters can characterize the individual performance deficit. Since pen grip force seems potentially sensitive to dystonia subtype, its measurement would also be favourable. The registration of the grip forces needed sophisticated techniques but less complex and higher integrated solutions may be available in the future.

For therapeutic purposes, both types of information (subtype of Writer´s Cramp and writing characteristics) are needed. As we found no strong relation between force and kinematic parameters, therapies basing on motor training should be tailored according to the individual pattern of kinematic and force deficits (Mai & Marquardt 1994). Baur et al. (2009 a, b) evaluated training therapies for writer’s cramp that based on these principles. The approaches based on motor training with modification of grip postures (Baur et al. 2009 a) and availability of an auditory grip force feedback (Baur et al. 2009 b). Both approaches were successful to decrease pen tip force as well as grip force in the patients after therapy. Force decrease was paralleled by reported reductions of pain during hand writing, suggesting that the amelioration of forces might be most relevant for the reduction of daily life impairment and must be regarded as a high priority goal during treatment.

To sum up, the present study showed that simple and dystonic WC patients do not have a different degree of impairment in handwriting. The similarity of deficits in both patient groups does not support the concept of a unitary progression of deficits in the patients causing a switch from simple to dystonic Writer’s cramp. Rather both subtypes may occur independently.

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3.2 Significance of finger forces and kinematics during handwriting in writer´s cramp (2nd study)

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Significance of finger forces and kinematics during handwriting in writer´s cramp

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Abstract

Muscular hyperactivity during handwriting, irregular and jerky scripts, as well as akward and slowed pen movements are the cardinal symptoms of writer's cramp. Accordingly, impaired kinematics and increased force have been reported in writer´s cramp. However the relationship between these symptoms has rarely investigated. In addition, measurements of finger forces have been restricted to the vertical pen pressure. In the present study, the pen of a graphic tablet was equipped with a force sensor matrix to measure also the pen grip force produced against the pen barrel despite highly variable pen grips of the patients. Kinematics of writing movements, vertical pen pressure, and grip force were compared in 27 patients with writer's cramp and normal control writers during writing of a test sentence. As expected, all measures revealed a significantly worse writing performance in the patients compared to control subjects. Exaggerated forces were more frequent than abnormal kinematics, and evidenced by prolonged movement times and reduced writing frequencies. Correlations were found neither between kinematics and force measures nor between the two forces. Interestingly, patients relaxed the grip force during short periods of non-writing by the same relative amount as of control subjects. The finding of a large heterogeneity of performance patterns in writer´s cramp may reflect the variability of dystonic symptoms as well as the highly variable compensatory strategies of individual patterns. Measurements of finger force and in particular of the grip force are valuable and important descriptors of individual impairment characteristics that are independent of writing kinematics.

1. Introduction

In writer´s cramp handwriting is disturbed by a hyperactivity of the involved musculature obvious as sustained muscle spasms and dystonic postures of fingers, hand, and arm. The pen is grasped with abnormal posturing of the fingers with highly idiosyncratic configurations such as extreme extension in the distal inter-phalangeal joints combined with flexion in proximal joint or whole hand grips where the pen is grasped between fingers and palm (Schenk, Baur, Steidle, & Marquardt, 2004; Sheehy & Marsden, 1982; Wissel et al., 1996). The whole upper extremity including the trunk maybe in an abnormal posture combined with increased tone and co-contraction. Abnormal posturing and muscle hyperactivity is frequently associated with pain at various locations (Sheehy et al., 1982). The writing of patients with writer´s cramp is characterized by irregular and jerky scripts which may be illegible in extreme cases (Mai & Marquardt, 1994; Sheehy et al., 1982). The production of the script is typically characterized by non-fluent, irregular writing movements and prolonged duration.

In number of recent studies, the alterations of the kinematics of writing movements in writers' cramp were precisely analysed using graphic tablets that register the horizontal movements of the grasped pen (Zeuner et al., 2007; Zeuner et al., 2005; Siebner et al., 1999; Schenk et al., 2004; Schenk & Mai, 2001; Baur et al., 2006; Mai et al., 1994; Chakarov, Hummel, Losch, Schulte-Monting, & Kristeva, 2006). These studies tested various writing tasks such as the repeated writing of standard sentences, the repeated writing of single or combined letters, or the production of superimposed circles or strokes. Patients with writers' cramp turned out to be impaired in several measures characterizing writing kinematics: The duration of writing a fixed sentences or word was prolonged, the frequency of up and down movements was decreased, measures of pen velocity were similarly decreased, measures of the regularity of the velocity profile indicated decreased fluency and automation, and various indicators of variability during repetitive writing of a constant letter or symbol were increased (Baur et al., 2006; Chakarov et al., 2006; Mai & Maquardt, 1994; Schenk et al., 2004; Schenk &Mai, 2001; Schneider et al., 2010; Siebner et al., 1999; Zeuner et al. 2007). Interestingly, from several studies it was obvious that some of the tested patients were still able to write with normal kinematics (Schenk et al., 2004; Zeuner et al., 2007).

In addition to the vertical pen pressure, the grip force produced against the pen barrel could be a highly sensitive signal of muscular hyperactivity in Writer's Cramp. From a biomechanical viewpoint, grip forces are not necessarily coupled with the vertical pen pressure. Grip forces can adopt arbitrary levels as long as a certain threshold to prevent slippage of the fingers is exceeded. The measurement of grip forces during hand writing is, however, hampered by space limitations to mount a sensor below the grasp points of the fingers. In patients with writer's cramp a measurement is additionally complicated by the fact that patients hold the pen with highly individualized finger configurations (Schenk et al., 2004; Sheehy & Marsden, 1982) and any attempt to measure forces with fixed force sensors would have unpredictable effects on performance. A solution to these complications is the use of pressure-sensitive sensor matrices. Such matrices are flat and flexible and can be wrapped around a pen. Force is measured at multiple sites across the sensor array, so that with an adequate distribution and spatial resolution of the elements, the pressure distribution of virtually every grip configuration can be measured. The feasibility of the instrumentation has recently been demonstrated in a study of hand writing in a sample of healthy children and children with cerebral palsy (Chau, Ji, Tam & Schwellnus, 2006).

We measured handwriting kinematics and pen pressure during writing of a test sentence in a larger sample of patients with Writer's Cramp using a graphic tablet. In particular, grip force was registered using a customized, flexible pressure-sensitive sensor matrix wrapped around the writing stylus. From the classical symptoms of Writer's Cramp and from the findings in studies of writing kinematics and pen pressure we expected impairments in all measures of writing performance. Deteriorations of the group means, however, do allow a conclusion about the correlation of these performance aspects across the individual patients. Such a correlation may be expected between forces and kinematics since increased finger forces may stiffen the fingers and the hand and thus restrict mobility and writing proficiency. However, considering the large heterogeneity in the clinical presentation of writer's cramp, individualized disturbance patterns may also be expected. In particular, correlation analyses may provide information about individual compensatory strategies employed by the patients.

We hypothesized that force increases may generalize across the different effectors and expected a stronger correlation between pen pressure and grip force compared to correlations between forces and kinematics. With the above reasoning, grip force may, however, also reflect individual performance patterns characterized by a small number of patients performing in the range of control subjects and manifold increases of the grip force in some others without concurrent adjustments of pen pressure and vice versa.

Finally, the measurement of grip force enabled the analysis of relaxation during the time intervals when the pen was lifted from the writing surface to pause or to move between words or letters. Grip force relaxation is an economic motor strategy to prevent fatigue and may be absent or reduced in writer's cramp due to dystonia (Prodoehl, MacKinnon, Comella, & Corcos, 2006). The relaxation may therefore provide another sensitive measure of the movement disorder.

2. Methods

2.1. Participants

Twenty-seven right handed patients with writer's cramp took part in the experiment (20 females, 7males, mean age ± SD: 43.9 ± 11.6 years). Frequency of female patients was relatively high compared to normally reported gender distributions in writer's cramp (Abbruzzese et al., 2008; Soland, Bhatia, & Marsden, 1996); we are, however, not aware of a selection bias. Inclusion criteria for the patients were the presence of disabling writer's cramp including muscular hyperactivity and abnormal posture during hand writing. None of the patients had evidence of other neurological deficits as revealed by neurological examination. According to the classification of Sheehy and Marsden (1982), 14 patients had simple writer's cramp with only hand writing being impaired, and 13 patients had dystonic writer's cramp with dystonic symptoms in other fine motor tasks. Mean duration of writer's cramp varied widely between 1 and 48 years (mean 12.5 ± 13.9 years). The majority of the patients (85.2%) experienced pain during writing and 33.3% had an additional tremor during writing. Arm dystonia was assessed with the Dystonia Scale proposed by Fahn (1989). Seven patients (25.9%) had been treated with Botulinum toxin injections a minimum of 3 months before the examination and 70.4% of the patients had tried other treatments such as physical, occupational, or psycho therapies. Table 1 displays clinical data of the individual patients.

The control group consisted of 14 healthy right-handed persons with a similar age and gender distribution as the patient group (11 females and 3 males, mean age ± SD: 42.1 ± 13.1 years).

Informed consent was obtained from all participants. The experimental protocol was conducted in accordance to the Declaration of Helsinki and was approved by the ethical committee of the Bavarian Medical Association.

2.2. Procedure and data recording

For the purpose of the present study subjects wrote the German sentence "Die Wellen schlagen hoch" ("The waves are surging high") on a blank paper sheet fixed on a digitizing tablet. Subjects were instructed to write in their normal everyday writing style during three trials. A digitizing tablet (Wacom IV, sampling rate 200 Hz, spatial resolution 0.05 mm) registered the horizontal position of the tip of the writing stylus. The pen pressure exerted orthogonally by the stylus against the writing surface (0–3 N) was determined from the axial force measured inside the pen adjusted for the angle of pen tilt (refill friction neglected) resulting in maxima lower than 3 N. It has to be noted, that the axial force sensor was not designed for high forces and the pen pressure produced by patients with pathological force increases may exceed the measurement range (see for example Siebner et al. (1999), see fig. 1). Recording started as soon as the subjects touched the digitizing tablet with the pen. The positional data were transmitted to a personal computer and analysed with special software (CSWin 2007, MedCom, Munich). Movement trajectories and corresponding velocity curves were calculated and smoothed by nonparametric regression methods (Marquardt & Mai, 1994). A force sensor matrix was used to measure the force exerted by the fingers against the pen during writing. The sensor matrix (sensor S2060, Pliance System, Novel, Munich, Germany) was wrapped around the stylus of the graphic tablet. The matrix is 0.5 mm thin and flexible. It is glued to the pen barrel surface and covered with silicon-elastomer. Eighty-eight force sensors are distributed across the whole surface of the stylus with a spatial resolution of 5 x 10 mm^2. The pressures range amounts from 500 to 20,000 hPa corresponding to 0.5 to 20 N/cm^2. The total error including hysteresis is smaller than 10%. The mounted device is calibrated with air pressure. The whole matrix was sampled with a rate of 50 Hz. The technique allowed the registration of the pen grip force for any individual grip type and without restriction for the finger positions.

Table 1 Clinical data of 27 patients with Writer´s Cramp

Code	Age (years)	Gender	WC type	Fahn scale[a] (%)	Pain (+ present, 0 absent)	Symptom duration (years)	Botox treatment (yes/no)	Other treatment (yes/no)
SK01	49	f	Simple	60	+	11	n	y
SK02	44	f	Simple	70	0	1	n	n
SK04	33	f	Simple	60	+	9	n	n
SK10	50	f	Simple	60	+	5	n	y
SK16	32	f	Simple	75	+	2	n	n
SK21	37	f	Simple	65	+	9	y	y
SK23	42	f	Simple	64	+	36	n	n
SK27	34	m	Simple	60	+	3	n	y
SK28	44	f	Simple	75	+	1	n	n
SK31	40	f	Simple	73	+	12	n	n
SK39	64	f	Simple	75	0	48	n	y
SK42	51	m	Simple	70	+	15	n	y
SK45	67	m	Simple	64	+	20	y	n
SK46	52	f	Simple	75	+	3	n	y
SK03	30	m	Dystonic	25	+	3	y	y
SK06	22	f	Dystonic	50	+	1	n	y
SK07	42	f	Dystonic	60	+	27	y	y
SK08	27	f	Dystonic	70	+	1	n	y
SK09	50	f	Dystonic	60	+	9	y	y
SK13	57	f	Dystonic	55	+	7	n	n
SK14	39	f	Dystonic	50	+	11	y	y
SK18	57	m	Dystonic	25	0	20	n	y
SK20	25	f	Dystonic	50	+	8	n	y
SK24	59	f	Dystonic	56	+	12	n	y
SK29	43	f	Dystonic	55	+	8	n	y
SK34	48	m	Dystonic	55	0	20	n	y
SK37	46	m	Dystonic	56	+	9	y	y

[a] Arm dystonia scale: 0%: severe dystonia and 100%: no difficulty (see Fahn, 1989).

2.3. Data analysis

To characterize the kinematics of the handwriting movements the time needed to write the sentence and writing frequency were calculated. The duration included movements of the lifted pen between words or letters as well as breaks. Frequency was calculated from the duration of individual upward and downward directed strokes and characterized the speed and fluency of writing (Mai & Marquardt, 1994; Schenk et al., 2004). Script size was calculated as the average stroke length in the up/down-direction. The total grip force exerted by the fingers and eventually other parts of the hand was calculated by integration across the forces measured by the matrix elements. Pen pressure and pen grip force magnitude are reported for the periods with the pen in contact with the paper. A grip relaxation measure was calculated by dividing the pen grip force during periods without pen contact (pen movements between words or letter, breaks with the pen lifted-off) by the grip force during contact periods. Kinematics and force measures were averaged across the three trials. t-tests were used to compare measures between control subjects and patients. The relationship between signals was analysed by correlation analyses. The relationship between clinical data and handwriting data was assessed with t-tests and correlation analyses. Mean measures of hand writing performance were calculated separately for kinematic and force measures. For this purpose, Z scores were calculated and averaged using the mean and the standard deviation of the control subjects for duration and frequency (kinematics) and pen pressure and grip force (force).

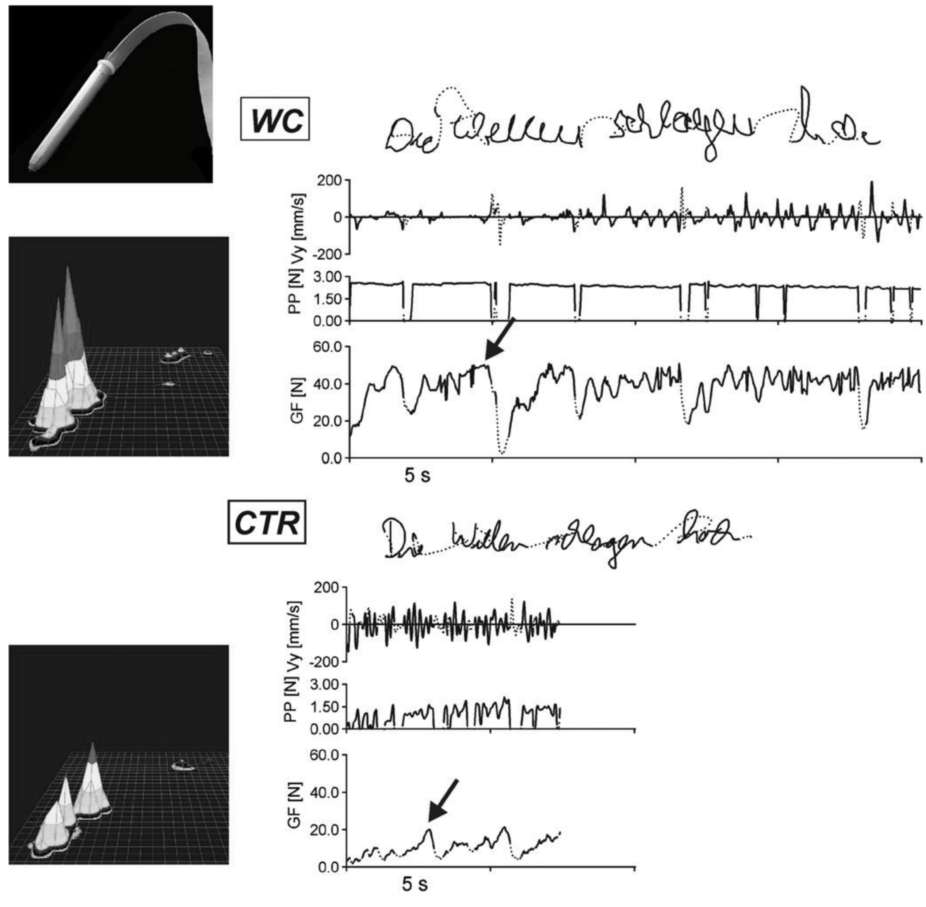

Fig. 1: Performance kinematics and grip force during writing the test sentence in a patient with writer´s cramp (WC) and a control subject (CTR). Upper Left: pen with force sensor matrix wrapped around the surface. Lower Left: pressure distribution across the unwrapped sensor surface (tip of the pen: lower left corner, back of the pen: right background). Right: reproduction of the script, upward/downward velocity (Vy), pen pressure (PP) and grip force (GF, integrated surface pressure distribution). The arrows indicate the time point corresponding to the pressure distribution shown on the left.

3. Results

Fig. 1 shows a handwriting specimen of a patient with dystonic Writer's Cramp and of a control subject. The reproduction of the script reveals that the patient succeeded to write the sentence in a legible manner although the trajectory seems partly irregular. He needed 20 s to write the sentence. The profile of the vertical velocity was also highly irregular with prolongations between consecutive velocity changes. In contrast to the patient's performance, the control subject needed much less time and produced a more regular velocity profile with a fast succession of velocity changes. The control subject also wrote smaller than the patient; however, script size did not differ significantly between the patient and the control group ($p > 0.05$). The left side of Fig. 1 reveals the pressure distribution across the pen barrel surface at selected time points during writing the sentence (see arrows). For the control subject, pressure peaks of three fingers can be discriminated. The small peak in the background resulted from contact of the back of the pen with the hand. Much higher peaks of the patient are indicative of exaggerated grip forces that seem to be produced mainly by two fingers. It has to be noted that the identification of individual finger was frequently less obvious than in the present example due to tight finger positions and flat contact areas. In addition, heterogeneity of grip type prevented the identification and analysis of individual finger forces in the present study. The time plots of the integrated grip force confirm a much higher grip force in the patient than in the control subject at virtually all time points of the recording.

The writing of each single word is obvious in the grip force profile of the patient and the control subject; both subjects relaxed their grip force between individual words. Pen lift-offs are also obvious from the time plots for pen pressure, the signal is, however, at ceiling for most of the writing of the patient (see section 2). Group results for the main measures of movement kinematics and grip force are displayed in fig. 2.

The duration of writing the sentence was clearly increased in the patients (mean WC: $t(39) = 4.75$, $p < 0.001$, Fig. 2A). Similarly, stroke frequency was significantly lower in the patients than in the control subjects ($t(39) = -2.95$, $p = 0.005$, fig. 2B). Grip force varied profoundly in the patients ranging from 4 N up to 62 N (fig. 2C). Thus, grip force was increased by up to a factor 4 in some patients if compared to the median of the control subjects, but normal grip forces were also observed in a substantial part of the patients (see also figs. 3 and 4). For the group of patients statistical analysis revealed a highly significant increase of the grip force ($t(39) = 3.14$, $p = 0.003$). In both groups, the relaxation was below 1 indicating that participants lowered their grip force in the time intervals when they did not produce script. The decrease of the grip force varied widely between 45% to only 95% of the grip force during writing (fig. 2D). In contrast to the other measures, relaxation was, however, similar in patients with writer's cramp and control subjects ($t(39) = 0.033$, ns). The amount of relaxation did not depend on the grip force level exerted by the participants (correlation $p > 0.1$ in both groups). In addition, the two patients with extremely high grip forces did not show extreme amounts of relaxation (SK14: 79%, SK16: 80%). The pen pressure was also clearly higher in the patients than in the control subjects (Fig. 2E, $t(39) = 4.01$, $p < 0.001$). It has to be considered that pressure values above 1.6 N do not necessarily represent the true physical pressure, because the reading was sometimes or even constantly at maximum during the writing (see fig. 1 and section 2). It is, however, remarkable that pen pressure nevertheless differentiated between patients and control subjects, even though the physical value was frequently underestimated in the patients. The various measures were compared separately within each group. Duration and frequency revealed a strong interdependence predominantly in the patient group (patients with writer's cramp–WC: $r = 0.83$, $p < .001$ and control subjects – CTR: $r = 0.59$, $p = 0.028$).

Fig. 3 shows the correlation between the grip force and the two measures of writing kinematics. It is obvious that grip force correlated with neither the duration nor the frequency in any of the groups (all $p > 0.2$). Similarly, pen pressure did not correlate with any of the kinematic measures (all $p > 0.2$).

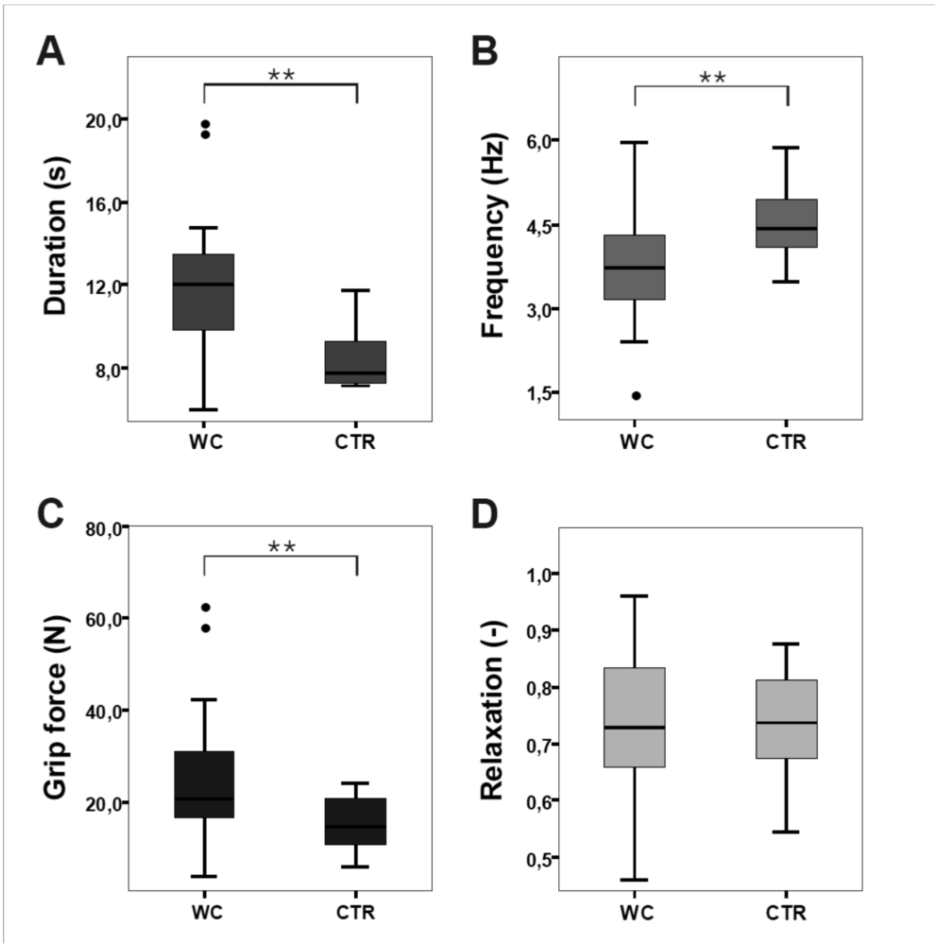

Fig. 2: Measure of movement kinematics and grip force in patients with Writer´s Cramp (WC, N=27) and control subjects (CTR, N=14). (A) Duration of writing the test sentence, (B) frequency of up-and downward strokes, (C) mean grip force, (D) relaxation defined as the ratio of mean grip force during non-writing versus writing episodes, and (E) pen pressure. Box plots indicate median, inter-quartile-ranges, maxima, minima and outliers (solid circles).

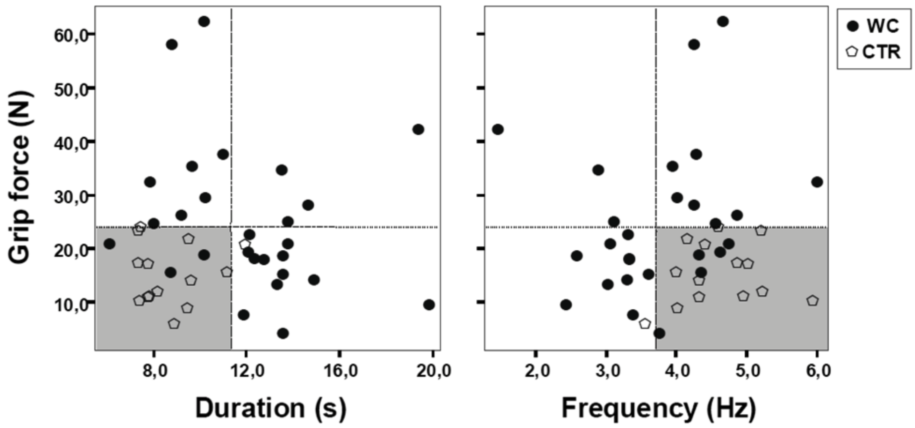

Fig. 3 Relationship between pen grip force and the two measures of movement kinematics (duration and writing frequency) in 27 patients with writer´s cramp (WC, closed symbols) and 14 control subjects (CTR, opensymbols). The normal range is indicated by the shaded area and thin lines; its limits were defined by the 90th (duration and grip force) or 10th (frequency) percentile of the performance of control subjects.

Fig. 4 displays the relationship between both finger forces. Due to the saturation of pen pressure during writing the relationship between both forces has to be considered with care (see Section 2). Particularly in the two patients with extreme increases of grip force the pen pressure was always at maximum during writing (due to the consideration of pen tilt the maximum value of pen pressure varied between patients even if the reading was always at maximum). However, also for data points with a pen pressure lower than the critical limit (approximately 1.6 N) no correlation between pen grip force and pen pressure is obvious. Defining the limit of normal performance as the 90 percentile (respectively 10 percentile for frequency, see fig. 3) of the distribution of the control subjects, 59.3% of the patients (16/27) needed an abnormally long time to write the sentence, and in a subgroup (48.1%, 13/27) also the frequency of writing was abnormally decreased. Force deficits were obvious in 74.1% (20/27) of the patients. The force deficits could be categorized into three groups: a general increase of both grip force and pen pressure in 25.9% (7/8), a selective increase of grip force in 18.5% (5/27), and a selective increase of pen pressure in 25.9% (7/27). Importantly, a general impairment of kinematics and force (at least one of the two force measures) was obvious in 37.0% of the patients (10/27), a selective deficit of kinematics was found in

22.2% (6/27), and a selective deficit of force control in 37.0% (10/27) of the patients. Only one patient (3.7%) did not reveal a deficit in any of the four measures investigated using the 90 percentile threshold of control subjects as the cut-off. In order to reduce the number of measures to classify patients' performance (also decreasing the risk of errors due to multiple comparisons), but preserve the distinction between kinematic and force measures, we calculated average measures for both aspects of hand writing. To this end, Z scores of duration and frequency (kinematics) and of pen pressure and grip force (force) were calculated on the basis of the controls' distributions and averaged (see section 2). Again considering the 90% percentile of the controls performance as a cut-off, none of the patients was in the normal range in both the kinematic and the force measure, while two control subjects exceeded the cut-off in at least one measure.

The type of writer's cramp had no effect on kinematic or force measures (t-test: $p > 0.1$, see Schneider et al. (2010)). The duration of symptoms and Fahn score had no or only very weak influences on kinematic and force measures in the patients ($p > 0.1$, exceptions: writing frequency versus symptom duration: $r = -0.39$, $p = 0.045$, writing duration versus symptom duration: $r = 0.41$, $p = 0.032$, see Zeuner et al. (2007)).

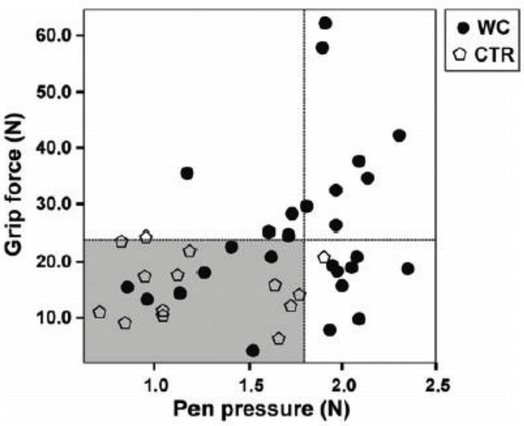

Fig. 4: Relationship between pen grip force and pen pressure in 27 patients with writer´s cramp (WC, closed symbols) and 14 control subjects (CTR, open symbols). The normal range is indicated by the shaded area and thin lines; its limits were defined by the 90[th] percentile of the performance of control subjects. Note that mean pressure magnitudes above approximately 1.6 N may be underestimated (see section 2 and fig. 1).

4. Discussion

In this study quantitative measures of writing kinematics and produced finger and hand forces during hand writing were investigated in 27 patients with writer's cramp. It turned out that the various measures were not correlated. In particular, a combined deficit of kinematics and forces were found in only a bit more than one third of the patients. Isolated force deficits were obvious with the same frequency. Isolated deficits of writing kinematics were less frequent, being obvious in every fourth to fifth patient. Accordingly abnormal kinematics was less frequent in the whole group (~ 60%) than exaggerated forces (~ 75%). The predominance of force deficits as compared to kinematic deficits has not been reported in previous studies that assessed kinematics and pen pressure (Chakarov et al., 2006; Schenk et al., 2004; Zeuner et al., 2007). The main reason is probably that the measurement of grip force added a novel physiological signal that either combined with an increased pen pressure or revealed a additional force impairment.

A novel technical approach was used to measure the grip forces produced by patients with writer's cramp against the surface of the writing pen. The technique allowed registration without restriction to the highly individualized grip types observable in patients with writer's cramp (Schenk et al., 2004; Sheehy & Marsden, 1982). As expected from the primary symptoms of writer's cramp, exaggerated grip forces were found that could be as high as four times the average value noted in control subjects. The finding of increased grip forces is in agreement with reports of increased pressure exerted by the pen against the writing surface which was also confirmed in the present study (Baur, Fürholzer, Jasper, Marquardt, & Hermsdörfer, 2009a, 2009b; Baur et al., 2006; Chakarov et al., 2006; Schenk & Mai, 2001; Schneider et al., 2010; Siebner et al., 1999; Zeuner et al., 2007). Since this force is measured by standard equipment the pen pressure was more frequently reported in writer's cramp. The measurement of pen pressure did, however, not capture all pathologically increased forces, as outlined in section 2 and as is obvious from the present data (fig. 1). Nevertheless the pen pressure differentiated with high significance between patients and controls and may still provide valuable information despite these limitations.

However, even if the technical limitations were considered there was no correlation between grip force and pen pressure. Rather both forces could be impaired together or in isolation with roughly equal frequencies. This finding was surprising since an association of strong finger grips and high writing pressure was expected. At least in the control subjects, a closer correlation between both forces had been expected due to the well known coupling between grip force and load in various object manipulation tasks (Flanagan & Johansson, 2002; Hermsdörfer, Hagl, & Nowak, 2004; Johansson & Westling, 1984). This coupling is most prominent for load variations within tasks, such as inertial loads during movements of grasped objects, while for comparisons across individuals, variations of finger friction or finger posturing may dominate the adjustment of grip force to a particular load. Especially during handwriting grip configurations are very variable even among normal writers. Dissociations between both forces have already been reported in earlier attempts to measure grip force and pen pressure in healthy subjects (Herrick & Otto, 1961). In patients with writer's cramp dissociations between both forces are even more conceivable: High grip force may be combined with stiffened hand and wrist, and this co-contraction may prevent high downward forces of the hand. On the other hand, abnormal ways to grasp the pen may be inefficient to generate a high grip force despite muscular hyperactivity, but nevertheless an exaggerated pen pressure may be produced. Thus, muscular hyperactivity in writer's cramp expresses itself in various ways and at different locations. The lack of a correlation between grip force and pen pressure proves that information about pen pressure is additive to information gained from grip force measurements and both forces can provide valuable information about individual disturbance characteristics. Decomposing the grip force into individual finger contributions and analysing finger force coordination may provide further information about general and individual mechanisms of writer's cramp. Due to technical reasons (see Section 3) finger forces were not identified in the present study but such analyses may be a promising target for future studies.

Different from the grip force, the degree of relaxation did not differ between writer's cramp patients and control subjects. Thus, despite patients produced abnormally high grip forces they decreased the force by the same relative amount as control subjects when the pen was lifted from the paper in order to move between words or letters. Relaxation of grip force outside the periods of writing can be considered as an economical mechanism to minimize fatigue and prevent increases of muscular tone. Obviously this mechanism was preserved in the patients, indicating that the writer's cramp had no impact on this highly automatised aspect of force control. Normal motor control has also been demonstrated in other aspects of hand writing, such as during writing senseless scribbles (Mai & Marquardt, 1994). The finding of a normal relaxation is surprising in view of a recent report of impaired voluntarily relaxation of arm and hand muscles in patients with Writer's Cramp (Prodoehl et al., 2006). However, the deficit was not obvious in the amount of relaxation; rather the duration of relaxation from a predefined force level until complete relaxation was prolonged between 20 and 70 ms. Therefore, if the slowing of force changes was present during the automatic grip force relaxation, it was not of a critical amount that could significantly impair this aspect of hand writing performance.

The forces and measures of movement kinematics did not correlate. Thus, slowed and hesitating writing was not associated with increased forces and writing kinematics could be normal despite increased forces. Patients could be classified into groups with either an isolated deficit of writing kinematics, or an isolated deficit of forces, and or an association of impaired performance of both aspects. Thus, there seem to be no causal relationship from dystonic muscular hyperactivity to increased force in manipulation of the pen and further to decreased speed and fluency of writing, that may have been expected a consequence of co-contraction, stiffening or fatigue of the hand and fingers. One possible reason for this independency of the deficits are highly individualized disturbance patterns: Many different constellations of muscular hyperactivity, co-contraction or wrong posture in proximal or distal joints, that frequently but not necessarily lead to increased grip forces, may impair the quality of hand writing. In addition, patients may have been able to keep the force at moderate levels if writing with reduced frequency and prolonged duration. Successful attempts to speed up may have been combined with massive increases of the grip force in some patients and additionally may have caused pain, as suggested by high incidence of pain in our sample. Although it cannot be conclusively determined from the present data how much of the force increase is a primary manifestation of dystonia and how much is attributable to compensation, the large heterogeneity of performance patterns among the patients with Writer's Cramp speaks for an important role of individualised compensatory strategies. The distinction between primary abnormal grip force control and a secondary increase in grip force is a highly relevant question for future research. Finally, the newly introduced measurement of grip force exerted against the pen has emerged as a valid and sensitive variable. Appropriately combined with measures of writing kinematics and of the pen pressure exerted against the writing surface, the performance of patients diagnosed with writer's cramp can be identified as pathological with very high sensitivity on the basis of writing a short test sentence. Force increase can be massive in some patients, is independent of writing kinematics, and is a promising target for motor training therapies. Indeed a motor training with the aim of reducing muscular hyperactivity decreased the pen pressure and the grip force in patients with Writer's Cramp (Baur et al., 2009a, 2009b). In parallel, pain during writing decreased in the patients. As maybe expected from the missing correlation between kinematics and force reported here, the training did not improve handwriting kinematics suggesting that therapy to improve handwriting speed has to address this aspect of hand writing more directly.

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3.3 Task specific grip force control in Writer´s Cramp (3rd study)

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Task specific grip force control in writer´s cramp

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Abstract

Objective: Writer´s Cramp is defined as a task specific focal dystonia generating hypertonic muscle co-contractions during handwriting resulting in impaired writing performance and exaggerated finger force. However, little is known about the generalisation of grip force across tasks others than writing. The aim of the study was to directly compare regulation of grip forces during handwriting with force regulation in other fine-motor tasks in patients and control subjects.

Methods: Handwriting, lifting and cyclic movements of a grasped object were investigated in 21 patients and 14 controls. The applied forces were registered in all three tasks and compared between groups and tasks. In addition, task-specific measures of fine-motor skill were assessed.

Results: As expected, patients generated exaggerated forces during handwriting compared to control subjects. However there were no statistically significant group differences during lifting and cyclic movements. The control group revealed a generalisation of grip forces across manual tasks whereas in patients there was no such correlation.

Conclusion: We conclude that increased finger forces during handwriting are a task-specific phenomenon that does not necessarily generalise to other fine-motor tasks.

Significance: Force control of patients with Writer’s Cramp in handwriting and other fine-motor tasks is characterised by individualised control strategies.

Key Words: Writer´s Cramp, focal dystonia, handwriting, force analysis, grip force

1. Introduction

Writer´s Cramp (WC) is considered as a task-specific form of focal hand dystonia with uncontrollable muscle co-contraction of hand and arm muscles during writing are the cardinal symptoms of Writer´s Cramp. Writer´s Cramp typically affects persons who have spent periods engaged in stereotyped and repetitive writing (Hallett, 2006). The script of patients with WC may still be legible, but script production is awkward, strenuous and slowed with the production of non-ergonomic, squashed and tremulous letters. Patients frequently report pain and loss of pen control during handwriting.

Two forms of Writer´s Cramp have been distinguished according to the co-occurrence of deficits in other fine motor tasks (Gowers, 1888; Sheehy and Marsden, 1982). In simple writer´s cramp (sWC) symptoms only occur while holding a pen and performing writing or drawing movements, while other manual tasks are carried out normally. By contrast, patients with dystonic or complex writer´s cramp (cWC) also report decrements of skill during other manual tasks such as drinking, eating, shaving/make-up application or computer work (Sheehy and Marsden 1982, Jedynak et al. 2001).

The etiology and pathophysiology of WC is still unclear but there are several hypotheses to explain the underlying processes. Hallett et al. (2006) defined three general physiological mechanisms (1) Loss of cortical inhibition was found in intra-cortical stimulation studies performed in patient with WC (Nakashima et al., 1989; Panizza et al., 1990; Chen et al., 1997; Sohn & Hallett, 2004; Quartarone et al., 2006; Torres-Russotto & Perlmutter, 2008); (2) Abnormal plasticity of the sensorimotor cortex may result from over-use as suggested by monkey experiments (Byl et al., 1996; Torres-Russotto & Perlmutter, 2008; Lin & Hallett, 2009); (3) Psychophysical tests of sensory perception revealed sensory dysfunction in patients with WC (Bara-Jimenez et al., 1998; Molloy et al., 2003; Lerner et al., 2004; Garraux et al., 2004). In addition, theories emphasising behavioral aspects point to a role of maladaptive control strategies in the genesis of WC (Mai,1995; Baur et al., 2009b).

In WC deteriorated handwriting fluency is associated with excessive forces that are frequently combined with abnormal writing posters of fingers, wrist, elbow, and shoulder (Sheehy & Marsden,1982; Mai & Marquardt, 1994; Schneider et al., 2010; Hermsdörfer et al., 2011). Several studies measured the finger forces produced during handwriting, and reported that the force exerted by the pen tip onto the writing surface (pen tip force) is elevated in patients with WC compared to healthy controls (Siebner et al., 1999; Schenk & Mai 2001; Zeuner et al., 2005; Zeuner et al., 2007; Chakarov et al., 2006; Baur et al., 2006; Baur et al., 2009a; Baur et al. 2009b; Schneider et al., 2010; Hermsdörfer et al., 2011). In addition, grip force, produced by the fingers against the pen barrel, was clearly increased in WC patients during writing (Baur et al., 2006; Schneider et al., 2010; Hermsdörfer et al., 2011). Both measures of finger force were found to be sensitive to muscular hyperactivity in WC patients and provided additive information on the individual disturbance pattern (Schneider et al., 2010; Hermsdörfer et al., 2011).

Since patients with dystonic/complex writer's cramp report additional deficits in non-writing fine-motor tasks it is tempting to objectively investigate their manual performance. Object manipulation tasks seem particularly well suited since they have been extensively used in studies of sensorimotor and cognitive control strategies in healthy humans as well as in studies analyzing the consequences of brain damage on manual functions (Nowak & Hermsdörfer, 2005; Flanagan et al., 2006; Hermsdörfer, 2009). For example, measurements of finger forces during grasping and lifting of a weight revealed that healthy subjects adjust their grip force precisely to the weight and other characteristics of the object (Johansson & Westling, 1984; Johansson, 1996; Flanagan & Johansson, 2002). Clinical studies showed that the precise control of grip force during object lifting was disturbed in neurological diseases such as basal ganglia disorders (Fellows et al., 1998; Nowak & Hermsdörfer, 2005), stroke (Hermsdörfer et al., 2003; Raghavan et al., 2006) and cerebellar diseases (Fellows et al., 2001; Brandauer et al., 2008).

Another sensitive paradigm in studies of object manipulation was based on the measurement of grip forces during the movement of grasped objects. Continuous vertical movements generate time-varying acceleration-dependent inertial loads that add to or subtract from the gravitational load. Healthy subjects precisely compensated the resulting load profile by time-synchronous grip force modulations (Flanagan & Wing 1995). However, patients with CNS diseases showed impaired grip force/load force coordination in this task (Hermsdörfer et al., 2008; Brandauer et al., 2010).

In those studies, healthy subjects used economical grip forces with small safety margins to prevent the object from slipping (Johansson & Westling, 1984; Johansson, 1996), whereas grip forces were almost invariably increased in patients with CNS disease.

The lifting task was tested in patients with writer's cramp. Patients used excessive grip force levels in relation to load force levels and grip forces in patients were increased compared to healthy controls (Odergren et al., 1996; Serrien et al., 2000; Schenk and Mai, 2001; Nowak et al., 2005b). In particular, Odergren et al. (1996) used lifting tasks with variations of the order of weight and found increased grip force levels in the static phase of lifting. The data of Serrien et al. (2000) confirmed deficits in grip force scaling while performing a drawer manipulation task. Odergren et al. (1996) and Serrien et al. (2000) concluded on the basis of their findings that disturbed sensorimotor processing is the cause for grip force deficits in WC patients. However, Schenk et al. (2001) investigated 22 WC patients and did not find a functional link between severity of deficits during handwriting and pen forces during handwriting as well as grip force during lifting an object. Nowak et al. 2005 (2005b) observed increased grip force while grasping and lifting of a cylindrical object in patients with focal dystonia (Writer´s Cramp, Musician´s Cramp) that rapidly decreased during repeated lifts, and concluded that elevated grip forces is more a pre-learned phenomenon than the primary disorder.

These previous studies of patients with WC did not directly relate grip force production in non-writing tasks to grip force deficits during handwriting. This is however particularly interesting if focal dystonia is supposed to spread from writing disturbances to other fine motor tasks. Therefore, we quantified motor performance during handwriting and during two object manipulation tasks in a sample of patients with WC and in control subjects. Handwriting performance was registered using a graphic tablet and a force sensor matrix that registered the grip force in arbitrary types of pen grip (see section 2 and Hermsdörfer et al., 2011). Object manipulation skills were assessed during grasping and lifting of boxes and during cyclic up-and-down movements of a grasped manipulandum. We were particularly interested in the grip forces exerted during both tasks, and in the relationship between these two grip forces and the grip force produced during hand writing. While the previous studies investigated only the lifting task in patients with WC, the cyclic task may closer match the demands during handwriting since the grip force has to be continuously modulated according to the varying dynamic loads. If grip force increases in writer's cramp generalise from handwriting to other fine motor tasks, increased forces during object manipulation have to be expected in those patients that used exaggerated forces during handwriting. Thus, correlations between the different grip forces are expected. If, on the contrary, WC is task-specific, no force increases during non-writing task and no corresponding correlation may be detected. It is conceivable that the outcome depends on the type of WC. Patients with simple and with dystonic/complex WC were therefore separated into two groups.

In addition to grip forces, sensorimotor integration and grip force coordination were evaluated in the object manipulation task. Sensorimotor integration was assessed as the ability to adapt forces to an unpredictable change of the weight of the lifted object (Johansson & Westling 1988) and grip force coordination was quantified as the precision of grip force modulation according to load variations in the cyclic movement task (Flanagan & Wing 1995). Since comparable basic sensorimotor skills in non-writing tasks have been shown to be preserved in patients with WC (Schenk & Mai, 2001; Nowak et al., 2005b; Hermsdörfer et al., 2011) we expected no performance decrements in these task aspects compared to healthy control subjects.

2. Materials and Methods

2.1 Subjects

We studied 21 right handed patients with Writer´s Cramp (17 females, 4 males, age: 41.1 ± 10.7 years; Table 1). The diagnosis was based on examination by a scientist experienced in the study of writer's cramp typically confirming earlier diagnosis by a neurologist. None of the patients had evidence of other neurological deficits as revealed by neurological examination. The group was divided into two subgroups according to whether the impairment was restricted to hand writing (simple WC) or also involved other fine motor tasks (dystonic/complex WC). Patients in the dystonic group reported impairments in one up to five other fine motor activities (see table 1). The group of patients with simple WC (sWC) consisted of 9 patients; 8 females and 1 male (age: 40.3 ± 6.8 years). Two patients classified as sWC reported impairments in motor tasks related to writing such as painting and drawing (table 1). The sample of patients with dystonic or complex Writer´s Cramp (cWC) consisted of 12 patients, 9 females and 3 males (age: 41.6 ± 13.1 years). The simple and dystonic WC patient groups did not differ in age (t-test: $t < 1$, $p > 0.1$). Symptom duration was longer in patients with cWC (mean 10.6 y) than sWC (mean 5.9 years), but the difference was not statistically significant ($t = 1.6$, $p > 0.1$). Pain during handwriting was reported by nearly all patients of both groups (SWC: 8/9; cWC: 10/12), while tremor during handwriting was more frequent in the cWC group (sWC: 1/9; cWC: 5/12). Severity of dystonia was rated with the arm-dystonia-disability-scale (ADDS), developed by Fahn in 1989 (Fahn 1989). Patients of the dystonic group revealed lower scores and accordingly more severe dystonia than patients with sWC (mean 50.9 % vs. 66.4 %, $t = 3.2$, $p = 0.005$). One patient with simple WC and four dystonic WC patients were previously treated with botulinum toxin. In all these cases the time since the treatment was longer than three months. The control group (Ctr) consisted of 14 healthy right-handed age-matched participants (11 females, 3 males, age: 41.1 ± 13.1 years; t-test: $t < 1$, $p > 0.1$). The control subjects had no history of any neurological disease or any relevant trauma to the arm or hand. None of them reported problems with handwriting. The profession was matched within the three groups.

Informed consent was obtained from all participants. The experimental protocol was conducted according to the Declaration of Helsinki and was approved by the ethical committee of the Bavarian Medical Association.

Table 1: Subjects characteristics

Legend: f= female; m= male, age and symptom duration in years

Pat.	Age	Gender	Type	Symptom duration	Impaired drinking	Impaired eating	Impaired make-up	Impaired shaving	Impaired PC work	Impaired other tasks	Fahn
WC 01	49	f	simple	11	no	no	no	no	no	yes	60
WC 02	44	f	simple	1	no	no	no	no	no	no	70
WC 04	33	f	simple	9	no	no	no	no	no	yes	60
WC 10	50	f	simple	5	no	no	no	no	no	no	60
WC 16	32	f	simple	2	no	no	no	no	no	no	75
WC 21	37	f	simple	9	no	no	no	no	no	no	65
WC 27	34	m	simple	3	no	no	no	no	no	no	60
WC 28	44	f	simple	1	no	no	no	no	no	no	75
WC 31	40	f	simple	12	no	no	no	no	no	no	73
WC 06	22	f	complex	1	no	yes	yes	no	no	yes	50
WC 07	42	f	complex	27	no	no	no	no	yes	no	60
WC 08	27	f	complex	1	no	no	no	no	yes	yes	70
WC 09	50	f	complex	9	no	no	yes	no	yes	no	60
WC 03	30	m	complex	3	no	yes	no	yes	yes	no	25
WC 13	57	f	complex	7	yes	no	no	no	yes	yes	55
WC 14	39	f	complex	11	no	no	no	no	yes	yes	50
WC 18	57	m	complex	20	yes	yes	no	yes	yes	no	25
WC 20	25	f	complex	8	no	no	yes	no	no	no	50
WC 24	59	f	complex	12	yes	no	no	no	no	no	56
WC 29	43	f	complex	8	yes	yes	yes	no	yes	yes	55
WC 34	48	m	complex	20	no	yes	no	no	no	no	55
NG01	21	m	control								
NG03	53	m	control								
NG04	21	f	control								
NG05	39	m	control								
NG06	26	f	control								
NG07	28	f	control								
NG08	54	f	control								
NG09	57	f	control								
NG10	48	f	control								
NG11	58	f	control								
NG12	52	f	control								
NG13	44	f	control								
NG14	46	f	control								
NG16	43	f	control								

2.2. Tasks

Three fine-motor tasks were tested in the subjects. The writing task assessed the subjects' ability to write a simple sentence, in the box lifting task the subjects were required to grasp and lift a box with two different weights, and in the cyclic movement task a grasped object was continuously moved up and down. In four patients with Writer's Cramp (4 cWC) and in two controls data for cyclic movements were missing due to failure during data acquisition. The measurements and analyses concentrated on the grip forces used during task execution, but other variables of fine motor skill were also assessed. The order of presentation was always the same with hand writing first, box lifting second and cyclic movements third.

2.2.1 Writing task

In our former studies (Schneider et al., 2010; Hermsdörfer et al., 2011) we showed that writing a test sentence is a highly sensitive tool to investigate impairments of hand writing kinematics and force production in writer's cramp. Accordingly, subjects wrote the German sentence "Die Wellen schlagen hoch" (The waves are surging high) with their dominant hand on a blank sheet of paper that was fixed on top a digitizing tablet. They were instructed to write in their normal everyday writing style. Three trials were recorded and results were averaged across trials.

A digitizing tablet (Wacon IV, sampling rate 200 Hz, spatial resolution 0.05 mm) registered the position of the tip of the writing stylus. A pressure sensitive stylus was used that measured the pen tip force exerted onto the tablet (0 - 2.5 N, sampling rate 200 Hz; resolution 0.01 N). The positional data were transmitted to a personal computer and analysed with the software CSWin 2007 (MedCom, Munich, see Marquardt and Mai 1994). The movement trajectories and corresponding velocity curves were calculated and smoothed by nonparametric regression methods (Marquardt & Mai, 1994).

A force sensor matrix was wrapped around the pen (see Schneider et al., 2010 for details) to measure the force exerted by the fingers against the pen barrel during writing (Pliance-system, Novel, Munich). Eighty-eight force sensors were distributed across the whole surface of the pen with a spatial resolution of 5 x 10 mm . In an area of one square centimeter, forces between 0.5 and 20 N could be measured. Pen grip force was calculated by integration across the force distribution. The total error including hysteresis was less than 10%. The sampling rate of the whole matrix was 50 Hz. This technique allowed the registration of grip force for any individual grip type and without restricting the finger positions.

Following performance measures were determined and averaged across the three trials. (cf. (Schneider et al., 2010):

- *Grip force writing [N] (GF Writing):* integral grip force exerted by the fingers against the pen averaged across periods when the pen was in contact with the paper.

- *Writing frequency [Hz] (Freq. Writing):* average number of up and down strokes per second derived from segmentation of the writing trajectory. Measure of handwriting speed.

- *Duration [s]:* time needed to complete the sentence. Measure of handwriting speed.

2.2.2 Box lifting

Each subjects sat comfortably at a table. A plastic box (depth x width x height = 9 x 9 x 7 cm) with a vertical disk-like handle (diameter 7.5 cm, width 2 cm) mounted onto the box was placed on a platform in front of the trunk (see fig. 1). The subjects were instructed to grasp the handle following a verbal command with their dominant right hand, lift the box 5 cm above the table surface (height indicated by a fixed marker), maintain this position stationary for about 5 s, and then replace the box on the table. The lifting should be performed with a whole hand precision grip (thumb and all fingers in opposition) and at a normal speed. Execution was demonstrated and explained in advance.

Subjects performed altogether 16 lifting trials of two boxes with different weight (300 and 600 g, including the handle). Weights were adjusted by different contents inside the boxes which were visually indiscernible. Subjects always started with the heavy box and switched to the light box after eight trials. Subjects were distracted during the change of the box and were never aware about the change before lifting.

The handle incorporated a force sensor (model BKS, Rieger, Rheinmünster, Germany) that measured the force exerted by the fingers orthogonally against the handle surface (cover material was fine grain sandpaper). Grip force in the range of 0-100 N were measured with an accuracy of ± 0.2 N. The platform on which the box was placed incorporated a force sensor (model PW, HBM, Darmstadt, Germany, 0-100 N, accuracy ± 0.1N) that measured the weight of the object. Data were sampled with 100 Hz and stored in a PC. A custom-made computer program (GFWIN) was used to analyse the signals.

The following measures were determined for each lifting trial (cf. Hermsdörfer et al. 2003):

- *Peak grip force lift = Max. Grip force lift [N] (GF max Lift):* maximum grip force during lifting, typically occurring shortly after the object lifts off from the platform.

- *Static grip force [N] (GF static lift):* grip force during stationary holding the object determined as the average grip force in a 1 s interval starting 2.5 s after the lift-off of the object (weight signal becomes zero).

- *Lifting time [ms] (T lift):* interval between contact with the handle (grip force signal increases) and lift-off of the object.

The values were averaged across the 16 trials.

2.2.3 Cyclic movements

The subjects sat on a chair and held a manipulandum approximately 30 cm in front of the trunk with the grip surfaces vertical and approximately parallel to the trunk. The manipulandum was disc-shaped with a diameter of 9 cm, a width of 4 cm, and a mass of 372 g covered on both sides with fine grain sandpaper (see fig.1). The subjects used their dominant right hand with the thumb on one side of the manipulandum and the other four fingers on the other side. Upon a verbal command the object had to be repeatedly moved up and down along a vertical line without tilting. Movement amplitude was approximately 30 cm. Subjects were instructed to increase the frequencies in three steps during each of three trials. They had to produce a minimum of 10 cycles for the three different frequencies from slow to moderately fast with smooth changes between frequencies. One test trial was performed before registration started.

The manipulandum incorporated a force sensor that measured the grip force (0–80N, accuracy ± 0.1N) and three acceleration sensors that measured the acceleration in the three spatial dimensions (± 50m/s , accuracy ± 0.2m/s). From the acceleration data and the manipulandum's mass (m) the load acting tangential to the grip surface was determined as the vectorial summation of the load due to weight of the object (m∗G) and the acceleration-dependent inertial loads in the vertical and sagittal directions (m∗AccZ, m∗AccY). Thus LF was calculated as: $LF= m*((AccZ + G) + AccY)^{1/2}$ (see Hermsdörfer et al., 2003 for details).

In order to select epochs with comparable frequency for data analysis following strategy was applied: each trial was segmented into three epochs for each of the three frequencies without the transitions. Maxima and minima and the vertical accelerations of each movement cycle were determined and averaged. Only those epochs with average accelerations between 7.0 and 13.0 m/s were used for further analysis. Each subject contributed at least one epoch for data analysis.

Following measures were determined for each selected epoch and then averaged across the available epochs (cf Hermsdörfer et al. 2003):

- *Average grip force = Mean grip force cycl. [N] (GF mean Cycl.):* Grip force averaged across the epoch

- *Grip force/load force ratio cycl. (GF/LF cycl.):* Maximum grip force values derived from segmentation of the grip force curves related to momentary load values averaged across the epoch. The ratio was preferred to the absolute grip force peaks since it controls for interindividual differences in load due to different accelerations.

- *Cross-correlation coefficient cycl. (R-XCorr cycl.):* The maximum coefficient of the cross-correlation between the grip force and the load signal quantifies the precision of coupling between both forces.

- *Time lag cycl. (LAG-XCorr cycl.):* The time lag resulting from cross-correlation analysis indicates the temporal relationship between the grip force and the load signal.

2.3 Statistical analysis

Separate analyses of variance (ANOVAs) were performed for the various measures with the three levels factor subject group (healthy controls vs. simple Writer's Cramp vs. dystonic Writer´s Cramp) for each of the three tasks (writing, lifting and cycling movements). The level of significance was set at $p < 0.05$. Post-hoc pair-wise testing was performed using t-test with Bonferroni correction.

The relation of the performance in the different tasks was analysed with pair-wise correlations (Spearman correlation). In particular, grip force measures were compared between tasks for each subject group.

A particular statistical analysis was employed in the lifting task to investigate the subjects' ability to adapt to the new weight after the unexpected weight change. The force measures produced during the last trials with the heavy box (trial 8) and the following two trials with the light box (trial 9 and 10) were subjected to a repeated measure ANOVA with the within-subject factor trial (levels: trial no 8, 9, 10) and the between-subject factor group.

3. RESULTS

3.1 Individual examples

In Figure 1 the performance during one trial in each of the three tasks is displayed for a patient with writer's cramp (WC14, dystonic/complex group) and a control subject (NG12).

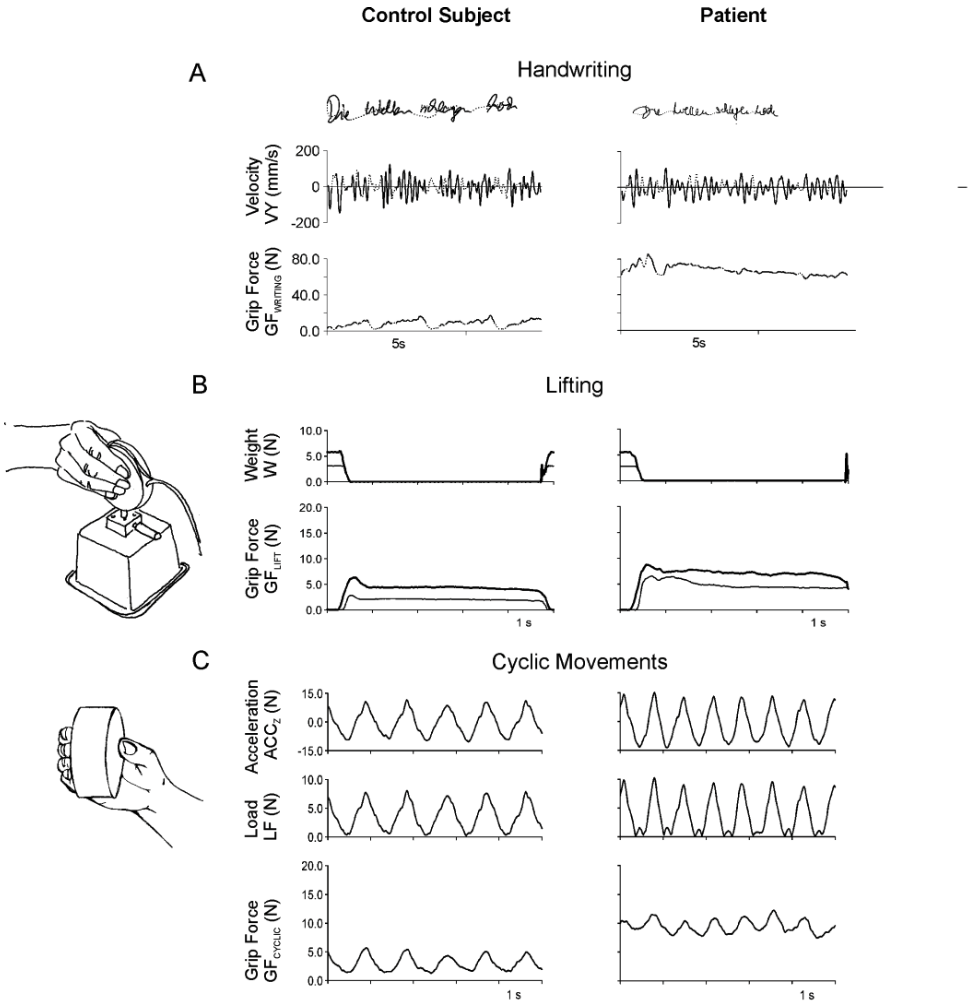

Fig. 1: Schematic drawings of the apparatus used for the lifiting and cyclic movement task and example profiles of characteristic task parameters in the three fine motor tasks tested in patients with writer's cramp and control subjects. Right: Patient with dystonic writer's cramp (WC14), left: control subject. A) Writing the test sentence: VY – vertical velocity, GF: grip force exerted against the pen. B) Grasping and lifting the test object: W, scale signal, GF: grip force, thick line: heavy weight, thin line: light weight. C) Cyclic movements of the instrumented object: ACC_Z – vertical object acceleration, LF: load force, GF: grip force. Figure 10: Schematic drawings of the apparatus and example profiles of the fine motor tasks

Fig. 1A shows the script and the corresponding time courses of the vertical velocity and the grip force during writing the test sentence “Die Wellen schlagen hoch”. In both subjects the script was legible. The velocity profiles of the control and the patient were both regular. The control subject needed less time to complete the sentence (Ctr: 7.7 s; Pat: 8.3 s). A massive difference was however obvious for the grip force. The patient produced grip forces that were nearly 6-times higher than the force produced by in the control subject (Ctr: 11.7 N; Pat: 67.8 N).

Fig. 1B illustrates the scale signal and the grip force for typical lifting trials of the heavy and the light box. Simultaneously with producing lifting force (reducing the scale signal) both subjects increased grip force. Grip force was higher for the heavier and lower for the light box with higher maximum values and higher static values in the patient.

Fig. 1C shows recordings of object acceleration, load force and grip force during vertical up- and down-movements. The patient moved with somewhat higher frequency and accelerations than the control subjects. Accordingly the load profile in the patients revealed small (negligible) upward load components at the upper turning points. In both subjects the grip force varied synchronously to the load with simultaneous peaks of grip and load force. The level of grip force modulation was higher in the patient than in the control subject.

3.2 Group effects

Table 2: Results of ANOVAs: Main results of the statistical analysis of characteristic task parameters: Means ± standard deviation for the three subject groups (Ctr: healthy control subject, sWC: simple WC, cWC: complex/dystonic WC); results of analyses of variance (ANOVA) with between-subject factor "group" (three levels: Ctr, sWC, cWC); results of post hoc pairwise testing with student's t-test (*: p < .0166 after Bonferroni correction).

	Ctr	sWC	cWC	ANOVA	Post hoc
Grip force writing [N] (GF writing)	15.39 ± 5.73	27.25 ± 15.58	27.47 ± 13.88	$F(2,32) = 4.3$; $p = 0.022$	Ctr < cWC: $p = 0.014$; Ctr > sWC: $p = 0.016$; sWC – cWC: $p > 0.1$
Frequency [Hz] (Freq. writing)	4.54 ± 0.63	3.87 ± 0.66	3.58 ± 1.22	$F(2,32) = 4.1$; $p = 0.027$	Ctr > cWC: $p = 0.016$; Ctr – sWC: $p = 0.023$; sWC – cWC: $p > 0.1$
Duration [s]	8.48 ± 1.47	10.74 ± 2.71	12.57 ± 3.80	$F(2,32) = 7.1$; $p = 0.003$	Ctr > cWC: $p = 0{,}002$; Ctr – sWC: $p > 0{,}1$ sWC – cWC: $p > 0.1$
Lifting					
Static grip force lift [N] (GF static lift)	6.0 ± 1.67	6.31 ± 1.98	6.88 ± 2.96	n.s. ($p = 0.61$)	–
Max. grip force lift [N] (GF max. lift)	7.72 ± 2.11	8.14 ± 2.04	8.45 ± 2.76	n.s. ($p = 0.73$)	–
Lifting time [ms] (T lift)	269.5 ± 82.9	277.5 ± 107.2	336.6 ± 132.2	n.s. ($p = 0.30$)	–
Vertically cycling					
Mean grip force cycl [N] (GF mean cycl.)	8.95 ± 3.86	9.96 ± 3.62	8.29 ± 3.64	n.s. ($p = 0.65$)	–
Grip force/load force ratio cycl (GF/LF cycl.)	1.36 ± 0.41	1.53 ± 0.51	1.29 ± 0.44	n.s. ($p = 0.53$)	–
Cross-correlation coefficient cycl (R-XCorr cycl.)	0.88 ± 0.08	0.85 ± 0.12	0.84 ± 0.06	n.s. ($p = 0.68$)	–
Time lag cycl. [s] (LAG-XCorr cycl.)	0.006 ± 0.016	−0.007 ± 0.015	−0.005 ± 0.008	n.s. ($p = 0.079$)	–

3.2.1 Writing task

Fig. 2A shows means and group variability of grip force and frequency during handwriting for the three subject groups. From the standard deviation of grip force it is obvious that the individual forces varied substantially in both patient groups. The corresponding ANOVA revealed a statistically significant main effect of group (F(2,32) = 4.3, p = 0.022). Post-hoc pair-wise comparisons (t-test) proved higher grip forces in both patient groups compared to control subjects and similar grip forces in the two patient groups (see table 2). Frequency of writing was decreased in patients compared to healthy controls (see fig. 2A). ANOVA revealed a statistically significant main effect of group (F(2;32) = 4.1, p = 0.027, see table 2) and pair-wise comparisons revealed group differences for the comparison of dystonic patients and controls, while the comparison of patients with sWC and control subjects did not pass Bonferroni correction (see table 2). Patients also needed more time to write the sentence (see table 2). As with frequency, ANOVA revealed a significant effect of group ($F(2,32) = 7.1$, $p = 0.003$, see table 2) and the post hoc tests indicated significant differences for the comparison of dystonic patients and healthy controls ($p = 0.002$), but not for the comparison of sWC patients and healthy controls ($p = 0.2$). The direct comparison of simple and dystonic/complex patients did not reveal any significant difference between the two patient groups (see table 2).

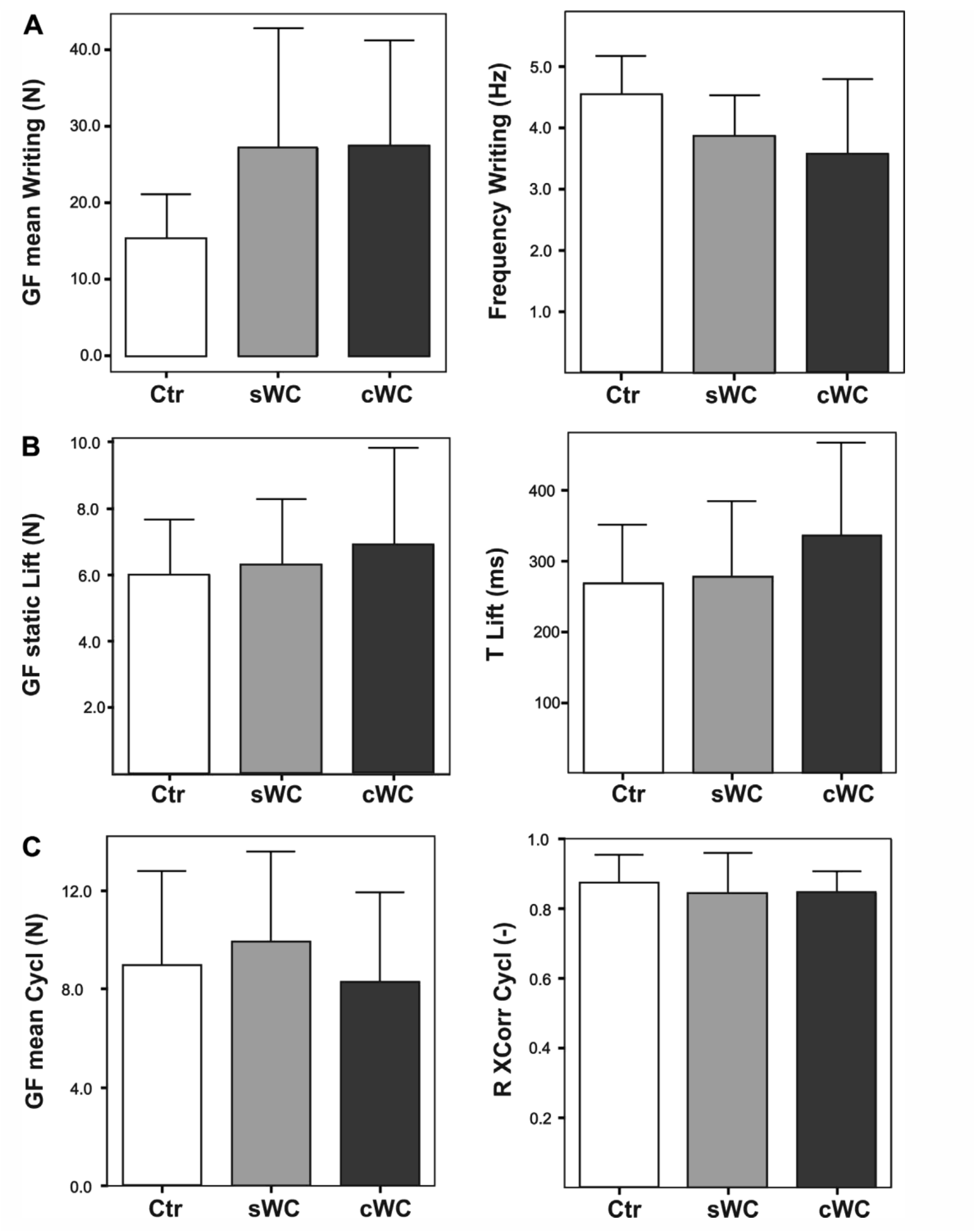

Fig. 2: Grip force parameters and temporal measures of different manual tasks. Grip force parameters and temporal measures for the three subject groups (Ctr: healthy control subject, sWC: simple WC, cWC: complex/dystonic WC) in the different manual tasks. Bars represent means and standard deviations. A) Grip force and writing frequency during hand writing. B) Static grip force and lifting time during object lifting. C) Mean grip force and coefficient of cross-correlation (GF/LF) for cyclic object movements

3.2.2 Lifting task

Fig. 2B shows the grand mean of grip forces during the static holding phase of the lifting trials and the time between object contact and lift-off for the three groups. Mean grip forces are higher and mean loading times are slightly prolonged in the group of patients with cWC, compared to group variability the effects seems small however. Accordingly, neither the ANOVA for the static grip force, nor the ANOVA for the loading time showed any effect of group (see table 2). Similarly, maximum grip force was slightly higher in patients than in controls but the difference did not reach statistical significance (see table 2).

Fig. 3 shows the grip forces across the 16 lifting trials with the unexpected change from the heavy to the light weight between trial 8 and 9. The maximum grip force that occurs in the initial phase of a lift (see fig. 1B) was lowered and adjusted to the lower weight in the second trial (no. 10) after the weight change. In contrast, the static grip force that was determined later during the lift (cf. Methods) was lowered already in the first trial with the lower weight (no. 9) indicating rapid adaptation to the new object conditions. Importantly, these time courses seem similar in the three subject groups. To confirm this observation statistically, an ANOVA with repeated measurement design was calculated for the trials just before and after the weight change (factor trial, levels: trial no. 8, 9, 10) and the factor group. This ANOVA revealed strong main effects of trial (GF max lift: $F(2,64) = 18.3$, $p < 0.001$; GF stat lift: $F(2,64) = 45.5$, $p < 0.001$) and no main effects of group (both $F(2,32) < 1$; $p > 0.1$). The interactions did not reach the level of statistical significance (GF max lift: $F(4,64) < 1$, $p > 0.1$; GF stat: $F(4,64) = 2.49$, $p = 0.052$).

Figure 3: Lifting trials

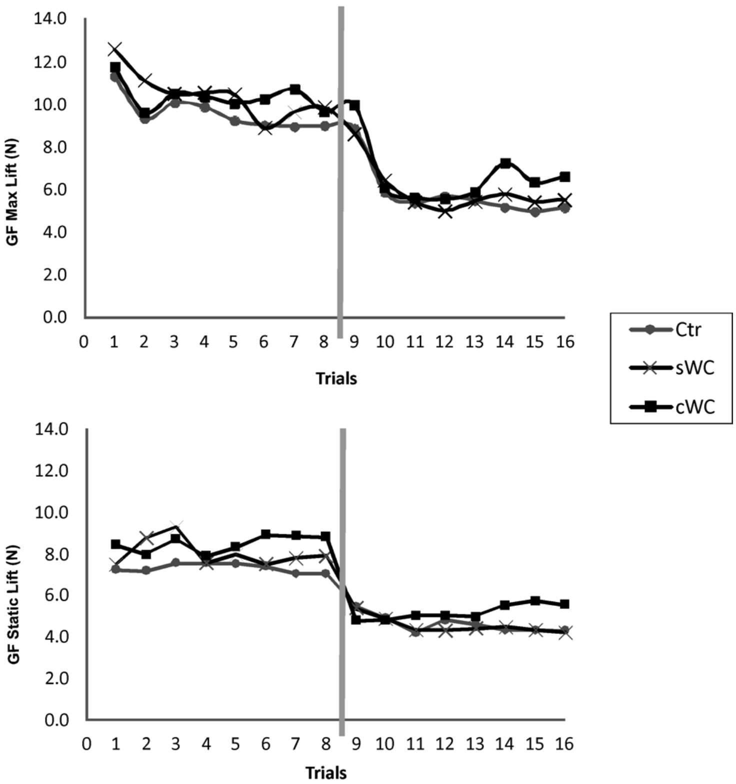

Fig. 3: Lifting trials. Profile of grip forces (GF max lift; GF static lift) across 16 lifting trials of two different boxes (300 and 600 mg, including the handle) for the three subject groups (Ctr: healthy control subject, sWC: simple WC, cWC: complex/dystonic WC). An unexpected change from the heavy to the light weight was done without awareness of subjects.

Legend: trial 1 to 8: light weight (300 g); trial 9-16: heavy weight (600 mg).

3.2.3 Cyclic movement task

The mean grip force produced to stabilise the manipulandum during the cyclic movements was comparable in the three subject groups, with sWC patients producing somewhat higher forces than cWC patients (see fig. 2C). ANOVA revealed no differences between groups (see table 2). Accordingly, the force ratios of grip and load force (GF/LF cycl.) did not reveal statistically significant differences, demonstrating that economic grip force production in relation to actual load requirements was preserved in patients (see table 2). The maximum coefficient cross-correlation (R-XCorr cycl.), a measure of precise coupling between grip force and load force, was similar in all subject groups (fig. 2C) and ANOVA revealed no significant difference among groups (see table 2). The time lag between grip and load force (LAG-XCorr cycl.) was in all groups near zero indicating that grip forces were modulated in close synchrony with the load forces and feed-forward mechanisms were preserved in patients.

3.3 Correlation between different forces

To detect functional linkage among finger force production in the different fine motor tasks we calculated the correlations between grip force variables in healthy controls and patients.

Fig. 4 gives an overview of correlations between grip forces in the three different tasks for the control subjects and the two patient groups combined. Healthy controls exhibited a clear positive correlation between the mean grip forces produced against the pen during handwriting (GF Writing) and the static grip forces during lifting an object (GF static lift) ($R = 0.59$; $p = 0.025$). Strong correlations were also found in control subjects between the static grip forces during lifting (GF static lift) and mean grip forces during cyclic object movements (GF mean cycl.) ($R = 0.79$; $p = 0.002$) as well as between max. grip force levels in lifting (GF max Lift) and cyclic movements (GF/LF cycl.) ($R = 0.64$; $p = 0.027$). Different from the other task-pairs, the correlation between the grip forces in handwriting (GF Writing) and grip forces during cyclic movements (GF mean cycl.) was less obvious in healthy controls ($R = 0.31$; $p = 0.33$).

In contrast to control subjects, none of the correlations between grip forces produced in the different tasks reached, or approached, the level of statistical significance in the combined patient group (see fig. 4, all $R < 0.33$, $p > 0.1$). Testing the correlations separately in both patient groups confirmed the results for the combined group (all $R < 0.33$, $p > 0.1$). It is obvious from fig. 4 that some patients with extraordinary high grip forces during handwriting produced forces in the two other tasks which were clearly in the range of control subjects. Some patients also produced relatively high grip forces during object lifting, however writing forces in these patients were not necessarily increased. Only few patients exhibited a generalised force increase across the tasks as suggested by the patient example shown in fig.1.

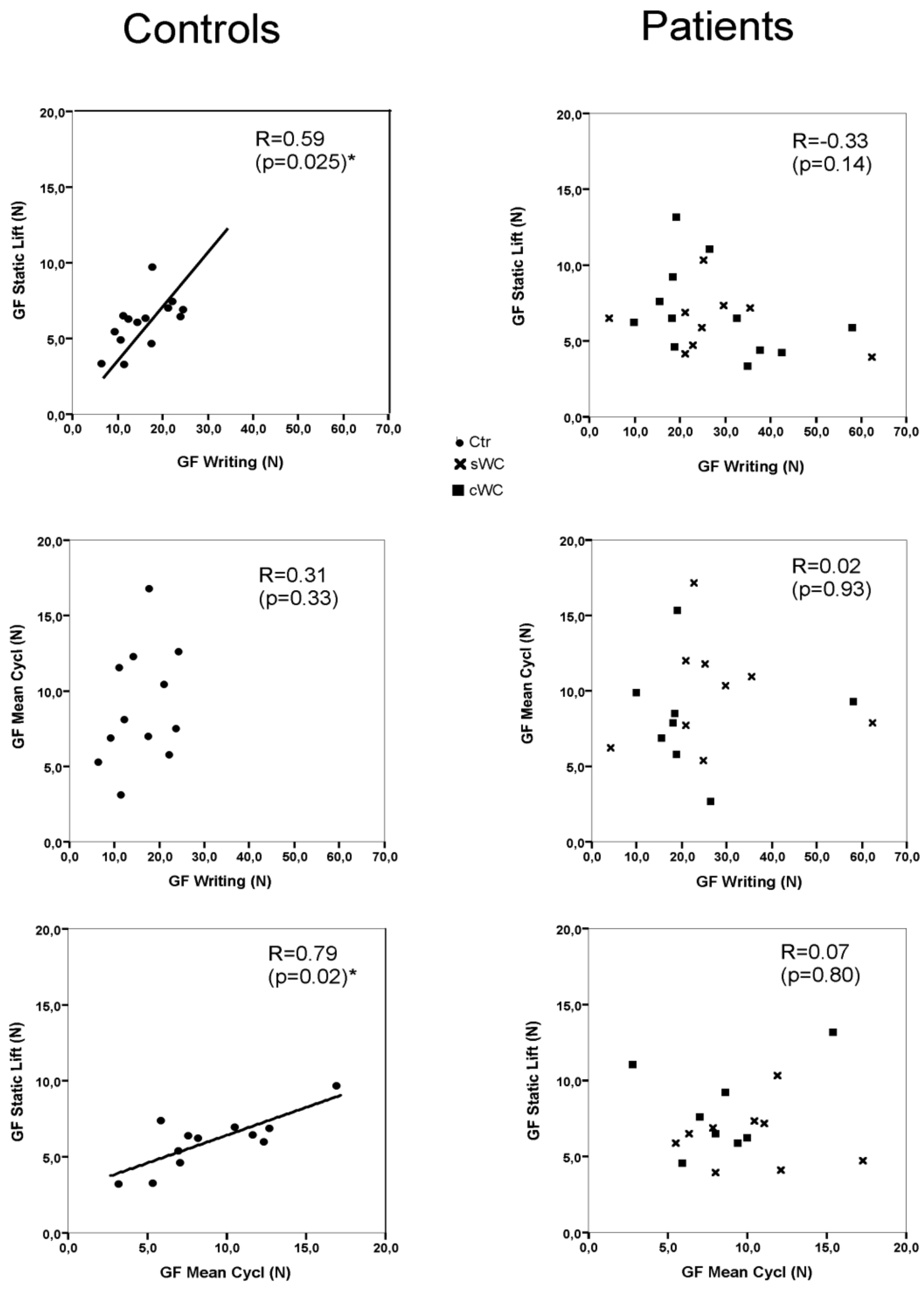

Fig. 4: Correlations between grip force parameters of the different tasks in healthy controls (left) and patients (right). A) Relationship between grip force during writing and static grip force during object lifting. B) Relationship between grip force during writing and mean grip force during cyclic movements. C) Relationship between static grip force during lifting and mean grip force during cyclic movements. Regression lines are displayed if the correlation was statistically significant.

4. Discussion

In this study we investigated grip force scaling and control among different manual tasks in WC patients and healthy controls. There are five main findings of this study. First of all, patients with writer´s cramp produced elevated grip forces during handwriting compared to healthy controls, but no group differences between patients and controls were found for box lifting and cyclic movements. Second, even patients that applied particularly high grip forces while writing the test sentence showed normal grip force levels in the other two manual tasks. Third, our results showed generalisation of grip force levels across tasks in healthy controls, whereas there was no such transfer in patients. Fourth, there was no difference in the application of grip forces between the two forms of writer´s cramp (sWC, cWC). Finally, aspects of fine motor performance during lifting and object movements, such as adaptation to a new weight or grip force/load force coupling, were preserved in patients.

4.1 Grip force levels

Our investigation was based on earlier studies on grip force control in WC patients in handwriting and lifting tasks, and was supplemented by a task with cyclic up and down movements. Our study is the first one to measure and directly compare grip force production during handwriting, lifting and cyclic movements, since previous studies (Serrien et al. 2000; Schenk & Mai, 2001; Nowak et al., 2005b; Odergren et al., 1996) were limited because they had no option to measure grip force during writing without hampering the writing process. In those studies, comparison of the grip forces in healthy subjects and patients was limited to a lifting (Schenk & Mai, 2001; Nowak et al., 2005b; Odergren et al., 1996), and a drawer manipulation task (Serrien et al., 2000), or axial pen pressure, and severity of handwriting deficit was compared with grip force values during object manipulation (Schenk & Mai, 2001). As expected, our findings for grip forces during handwriting revealed elevated forces of WC patients compared to healthy controls (Hermsdörfer et al., 2011; Schneider et al., 2010). Our results, however, contrast the findings of previous studies (Odergren et al., 1996; Schenk & Mai, 2001; Nowak et al., 2005a) which have reported abnormal grip force levels in patients during lifting. For example, Odergren et al. (1996) tested different lifting task in six patients with WC and found increased peak grip force levels in the static phase of lifting. Schenk et al. (2001) registered elevated values in 12 out of 22 patients, and Nowak et al. (2005b) measured increased forces in all of the 9 patients with focal hand dystonia (4 patients with WC and 5 patients with Musician´s Cramp) during lifting. In the view of these studies, and that involuntary muscle co-contractions and hyperactivity are the cardinal symptoms when patients attempt to write, the missing group effect for grip forces during non-writing tasks came as a surprise. One obvious reason may be characteristic differences in the patient samples. Apart from the study by Schenk et al. (2001), sample size was relatively small in previous studies, and the pathological conditions of these patients may have been more severe compared to the patients of the present study. In addition, variability of patients' forces within the present groups was relatively high so that small increases of the group means did not reach the level of statistical significance. It is, however, clear that no force deficit in the other tasks comparable to that during hand writing was found in our relatively large patient sample.

One reason for the discrepancy between the patients' performance during hand writing and object manipulation may be that controlling grip force during writing is a more complex task than controlling finger forces during lifting and moving an object. Only very complex tasks may challenge the underlying neural processes to such an extent that the dysfunction is visible (see for example Havrankova et al., 2012). Indeed, hand writing requests extensive and very precise coordination of various finger and hand joints. However, also grip force control requires refined coordination as demonstrated in many studies. EMG recordings show for example that nearly all muscles of the hand act in a coordinated manner (Maier and Hepp-Reymond, 1995 a,b). In addition, skilled control of grip forces requires a long process during development (Forssberg et al., 1991, 1992). In our own work we have demonstrated deficits of grip force control in many neurological conditions (Nowak & Hermsdörfer,2005; Hermsdörfer et al., 2003). Nevertheless, a particular complexity of hand writing cannot be excluded. It would be interesting to study other manual tasks that require extensive fine motor control using quantitative methods, such as activities during grooming or professional work.

Healthy control subjects generalised grip forces across the different tasks (i.e. grip forces during writing and lifting as well as grip forces during lifting and cyclic movements) showed significant correlations. Thus, a person that uses relative low grip forces during hand writing tends to use relatively low forces for box lifting, and the later feature is typically coupled with relatively low forces during cyclic movements. The coefficient of the correlation between grip forces during writing and cyclic object movement was also positive, suggesting an association between the forces. However, contrary to our expectations, this correlation failed to reach statistical significance. It therefore seems that in terms of grip force control the cyclic movements with a relatively heavy object differ from the movements of a light pen, when loads mainly result from the movements of the pen on the paper. The stationary holding task seems intermediate with respect to force control. This interpretation is, however, speculative and invites further investigation.

In contrast to the control subjects, patients showed no functional linkage between grip forces in the three different manual hand tasks. Even patients that applied greatly increased grip forces while writing the test sentence showed normal values in the other two manual tasks. Some patients behaved in a more consistent fashion observed in previous studies (Odergren et al., 1996; Schenk & Mai, 2001; Nowak et al., 2005a) producing exaggerated forces during the non-writing tasks, but these patients did not necessarily exert high forces during writing. Interestingly, also Schenk et al. (2001) could not find a correlation between elevated grip forces during lifting and the pen tip pressure during writing. Since pen tip pressure is not necessarily related to the grip force (Hermsdörfer et al., 2011), this observation can however not directly be related to the present findings.

Patients with Writer's Cramp neither generalised increased grip force levels during handwriting nor individual force preferences across different tasks. The later phenomenon may actually be not related to handwriting since the correlation was also absent between the two object manipulation tasks. This finding, therefore, could be taken as an indicator of a more general deficit to generalise force control across different manual fine motor tasks. Since, however, control subjects also did not consistently exhibit strong correlations between the investigated tasks, the later notion has to be considered with care. The finding may nevertheless be indicative of more subtle deficits in the patients that also may be reflected by the patients` self-reported impairments in non-writing tasks within the dystonic group.

4.2 Group differentiation

Post-hoc pair-wise tests did not reveal any statistically significant differences in the grip forces in all three manual tasks between subgroups of WC as defined by Sheehy and Marsden (1982). We therefore replicate the findings of Schneider et al. (Schneider et al., 2010) who reported similar force deficits of simple and dystonic/complex WC patients during writing, as well as Jedynak et al. (2001) who reported similar writing deficits in both patient groups. The WC patients of former studies who produced exaggerated forces during lifting (Odergren et al., 1996; Serrien et al., 2000; Schenk & Mai, 2001; Nowak et al., 2005b) may have been in more advanced stages of the disease, or there may exist differences in etiology that are not yet established. Similarly to absent differences in the grip force level, the missing correlation of force levels between tasks-pairs was also evident in both patient groups. Differences between the simple and the dystonic/complex form of writer's cramp were, therefore, not reflected by characteristics of force control.

4.3 Underlying pathological mechanism

Grasping with application of grip forces and lift force are based on a complex system of interaction between sensory feedback and muscle activity of hand and arm (Nowak, 2008; Johansson & Westling, 1984, 1988). It has been stated that inefficient grip force scaling in movement disorders is due to deficits in sensory feedback mechanism and inadequate force scaling relies on abnormalities in temporal-spatial processing in patients (Abbruzzese & Berardelli, 2003). It might therefore be considered surprising that the regulation of grip force level in non-writing tasks is preserved in WC patients, and no deficits were evident in manipulative control while lifting and moving a hand-held object. The question arises what underlying pathological mechanisms account for the deficits in handwriting, but do not cause deficits in other object manipulation tasks.

Although it has been demonstrated that sensory deficits can be particularly detrimental in grip force control (Johansson & Westling 1984, 1991), applied grip force level is under voluntary control and therefore depending on expectations and pre-learned motor strategies (Gordon et al., 1991). Excessive forces in WC patients in writing tasks could, therefore, be considered as the consequence, rather than, the cause of WC. This assumption is consistent with the findings of Odergren et al. (1996) who observed that a period of handwriting induced an increase in grip force in WC patients. Similarly, a short training session to ameliorate exaggerated force production in patients with writer's cramp normalised the grip forces used for lifting (Schenk & Mai, 2001). In agreement with our findings former studies did not find a correlation between severity of handwriting deficits and the amount of grip force elevation (Schenk & Mai, 2001; Nowak et al., 2005b). The present findings, therefore do not support the notion that disturbed sensorimotor processing is the cause of disturbed force regulation in patients with writer's cramp (Serrien et al., 2000; Odergren et al., 1996), but rather emphasize task-dependency.

In addition to normal force levels other aspects of fine motor performance were also preserved in the two non-writing fine motor tasks of the present study. Grip forces in both healthy subjects and patients varied synchronically with load forces that were self-generated by object movements. Grip and load forces are produced by different muscle synergies, and synchronicity suggests preserved feed-forward-control mechanisms (Flanagan & Tresilian, 1994; Wolpert & Flanagan, 2001; Hermsdörfer et al., 2004). Further, sensorimotor integration of grip and load forces according to weight changes was as efficient in patients as in healthy controls. This was shown by the fast adaption of grip forces to weight changes from heavy to light, that was indiscernible in patients from control subjects.

These findings add to former demonstrations of preserved capacities in basic aspects of sensorimotor control reported in previous studies of object manipulation in patients with WC (Schenk & Mai, 2001; Nowak et al., 2005a; Hermsdörfer et al., 2011). Clinical and experimental findings therefore suggest that impairment in focal dystonia pertains to an abnormality of specific motor programs and are often highly contextual and task-dependent (Abbruzzese & Berardelli, 2003).

5. Conclusion

Exaggerated grip force levels in handwriting combined with normal values in the other two fine motor tasks in our sample of patients with writer's cramp suggest a task-specific phenomena and do not support the idea of a primary deficit in sensorimotor control (Mai and Marquardt C. 1994; Nowak and Hermsdörfer 2005). The characteristics of force control in different manual tasks seem to be independent and may vary from patient to patient (Hermsdörfer et al., 2011). These findings show that the behavioral characteristics of writer´s cramp are highly task-specific, possibly due to highly individualised ways to cope with the impairment of handwriting.

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4. Discussion

The main findings of this thesis and the included three studies can be summarized as follows: Patients with Writer´s Cramp showed elevated grip force and pen tip forces as well as reduced automation and writing frequency during handwriting compared to healthy controls measured by a digitizing tablet and a pressure-sensitive matrix wrapped around the writing stylus. Investigations of two other fine motor tasks (lifting of an object and cyclic vertical movements) compared with effects in handwriting showed no group differences between controls and patients for the fine motor tasks despite elevated force levels and reduced kinematic measures during handwriting.

Further the parameter grip force during hand writing turned out to be a sensitive and valid measure for the major symptom of co-contractions in WC. Neither a general aggravation was seen for dystonic/complex WC patients compared to the group of simple WC patients nor for increased complexity of writing material ranging from "o"-like circles over writing a test sentence to copying a longer text nor a generalisation of symptoms from handwriting to other fine motor tasks in patients.

4.1 Group differentiation (simple vs. dystonic/complex)

In general we did not find significant differences in neither investigated kinematic nor kinetic parameters for all investigated fine motor tasks (handwriting, lifting and cyclic arm movements) between simple and dystonic/complex WC patients (1st and 3rd study). However, there were some indirect hints for a difference of the two subgroups as the parameter grip force was elevated during writing and both writing frequency and writing duration were reduced in the group of dystonic/complex WC patients compared to control whereas there was no such distinction between simple WC patients and healthy control (1st and 3rd study). Further we found a reduced automation (NIV) in simple WC patients when compared to controls but not in comparison of dystonic/complex Writer´s Cramp and controls.

As we could not find any significant differences between both patient groups we were able to confirm the results of Jedynak et al. (Jedynak et al., 2001) who found similar legibility and deficits in handwriting for simple and dystonic patients. Further generally we have to decline the findings of DAS et al. (2007) and Schenk & Mai (Schenk & Mai, 2001) that found differences in handwriting performance, longer disease duration and a higher severity score. An explanation for that divergence is that case and symptom history was mainly based on self reports hence subtype classification could not be considered as secure. Further we did not take a third subtype called progressive WC into account. This subtype is defined as initially only having problems during handwriting, like simple WC, and later these patients develop difficulties in other fine motor tasks, like dystonic/complex WC (Sheehy & Marsden, 1982). Hence another explanation for the missing group differences between simple and dystonic patients could be that our so-called group of dystonic patients consisted of progressive and dystonic patients (1st study).

4.2 Task specifity

All WC patients showed abnormal handwriting performance independent of complexity of writing material (ranging from “o”-like circles over writing a sentence to copying a longer text). It seemed that different demands of writing material did not deteriorate the performance of writing and outcome of investigated parameters.

Conclusively as patients did show similar impairments in all handwriting sets and neither length nor semantic content nor spatio-temporal did influence handwriting in patients, deficits seem to be related to elementary script production independent of content (3rd study). Our results contrast the findings of Zeuner et al. (2007) who reported a dependency on task complexity in handwriting comparing drawing of superimposed circles with writing of a test sentence with worse performance while writing the sentence. An explanation for this discrepancy could be that as this has been an experiment to test training purposes and instructions have been made before writing of the test sentence concerning speed and writing style (everyday writing style and speed). Conclusively this may have influenced the results as script production normally is done spontaneously (1st study). Hence instructions made during handwriting for training purposes of Writer´s Cramp can induce performance alterations of handwriting tasks (Baur et al., 2006; Mai & Marquardt C., 1994; Zeuner et al., 2002, 2005, 2007).

Our investigations of task specificity showed no statistically significant differences in investigated kinetic parameters, especially the application of grip forces by comparing handwriting, lifting and cyclic arm movements of WC patients and healthy controls (3rd study). Further healthy controls generalised grip force levels during different tasks. In this perspective as patients only used exaggerated forces during handwriting the usage seems to be highly task specific as grip force application during lifting and cyclic movements were at the same force level with healthy controls. Our findings are an essential contribution to the genesis of writer´s cramp with the question of specificity but they challenge the findings of previous works (Odergren et al., 1996; Schenk & Mai, 2001; Nowak et al., 2005) and our own hypotheses as muscle co-contractions and hyperactivity are the cardinal symptoms of WC. The above noted studies reported abnormal and elevated grip force levels in patients during lifting. One reason for the discrepancy to our study could be that our patients showed a relatively high variability of grip forces during lifting and moving objects. Therefore small increments of group means did not show a significant difference.

Another reason could be that grip force control during handwriting may be more complex than control during lifting and cyclic movements. An alteration of neural processes may not be initiated until more complex tasks are executed (Havránková et al., 2012; 3rd study)

4.3 Pathophysiology

As the pathophysiology of Writer´s Cramp still remains unclear (see background section) our scientific work contributes to and somehow can challenge the view. The important underlying question is to know which mechanism accounts for handwriting deficits but does not affect other object manipulation tasks.

Precise grip force control while grasping and lifting is based on complex interactions between sensory feedback and coordination of hand and arm muscles (Nowak, 2008; Johansson & Westling, 1984, 1988; 3rd study).

One hypothesis for the underlying pathophysiological mechanism **is abnormalities in sensory feedback mechanism,** and inadequate application of forces seems to be due to deficits in temporal-spatial processes during movements (Abbruzzese & Berardelli 2003; Macefield et al., 1996). For example Murase et al. (2000) showed abnormalities in sensory gating before onset of movement by investigating gating of SEP (Somatosensory Evoked Potentials). Two other studies (Odergren et al. 1996; Serrien et al. 2000) concluded on the basis of their results that grip force deficits during their experiment may be due to inadequate sensorimotor processing.

Odergren et al. (1996) performed four different lifting tasks and their results indicated an impaired capacity to integrate sensory information in motor programming and force regulation despite a normal sensibility. Their interpretations were either a general deficit in sensorimotor integration or grip force deficit may have been the consequence as a period of handwriting induced an increase in grip force in WC patients. Serrien et al. (2000) used a drawer-opening task and applied load and vibratory disturbances to investigate grip force control. WC patients showed increased grip forces compared to healthy subjects and stronger modulations of grip force in the symptomatic hand and therefore concluded a deficit in sensorimotor integration.

However, our own results do not support the idea of inadequate sensorimotor processing being the cause of inadequate force regulation in WC. In fact we agree with the findings of Schenk and Mai (2001) and Nowak et al. (2005) that did not find a linkage between severity of handwriting deficits and applied grip force levels and showed that short training sessions of lifting trials restored normal grip force levels. Further it has to be noted that former studies proved that not all grip force deficits rely on failures in the sensorimotor system as grip force control possibly is under voluntary control (Johansson und Westling, 1984, 1991; Gordon et al., 1991).

The second hypothesis explaining a pathological mechanism is **loss of cortical inhibition / exaggerated cortical inhibition** which can be to some extend responsible for muscle co-contractions and voluntary movements in dystonia due to a failure of surround inhibition which is a consequence of loss in inhibition (Ibáñez et al., 1999; Hallett 2006, 2011).

Surround inhibition describes a mechanism that suppresses excitability around an area of an activated neural network (Beck, 2008; Cohen & Hallett, 1988) and if this mechanism is decreased it is likely to induce overflow of activity in muscles not intended in the task resulting in excessive movement and co-contractions (Hallett, 2011, 2004). Further surround inhibition which is a neural mechanism to improve contrasts between signals may be involved in movement initiation in the primary motor cortex (Beck et al., 2008, Hallett, 2011).

Loss of inhibition seems to play a role in skilled finger movements like writing or playing an instrument whereby fine tuning at low force levels plays an important role (Beck et al., 2009). Further Beck et al. (2010) demonstrated that the mechanism of surround inhibition might be influenced by task complexity. As writing or playing a musical instrument represent extremely skilled and complex movements in comparison to manual tasks as lifting and cyclic movements this mechanism may be a concept to explain our findings (Zeuner &Volkmann, 2013).

The third suggested underlying mechanism is an **abnormal plasticity of the sensorimotor cortex by over-use** (Quartarone et al. 2003; Quartarone et al. 2005; Blake et al. 2002; Byl et al. 1996). Our clinical findings matched such a mechanism as our patients only showed worse performance during handwriting and not while performing the other two manual tasks that were completely new to them and which patients haden´t practiced in a repetitive manner.

The same is true for the suggested mechanism of Mai and colleagues (Mai & Marquardt, 1994; Mai, 1995). In our perspective Writer´s Cramp and grip force elevation during handwriting could be indeed a vicious circle with an initial perturbation of an unknown cause followed by compensative strategies and inadequate motor learning processes.

4.4 Conclusion

Kinematic and force parameters seem to be useful tools for the diagnosis of WC patients. As there were no differences for analysing purposes by using varying text material the test sentence 'Die Wellen schlagen hoch' (Engl.: 'The waves are surging high') seems to be an appropriate and sensitive tool. Moreover instructions can be kept simple and the interference level is lower than for the other tested writing tasks.

Subtypes in WC, simple versus dystonic/complex WC, did not show a different amount of detriment in kinetic and kinematic parameters both during handwriting and the two other fine motor tasks (lifting and cyclic movements). Our results did not confirm that neither dystonic/complex WC is an aggravated form of simple WC nor that there is a hint for a unitary progression or spreading process from simple to dystonic/complex WC. These two subtypes seem to be independent of pathogenesis. But we see no need to abandon the classification as it is very important for therapeutic strategies.

Impairments in grip forces during handwriting associated with normal grip force levels in the other two fine motor tasks in our investigated patient sample indicate that WC seems to be task-specific. Grip force control seems to have individual control mechanisms.

Moreover the pathological profile of writer´s cramp seems to be highly individual.

Further our findings do not support the idea of a primary deficit in sensorimotor control. Other pathophysiological substrates could not be assessed conclusively with our study design.

Ongoing studies should be designed to test other pathophysiological mechanisms with similar designs or tasks. In addition more complex tasks as the tested ones should be used to find out if task specificity depends on complexity.

5 Appendix

5.1 References

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5.2 Table of figures

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Eidesstattliche Versicherung

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Ich erkläre hiermit an Eides statt,

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