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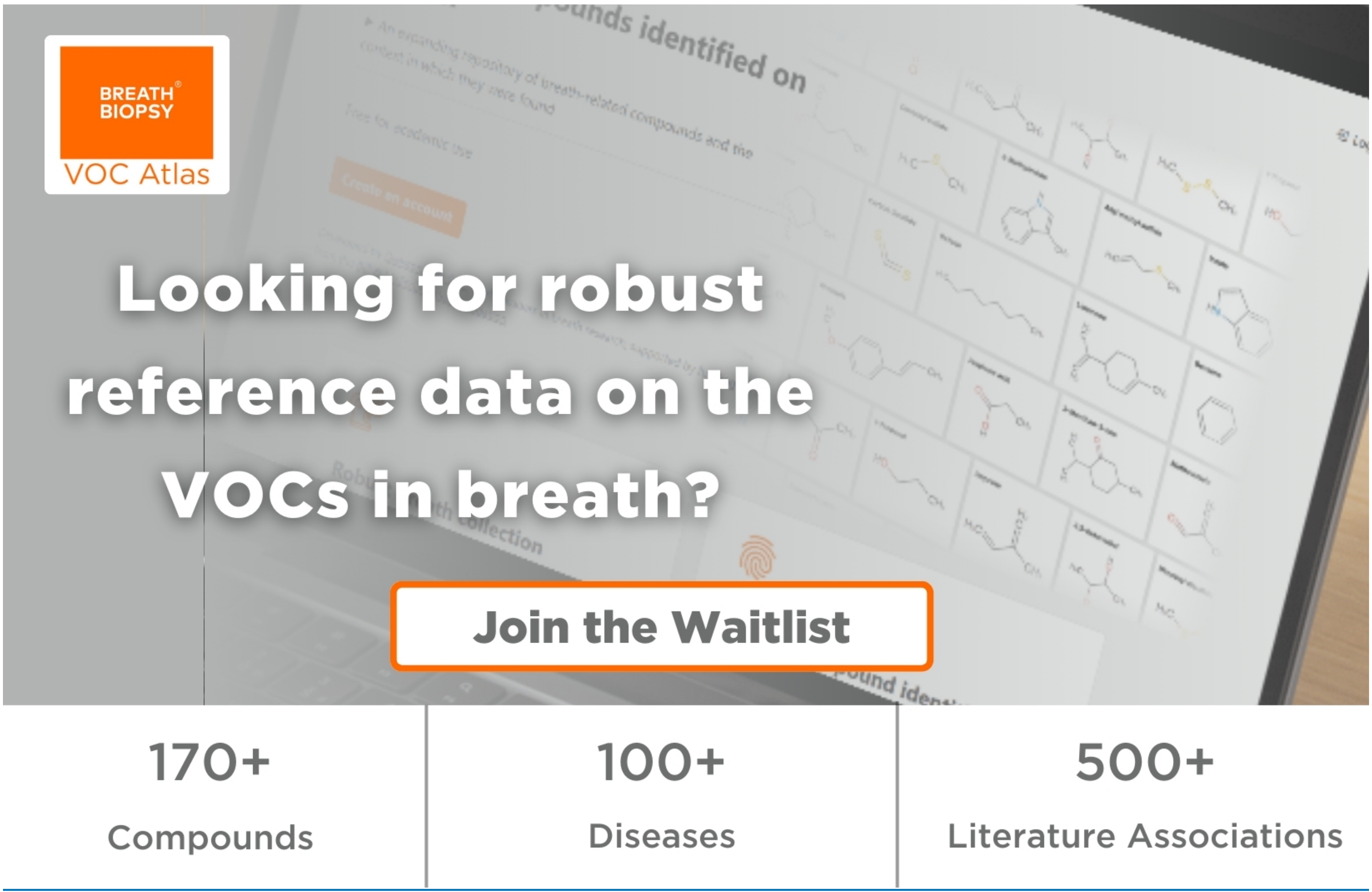

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Evaluation of a wearable orthosis and an associated algorithm for tremor suppression

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Abstract

We describe a wearable orthosis and an associated algorithm for the simultaneous assessment and treatment of essential tremor, one of the most common movement disorders in humans involving an overactivity of the olivo-cerebellar pathways. A motor providing effective viscosity is fixed on a wearable orthosis in the upper limbs. The motor is controlled by a personal computer with software processing in real time the position and rate of rotation of the joint detected by a chip gyroscope. The orthosis can be used in a monitoring mode and in an active mode. The range of tremor suppression of the signals above the orthosis operational limit ranges from about 3% (percentile 5) to about 79% (percentile 95) in relation to energy in the monitoring mode. Considering both postural and kinetic, the mean tremor energy decreased from 55.49 ± 22.93 rad^2 s^{-3} in the monitoring mode to 15.66 ± 7.29 rad^2 s^{-3} in the active mode. Medians of power reduction were below 60% for the wrist and the elbow. In addition to supplying new information on the interactions between kinematics, dynamics and tremor genesis, this non-invasive technique is an alternative to current therapies. This new approach will provide new insights into the understanding of motor control.

Keywords: essential tremor, cerebellum, human, robotics, viscosity, orthosis

(Some figures in this article are in colour only in the electronic version)

Introduction

Tremor is defined as a rhythmic oscillatory activity of body parts (Findley and Koller 1995). The oscillatory activities are related to various combinations of four basic mechanisms: (a) mechanically induced oscillations, (b) oscillations due to reflexes, (c) oscillations generated by neuronal generators in the central nervous system, (d) oscillations resulting from impaired feedforward and feedback loops (Deuschl *et al* 2001).

Essential tremor (ET) is a bilateral postural tremor involving mainly the upper limbs (Findley and Koller 1995). A kinetic tremor is often observed in association with the postural oscillations, and a head tremor can also be noticed (Leegwater-Kim *et al* 2006). Some patients develop a rest tremor, with electrophysiological features consistent with mild Parkinsonism (Cohen *et al* 2003). Tremor amplitude tends to increase and progresses more medially (from distal to proximal joints) over time, while tremor frequency tends to be inversely related to age (Rajput *et al* 2004). More than 90% of patients who come for medical attention report disability (Louis 2005a). ET affects approximately 4% of the population above 65 years of age, representing the most common movement disorder in the elderly (Benito-Leon *et al* 2003, Louis *et al* 2005b, Thanvi *et al* 2006).

Neuronal networks in posterior fossa are incriminated in the generation of ET. Animal models of ET and functional studies in patients indicate that an abnormal olivo-cerebellar activity could cause an enhanced oscillatory activity in the cerebellum and its targets, especially thalamic nuclei (Jenkins *et al* 1993). However, recordings of neurons in human have provided conflicting results with the hypothesis of continuous olivo-cerebellar driving of the motor cortex via thalamic connections (Hua and Lenz 2005). ET might result from networks enabling tremor-related activity during voluntary movement and by increased access to sensory feedback. A pathological coupling between sensory inputs and motor output could, in theory, participate in the genesis of ET (Gibson *et al* 2004, Manzoni 2005). The clinical similarities between symptoms of ET and the symptoms in classical cerebellar disorders are noticeable (Findley and Koller 1995, Glickstein *et al* 2005, Manto 2005). The beneficial effect of ethanol reported in ET could be due to an effect on inferior olive or an effect on alcohol-sensitive GABA receptors within the cerebellum (Manto *et al* 2005).

Current strategies in the treatment of ET are based on drugs (mainly the front-line agents primidone and propranolol), and surgery (thalamotomy and deep brain stimulation) in those patients being refractory to drugs (Louis 2005a, Ushe *et al* 2004). Gamma knife thalamotomy could represent an option for difficult cases (Niranjan *et al* 2000, Young *et al* 2000). However, (a) ET is not managed effectively or sufficiently in about 25% of patients, (b) the drugs used often induce side effects, may be contra-indicated or do present potential side effects or contra-indications which make their use more difficult and (c) surgery is associated with a risk of haemorrhage and psychiatric manifestations (Binder *et al* 2003). In particular, a high rate of suicide (4.3%) has been recently found in patients treated with deep brain stimulation (Burkhard *et al* 2004). Therefore, further research and new therapeutic options are required to manage ET most effectively.

We designed a new tool which allows not only the experimental online assessment of ET under various viscosity conditions in order to characterize the role of neuronal networks in tremor genesis, but also its direct cancellation. This pathophysiological and therapeutic tool involves a robotic wearable device called wearable orthosis for tremor assessment and suppression (WOTAS), which acts in parallel to the affected limb and is able to apply damping or inertial load to a selected set of limb articulations. We assessed this new technique in patients exhibiting ET.

Materials and methods

The effects of load and force on tremor have received considerable attention by the research community. Amongst others, Adelstein (1981) has conducted a thorough analysis of the effect of viscous loading as a means for active reduction of intention tremor. As a result, Adelstein

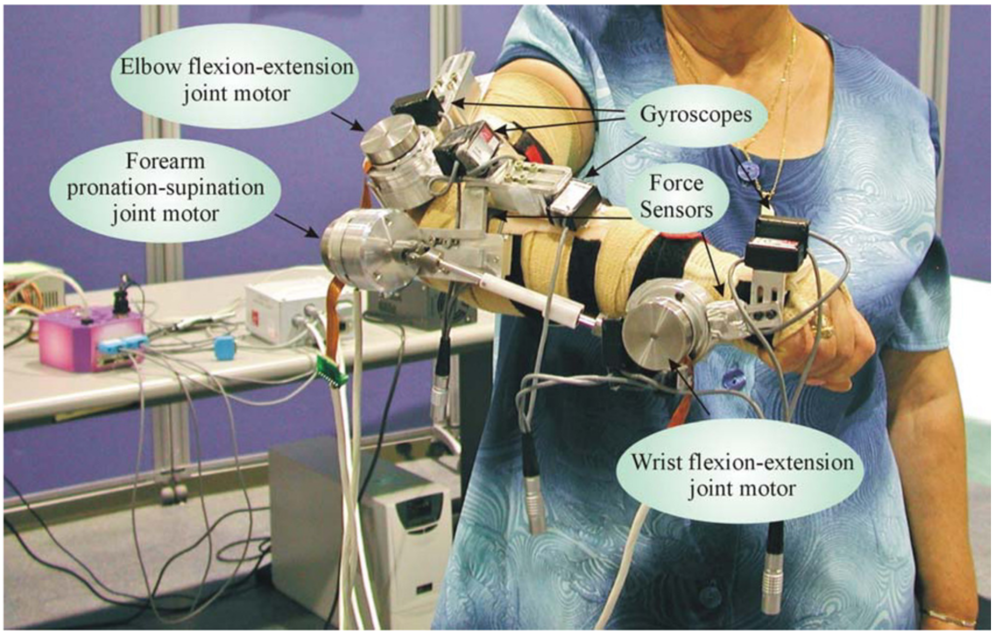

Figure 1. Patient using the WOTAS orthosis affixed on the right upper limb. This robotic device spans the elbow and wrist joints, being able to apply independent tremor suppression strategies to elbow flexo-extension, wrist flexo-extension and wrist prono-supination.

reports that significant and steady reductions of tremor amplitude are observed as the viscous loading increases. This phenomenon gives rise to the possibility of an orthotic management of tremor. An orthosis is defined as a medical device that acts in parallel to a segment of the body in order to compensate some dysfunction. In the case of tremor management, the orthosis must apply a damping or inertial load to a selected set of limb articulations. As a wearable device, it must exhibit a number of aesthetics, cosmetic as well as functional characteristics. Aesthetics and cosmetics are more directly related to size, weight and appearance of the orthosis. Functionality is more related to the trade-off required in terms of required torque and velocity and to the robustness of operation.

Description of the technique

An active orthosis (exoskeleton), able to apply effective viscosity or inertia, is attached to the upper limb of the patient (figure 1). This active orthosis is designed according to the shape and function of the human upper limb; segments and joints correspond to some extent to those of the human body while the system is externally coupled to the person. The exoskeleton developed activates the elbow and wrist joints, being able to measure and apply forces on three movements of the upper limb: elbow flexion–extension, forearm pronation–supination and wrist flexion–extension. The exoskeleton is activated by a set of rotary flat dc motors (EC 45 Flat Brushless DC motor, Maxon Inc.) and harmonic pancake transmissions (Rocon *et al* 2005). This solution was selected on the basis of a comparison of available technology for actuation and represents a compact and light solution suitable for wearable devices.

The mechanical design of the exoskeleton elbow joint is based on a hinge joint with the axis of rotation placed in the line between the two epycondyles. The actuator solution adopted is attached to the structure with its rotary axis aligned with the elbow joint of the exoskeleton. The wrist joint adopted the same solution, but with the axis of rotation placed in the line between the capitate and lunate bones of the carpus. The solution developed for the control of pronation-supination movement is novel and based on controlling the rotation of a bar placed parallel to the forearm, see figure 1. The total weight of the final system is roughly 850 g.

The active orthosis aims to allow both monitoring of upper limb movements and implementation of tremor suppression strategies. Therefore, it is equipped with kinematics (angular velocity) and kinetic (interaction force between limb and orthosis) sensors. The rate of rotation of each activated joint is detected by a sensor system based on a combination of two independent chip gyroscopes (ENC-03J manufactured by Murata Inc.), placed distally and proximally to each activated joint. The angular position and acceleration information are obtained through mathematical operations. The interaction force between the exoskeleton and the user is measured by a force sensor based on strain gauges (Rocon *et al* 2005).

Another important aspect of the design of active orthosis that will apply dynamic force between segments of the human limbs is the transmission of forces through the soft tissues to the human skeleton. In order to minimize this difficulty, the orthosis is adaptable to each configuration of the joint between different patients owing to the use of thermoplastics, see figure 1. In addition, a textile substrate was used to compress the soft tissues and enhance the performance of the fixation supports.

The active orthosis is controlled by a computer with a dedicated software application that implements an algorithm to be able to distinguish in real time tremorous from voluntary movement and to calculate the force applied by the active orthosis over the upper limb in order to change its biomechanical characteristics and, consequently, suppress tremor. In summary, the control system works as follow:

(1) the sensors coupled to the limb measure its motion,
(2) an error cancelling algorithm performs a real-time discrimination of the undesired component of motion,
(3) tremor information is sent as the input to the controller in order to generate the desired exoskeleton performance to suppress the tremor (see figure 2(a)).

In this approach, the musculo-skeletal system (each upper-limb joint contributing to tremor) is modelled as a second-order biomechanical system exhibiting a low-pass filtering behaviour. The cut-off frequency of this second-order system is directly related to the biomechanical parameters of the second-order system, i.e. inertia, damping and stiffness. Our approach consists in selecting the appropriate modified values of inertia and damping of the musculo-skeletal system, so that the cut-off frequency lies immediately above the maximum frequency of the voluntary motion and well below the tremor frequency, see figure 2(b).

For a successful active tremor absorption mechanism, a means for intelligent detection of tremor versus voluntary motion is required. To this end, a model of the tremor motion is proposed. The algorithm developed is based on a two-stage method that estimates voluntary and tremorous motion with a small phase lag (Rocon *et al* 2005). It is well known that the frequency of the voluntary motion of activities of daily living, ADL, occurs at frequencies lower than the tremorous movements (Riviere 1995). Based on this statement in the first stage of the algorithm, the voluntary motion is estimated using a Benedict–Bordner filter tuned to estimate low frequency movements. In the second stage, the estimated voluntary motion is removed from the overall motion and the assumption that the remaining movement is tremor is made. Next, an adaptive algorithm estimates tremor using a sinusoidal model, estimating its time-varying frequency, amplitude and phase (Riviere 1995). This algorithm developed

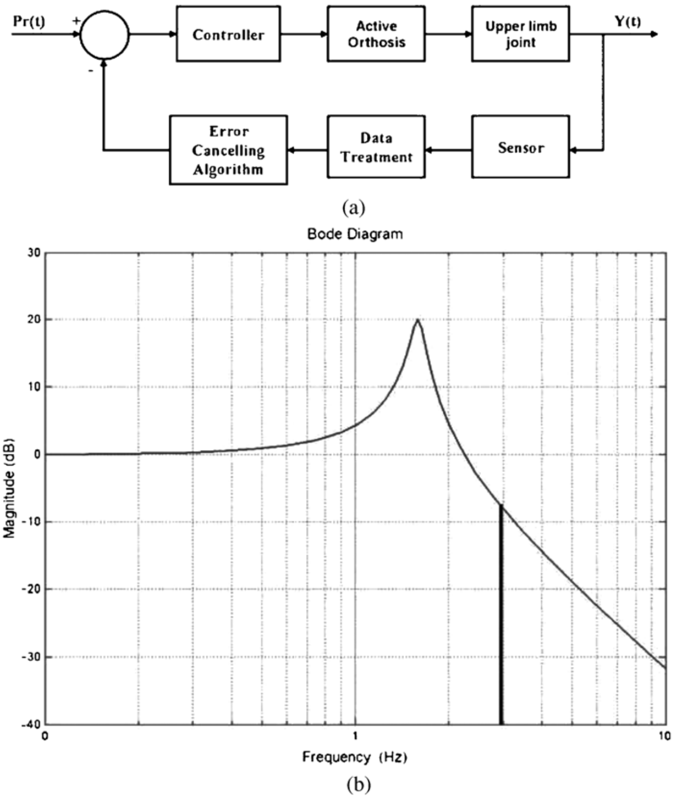

Figure 2. (a) Tremor suppression control system. The movement of each upper limb joint is detected by gyroscopes. An error cancelling algorithm performs a real-time discrimination of the tremorous (undesired) component of motion. The angular velocity information from the estimated tremorous component is used to calculate the reference mass and damping characteristics of the upper limb. This process defines the actual impedance force of the system, defining the apparent impedance of the upper limb and consequently reducing the tremor. (b) The musculo-skeletal system is modelled as a second-order biomechanical system. The active orthosis is used to modify the apparent biomechanical characteristics of the upper limb so that the cut-off frequency, *fc*, lies between the frequency range of voluntary and tremor motion.

was evaluated with 33 subjects presenting different tremor diseases. Results demonstrated the correct operation of the algorithm being able to estimate with a small phase lag (roughly 1 ms of time delay introduced) the voluntary and tremor components from the overall movement.

Experimental protocol

The performance of the active orthosis developed was evaluated in an experimental phase involving six patients suffering from ET (three females, three males; mean age 72.3 ± 4.3 years). These patients exhibited a bilateral postural/kinetic tremor in upper limbs at intensities of 2/4 to 4/4 despite regular intake of medication (primidone up to 500 mg/day, propranolol up to 160 mg/day or a combination of both), in agreement with the criteria of ET (consensus statement of the MDS). Regular anti-tremor medications were maintained stable during the week preceding the assessment. The investigation was approved by the ethical committee, and patients gave their written informed consent.

The effects of adding effective viscosity were investigated for the upper limb on one side during the execution of different clinical tasks (keep the upper limbs outstretched in a horizontal position, point the nose with the index starting from the thigh and keep the arm in a rest position over the thigh). These tasks have been previously used to characterize tremor movement (Belda-Lois *et al* 2004).

During the experiments, WOTAS operated basically in two different control modes as follows.

(1) *Monitoring mode*. WOTAS operates in the free mode (no force is applied on the upper limb) and monitors tremor parameters of the patients.
(2) S*uppression* mode. WOTAS is able to change biomechanical characteristics of the upper limb, such as viscosity or inertia, in order to suppress tremor.

The order in which the modes have been applied has been alternated, as well as the order in which the patients have executed the tasks. This approach was adopted in order to avoid interactions in the analysis as well as learning effects (Belda-Lois *et al* 2004). During the experiments, the patient did not know when the systems were applying a suppressing strategy or when they were operating in the monitoring mode. It was only the computer operator who knew when the systems were applying the suppression strategy. For formal purposes, we consider this arrangement equivalent to a double-blind trial in order to reduce the placebo effects in the experimentation phase (Belda-Lois *et al* 2004).

The data analysed and presented here were the output voltage coming from the gyroscopes placed on the active orthosis. The data were filtered by means of a kernel smoothing algorithm. The duration of the acquisition was 10 s for each task.

Results

The effects of adding effective biomechanical loading were investigated for the upper limb during the execution of the different clinical tasks. During the trials, some patients were able to identify when the system was operating in a suppression mode, relating to the clinician's either 'now the system is suppressing my tremor' or 'now it is not'.

Figures 3(a) and (b) illustrate the effects of WOTAS on the tremorous movement when operating in the *suppression* mode in one patient with a severe ET. Figure 3(a) shows the time series corresponding to the tremorous movement of the wrist joint during the arm outstretched task of one patient exhibiting a severe essential tremor. The top part of the figure shows the time signal with WOTAS in the *monitoring* mode (left) and in the *damping* mode (right). Note that the amplitude of the tremor is clearly lower under the *damping* condition as compared to the *monitoring* mode. The bottom panels illustrate the same reduction in the frequency domain. The power spectrum density (PSD) has been obtained from the part of the signal with a detectable tremor. A clear peak of tremor activity close to 6 Hz is identified. The peak of energy corresponding to the tremorous activity when WOTAS is operating in the *suppression* mode presents a clear reduction. The reduction of the power spectral density was 80.4% in this patient. Note that the dominant tremor frequency is stable despite the reduction in its amplitude. Figure 3(b) illustrates a similar phenomenon for the elbow. Figures 3(c) and (d) show the effects of the active orthosis on the kinetic tremor associated with a finger-to-nose test. A strong reduction in tremor was observed.

The efficiency of the active orthosis increases as tremor power increases. A statistical analysis has been made to characterize tremor suppression. The statistical study has been made using R. A second-order polynomial fitting has been performed with the natural logarithms of power spectra in free and suppression modes. This method allows us to identify a lower limit

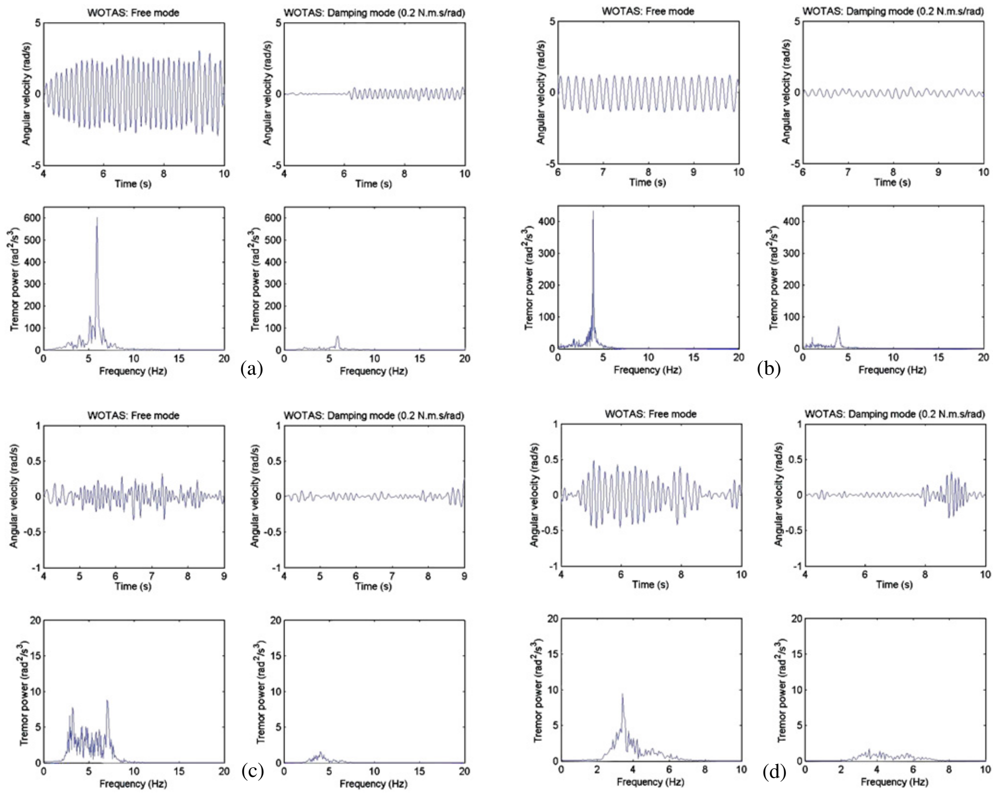

Figure 3. This figure illustrates the oscillations of the wrist with the associated power spectral density (PSD) of tremor with the motor in a free mode (left panels) and providing viscosity of 0.2 N ms rad^{-1} (right panels) in one of the patients. Note the strong reduction in the PSD when viscosity is applied. Oscillations are expressed in rad s^{-1} and PSD is expressed in rad^2 s^{-3}. (a) Reduction of postural tremor of the wrist with WOTAS, (b) reduction of postural tremor of the elbow with WOTAS, (c) reduction of kinetic (intention) tremor at the elbow with WOTAS, (d) reduction of tremor at the elbow level in a patient performing a finger-to-nose task.

for efficient tremor suppression; this limit is roughly 0.15 rad^2 s^{-3}. This shows a lower limit for efficient tremor suppression. It was possible to estimate the range of tremor suppression of the signals above the orthosis operational limits, ranging from 2.9% (percentile 5) to 78.5% (percentile 95) in relation to energy in the *monitoring* mode.

Figure 4 shows the reduction in tremor energy when the active orthosis is operating in the suppression mode, focusing on the most intense reductions obtained with the orthosis in each patient. The results of the experiments indicated that the device could achieve a consistent 40% of tremor power reduction for all patients, being able to attain a reduction ratio in the order of 80% tremor power in specific joints of patients with a severe tremor. Figure 5 illustrates the effects of the damping mode on the means, medians and centiles 10/20/80/90 of power spectra for each joint. The results indicated an effect for the wrist and the elbow.

In one patient, the reduction of tremor in the wrist and elbow was associated with a possible rise in tremor intensity at the shoulder level. However, in the majority of patients there was no visible displacement of tremor movement from distal to proximal joints. We call this phenomenon distal to proximal tremor shift (DPTS). The authors believe that it is

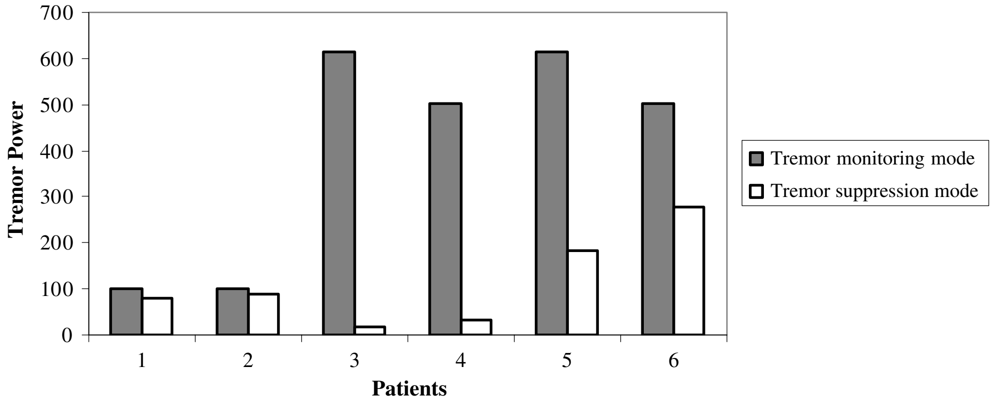

Figure 4. Tremor in a damping mode (white bars) and monitoring mode (grey bars) for the six patients. The trials with the highest tremor energy in the monitoring mode are shown. Note the marked tremor reduction. Tremor power expressed in rad^2 s^{-3}.

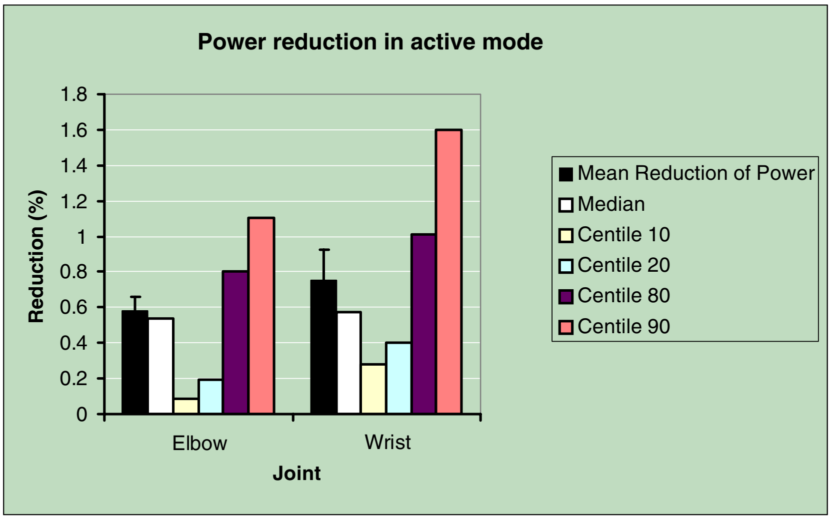

Figure 5. Power reduction (0: total disappearance of tremor, 1: tremor unchanged) achieved by the exoskeleton in the active mode for each joint (wrist, elbow). Means, medians and centiles 10/20/80/90 are illustrated.

important to investigate and define the profile of the users who might be affected by this new phenomenon.

Considering the group of patients, the mean tremor energy under postural/kinetic conditions was 55.49 $\pm$ 22.93 rad^2 s^{-3} in the monitoring mode and 15.66 $\pm$ 7.29 rad^2 s^{-3} in the active mode. There is a consistent reduction in the tremor energy when the orthosis is active (damping effect: $p = 0.018$ when both joints are considered).

There are hints that the mechanical suppression of tremor could produce a 'positive' feedback to essential tremor patients. Patients reported that when they realized that the orthosis was suppressing the tremor, they felt more and more confident to accomplish the task. This behaviour has been detected in patients with a severe tremor, and requires further research to be confirmed and investigated in depth.

Overall, patient tolerance was good. No lesions were observed on their skin, except for a moderate and transient change in skin aspect due to the orthosis. A slight discomfort was reported by some patients.

Discussion

This paper describes a new solution for tremor assessment and suppression in humans using an active orthosis based on dc motors and able to change upper limb biomechanical characteristics in a real-time fashion. The main innovations of the technique presented are that the active orthosis is able to apply forces between segments of the upper limb and the intelligent detection of tremor versus voluntary motion, in such a way that the orthosis does not load the voluntary movement of the patient.

The lower limits for tremor suppression efficiency are mainly related to the interface of the orthosis with the upper limb since stiffness between the orthotic device and the body is a key factor to control a dynamic process such as tremor. Therefore, the characteristics of the transmissions through the soft tissues play an important role in the efficiency of tremor suppression.

The main drawback of the technique presented is that the patients considered that the use of such device would cause social exclusion. This was expected by authors since the exoskeleton was developed as a platform to evaluate the concept of mechanical tremor suppression and not as a final orthotic solution. Despite the available miniaturization provided by microelectromechanical systems (MEMS), which allows for the reduction of sensors as well as the miniaturization of the available controllers, a DSP could implement the control strategies of the exoskeleton; the main technological challenge for the reduction of the orthosis size is the actuator technology. In the authors' opinion, there is no available technology that allows for the construction of an orthotic device which could be accepted by the patients as a final orthotic solution. Patients require a device that could be hidden under their clothes. Furthermore, there are evidences that there is a physical limitation for tremor suppression through wearable devices due to force transmission through soft tissues.

The adaptive viscous control method is non-invasive and painless. It may be effective in patients who are insufficiently responsive (or have adverse reactions) to drugs or in whom surgery is counter-indicated. We avoid the potential side effects of drugs and the risks of surgical procedure. Although deep brain stimulation has provided remarkable benefits for people with a variety of neurologic conditions (Perlmutter and Mink 2006), alternative solutions are of interest for refractory cases. From the motor control point of view, deep brain stimulation has also the disadvantage of impairing the adaptative control of reaching (Chen *et al* 2005). In ET patients with electrodes placed in the cerebellar thalamus, the larger the stimulation voltage the greater the reduction in rates of adaptation. In patients with unilateral thalamotomy, the adaptation in the contralateral arm is also impaired as compared to the ipsilateral arm (Chen *et al* 2005). Therefore, although both central neurostimulation and lesions are effective to manage tremor in many cases, both techniques significantly impair the capacity of the brain to form internal models of action, the adaptative control of reaching depending on the integrity of the cerebellothalamocortical pathway (Chen *et al* 2005, Diedrichsen *et al* 2005, Kawato and Wolpert 1998, Nowak *et al* 2004, Obayashi 2004).

Despite the benefits provided by drugs, there is still a high non-response rate in ET (Louis 2005a). Primidone appears superior to phenobarbital in the reduction of tremor (O'Suilleabhain and Dewey 2002). Nevertheless, tolerability remains a common issue. In our experience, more than one-fourth of patients treated with primidone will require a discontinuation of the medication due to intolerance, despite very low doses at the initiation of the treatment and a graduated titration. Regarding gabapentin, topiramate, clonazepam, alprazolam or calcium channels antagonists, there are responders amongst the heterogeneous population of patients exhibiting ET. The reduction of tremor appears lower than the reduction observed with propranolol or primidone, and the anti-tremor effect is usually observed at a dose associated with sedation, especially for benzodiazepines. Gabapentin administration may be associated with the improvement of the kinetic tremor. Although intramuscular botulinum toxin injections may decrease tremor by inducing muscle weakness, the effects upon the upper limb function are a matter of debate and patients may complain of hands' and fingers' weakness.

Oscillations occur frequently in biological systems (Kawato and Wolpert 1998). Interactions with the environment induce oscillations in the human body. The mechanical properties of the neuromuscular system and the effects of reflexes contribute to the features of oscillations. Because muscles can be compared to viscoelastic structures, they are involved in damping, the dissipation of mechanical energy. Potentially, reflexes can modulate the relative magnitudes of the viscous and elastic components of the mechanical impedance provided by muscle (Lin and Rymer 2000, Kawato and Wolpert 1998). The technique described here may be seen as an adaptative device which cancels oscillations of tremor by governing and redirecting the movement at the effector level.

The potential compensatory mechanisms which might occur in the central nervous system after redirecting the involuntary motion remain to be defined. Further research in the field of actuators will clarify our understanding of the short-term, middle-term and long-term adaptation of human motor behaviour to wearable active orthosis (Manto *et al* 2003). Improvements of comfort issues and reduction of size, weight, portability of the orthosis will increase the impact of this new strategy on the understanding and management of movement disorders during daily practice.

These results suggest this new technique as a possible therapy for tremor suppression in human disorders characterized by postural/kinetic tremor in upper limbs. It opens possible perspectives for disabling forms of tremor, such as tremor encountered in cerebellar and/or brainstem disorders.

Acknowledgments

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