Neck rigidity in Parkinson's disease patients is related to incomplete suppression of reflexive head stabilization

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A R T I C L E   I N F O
Article history:
Received 12 January 2009
Revised 10 March 2009
Accepted 13 March 2009
Available online 21 March 2009

Keywords:
Parkinson's disease
Rigidity
Passive head rotation
Dynamic model
Suppression of reflexive head stabilization

A B S T R A C T
Muscle rigidity in PD (Parkinson's disease) patients represents an involuntary increase in muscle tone that stands out upon passive rotation of a joint. The pathophysiology of rigidity is still not well understood. We measured head-trunk torque in PD patients and normal controls during transient passive head rotations by means of servomotors under the instruction to the subjects to relax the neck muscles. We observed that rotation onset was followed by an initial rapid rise in resistive torque, similarly in both subject groups. It then leveled off or declined in controls. With PD patients, in contrast, the rise continued roughly proportional to head eccentricity almost until the end of the rotation. These observations led us to the hypothesis that the initial rise in torque represents reflexive head stabilization that normal subjects in the course of the rotational stimulus are able to suppress, whereas PD patients are less effective in doing so. The hypothesis was implemented into a dynamic control model of active and passive head rotation. Model simulations successfully reproduced the torque responses of normal subjects and PD patients in the present and previous studies.

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Introduction
Increased resistance to passive joint rotation, i.e. rigidity, is one of the cardinal signs of Parkinson's disease (PD). It is assessed clinically by slowly and unpredictably rotating the joint of interest while asking the patient to relax and remain passive. Rigidity tends to be sustained throughout the passive movement, unless occasionally additional tremor leads to cogwheel-type interruptions. The underlying pathophysiology is still not well understood (Lee, 1989; Delwaide, 2001; Hallett, 2003). A current hypothesis considers suppression of automatic postural activity a function of the basal ganglia (cf. Mink, 1996). We therefore asked whether PD rigidity reflects joint stabilization by long-latency proprioceptive reflexes, which patients, unlike normal subjects, cannot voluntarily control. This study explores into the hypothesis of an impaired voluntary suppression of reflexive neck stabilization as the cause of neck rigidity in PD patients.

There is a considerable amount of electrophysiological work on PD rigidity that focused on the role of spinal mechanisms and proprioceptive afferents. Foerster (1921) found that rigidity was abolished after section of the dorsal roots. Yet, the spinal proprioceptive reflex loop, fusimotor activity, and the gain of α–γ co-activation are normal in PD (Burke et al., 1977), in accordance with the clinical experience that tendon jerks are not exaggerated. Thus, with PD rigidity, unlike with spasticity, short-latency components of the stretch reflex are normal, whereas late components, starting in the 50–100 ms latency range, are enhanced (Tatton and Lee, 1975). Their augmented magnitude has been claimed to correlate to rigidity (Tatton et al. 1984). The long latency of these components has been attributed mainly to low-conduction-velocity secondary spindle (group II) afferent inflow by some authors (Berardelli et al., 1983; Cody et al., 1986). Others, in contrast, related it to the involvement of long neural loops through supra-spinal centers including the cerebral cortex, arising mainly from primary muscle spindle (Ia) input (Rothwell et al., 1983). Few studies related rigidity to reduced group Ib (Golgi tendon organ) inhibition of motoneuronal activity (Delwaide et al., 1991; Burne and Lippold, 1996).

While the short-latency reflexes are considered stereotypical autogenic local spinal responses, the subsequently occurring long-latency reflexes appear to be involved in supra-spinal multi-joint contextual responses to external disturbances (Marsden et al., 1983; also Kurtzer et al., 2008). The latter appear to involve the basal ganglia. A lesion study in primates suggests that the basal ganglia are important for controlling the sensitivity of flexors and extensors to stretch (Rea and Ebner, 1991). Furthermore, it has been shown that PD patients, unlike normal subjects, have difficulties adjusting long-latency reflexes to the postural context (Diener et al., 1987). The amount of PD rigidity seems to correlate with electromyographic activity in the corresponding muscle and may be used for quantifying and monitoring it over time and treatment (Meara and Cody, 1992; Levin et al., 2009).
In behavioral studies, several proprioceptive functions have been shown to be impaired in PD patients. Conscious perception of proprioceptive stimulation by joint rotation is abnormal (Zia et al., 2000; Maschke et al., 2003). Additionally, arm pointing under pure proprioceptive control is abnormally slow and under-shooting, while it improves when visuo-proprioceptive movement control is added to the proprioceptive-motor integration (Klockgether and Dichgans, 1994; Klockgether et al., 1995; Adamovich et al., 2001). Proprioceptive-motor integration appears to be abnormal as well in stance stabilization of PD patients (Bloom et al., 2001; Rocchi et al., 2002; Maurer et al., 2003) and in walking (Jacobs and Horak, 2006). The deficit is related to a general difficulty in task- and set-switching (Fimm et al., 1994; Cools et al., 2001), which becomes especially pronounced when the patients have to use internal cues and self-initiation instead of external input (Brown and Marsden, 1988; Kimmig et al., 2002; Werheid et al., 2007). There are studies on neuronal activity in the basal ganglia, which suggest that suppression of automatic postural reactions is a relevant constituent of the PD motor impairment (Mink and Thach, 1991; Mink, 1996).

It is still unknown, however, how PD rigidity relates to the presumed impairment of proprioceptive-motor integration. A hypothesis, to be valid, would have to address not only the just mentioned electrophysiological and behavioral aspects, but also quantitative characteristics of the abnormal motor resistance. There are several studies that measured torque of limb joints or EMG activity in response to passive movements, but did so mainly in order to quantitatively distinguish PD rigidity from normal muscle resistance and spasticity or to evaluate therapy effects (e.g. Webster, 1960; Prochazka et al., 1997; Mak et al., 2007; Shapiro et al., 2007, to name a few). Some of them characterized rigidity in terms of its stimulus velocity and position dependency, though with differing results (Berardelli et al., 1983; Rothwell et al., 1983; Teräväinen et al., 1989; Lee et al., 2002; Mak et al., 2007). Also the damping in a leg pendulum test was evaluated (Le Cavorzin et al., 2003). However, a systems analysis approach that addresses the signal processing deficit of rigidity using a dynamic model of voluntary stiffness control has not yet been published to our knowledge.

In addition to affecting limb muscles, PD rigidity may also affect axial muscles (Wright et al., 2007) including those of the neck (Kroonenberg et al., 2006). Axial rigidity is of functional relevance to the extent that precise distal segment movements depend on exact tone regulation of the more proximal and axial muscles (Diener et al., 1989). Tone regulation of axial muscles has been considered to differ somewhat from that of distal muscles (Gurfinkel et al., 2006). This notion has been extended to rigidity (Wright et al., 2007). However, the issue is still unresolved due to major methodological differences between studies.

This study investigated axial rigidity at the neck level. Reasons for this are that our laboratory has expertise with head movement control in the horizontal plane and that there already exist corresponding dynamic models of reflexive head control from other laboratories (Schor et al., 1988; Keshner and Peterson, 1995; Keshner et al., 1999; Peng and Hain, 1996; Tangorra et al., 2003). The models consider mainly two head stabilizing mechanisms that have originally been identified in animal experiments (Outerbridge and Melvill-Jones, 1971; Goldberg and Peterson, 1986). One is neck proprioceptive head-trunk stabilization, the cervico-colic reflex, the other, vestibular headspace stabilization, the vestibulo-colic reflex. Their presumed action in adult humans depends to a large extent on the experimental situation in which they are tested (Schor et al., 1989; Keshner and Peterson, 1995).

We assessed transient neck torque responses upon passive horizontal head rotations with different peak angular velocities (2.3, 4.6, and 18.4°/s) while keeping peak displacement constant. Furthermore, we applied proprioceptive and vestibular stimuli and a combination of both. This study extends the previous work of Wright et al. (2007) who applied inter-segmental rotations at the level of the hips and shoulders, using periodic stimuli with very low angular velocity (1°/s). These authors focused on directional asymmetries, relations of rigidity to motor symptoms in the UPDRS, and on treatment effects by levodopa. In contrast, our study aimed at a formalized explanation of rigidity in terms of a dynamic control model to be derived from the experimental findings. Since passive tissue resistance may contribute considerably to PD rigidity (Dietz et al., 1981; Watts et al., 1986), our study took care to measure foremost active muscle force rather than intrinsic mechanical properties. This was accomplished by using small excursions about primary position (within the so-called neutral zone; Kumar, 2004) and omitting severely affected patients with secondary changes of the mechanical properties.

**Methods**

**Patients and control subjects**

Fourteen PD patients (63 ± 8 yrs; seven females and seven males) were compared with 23 age-matched normal controls (55 ± 13; eleven males and twelve females). All subjects gave their informed consent to the study, which was approved by the local ethics committee. Patients' clinical data are given in Table 1. Disease duration ranged between 1 and 10 yrs. The patients were moderately affected (average UPDRS scores just prior to measurements, 36 ± 12; Hoehn and Yahr stages I, II or III, assessed by the same neurologist). Rigidity was mild to moderate (most affected arm, score 1–3). All patients received L-dopa (some in addition selegiline, amantadine, or agonists). Measurements took place in the early morning so that at least 10 h had elapsed after the last medication. Six of the fourteen patients had received brain imaging that showed no pathological findings. None of the patients showed signs of considerable structural brain damage. None of the patients complained of neck pain or had a history of cervical syndrome.

**Apparatus, stimuli and protocol**

Subjects (Ss) were seated on a Bärany chair (Toennies, Freiburg) in the center of a cylindrical screen of 0.8 m radius. Their heads were stabilized by means of a dental bite board during presentation of the stimuli. The board was attached to a head holder that was mounted on the chair, but could be rotated independently from the latter in the horizontal plane (see inset of Fig. 1). The shaft of the head holder contained a device for measuring horizontal head torque (Burster, Gernsheim, Germany; range 0–20 Nm, nonlinearity < 0.2% of r.o.). The

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<th>Patient Age</th>
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Fig. 1. Experimental paradigm and representative examples. Resistive head–trunk torque responses (upper panel) exerted by normal subject (thin curve) and PD patient (bold). Responses are counter to rightward head–trunk rotation stimulus of 4.6/°s peak velocity (‘trunk-only’ stimulus). The stimulus curves (below): head–trunk rotation is rightward, heavy line, while trunk-space rotation is leftward, dashed curve, so that head remains stationary in space, thin curve. Stimulus setup is given in inset (subject sitting on turntable, head fixed via bite board to chair-mounted head rotation device). In the torque response curves, arrows indicate begin of leveling off of torque (phase I end) in normal subject at about 0.1 Nm, after which it starts to decline, and in patient, after which it still continues to rise and starts to decline only at about stimulus end.

The model simulations were performed using MATLAB/SIMULINK (The MathWorks Inc., Natick, MA, USA). This program was also used to compute the time vector and the slopes change with respect to stimulus onset (referred to as ‘phase I’). The slopes of the phase I and phase II were approximated by straight line fits in order to obtain torque measures and the time of slope change with respect to stimulus onset (referred to as ‘duration of phase I’) for statistical purposes. The same procedure was applied to the responses of the patients where the torque responses were more variable and the slopes change showed, in most cases, only a reduction rather than a reversal.


Statistics

Torque responses were analyzed by repeated measures ANOVA, unless otherwise stated, with stimulus peak velocity (2.3, 4.6, and 18.4°/s) and stimulus condition (trunk-only rotation, head-only rotation) as within-subject repeated measures factors and group as the between groups factor (patients vs. normal subjects). The responses to head + trunk rotation were not included for simplicity, since this rotation evoked a qualitatively different response upon the physiological motion range and neutral zone (McClure et al., 1998; Takahiro et al., 2004).

The stimuli were always applied in darkness. Subjects’ ears were plugged in order to minimize auditory spatial orientation cues. The stimuli were presented in 18 separate trials (3 stimulus peak velocities × 2 directions × 3 different stimuli) in random order within a recording session that lasted 30–40 min.

Instructions

Care was taken to guide subjects’ spatial attention appropriately prior to each rotational stimulus. To this end, the afore mentioned light spot was transiently switched on and subjects adjusted its position by means of a remote control to their subjective visual straight ahead direction (for details, cf. Maurer et al., 1997). During the time of the subsequent rotation stimuli, subjects were asked to relax the neck muscle and to neither assist nor resist the rotation. Rest periods of several minutes were given after 3–4 trials with the room lights on. In darkness, the experiments were continuously checked through an infrared video camera.

Data acquisition and analysis

Position readings of the chair and head holder potentiometers (in deg), of the torque applied to the head holder (in Nm), and of the stimulus trigger signals were sampled at 200 Hz and stored in a computer for off-line analysis. The torque 5 s prior to stimulus onset was averaged and taken as baseline. It was close to 0 Nm in approximately all subjects, meaning that they exerted no considerable force on the bite board at rest. In grand average torque curves, an initial response (‘phase I’) to the trunk-only and head-only rotations stood out clearly (Fig. 2; individual examples in Fig. 1). In normals, it was followed by an abrupt trend change in that the torque decreased or leveled off (see Figs. 2 and 4; ‘phase II’).

Occurrence of a trend change in slope at a certain instant \(t_p\) after stimulus onset was tested by means of a linear regression model

\[
Y = b_0 + b_1 \cdot t + b_2 \cdot D + b_3 \cdot t \cdot D + \varepsilon,
\]

where \(Y = [Y_i]_{1 \leq i \leq n}\) is the torque development vector defined on the time vector \(t = [t_i]_{1 \leq i \leq n}\), \(\varepsilon = [\varepsilon_i]_{i = 1,...,n}\) is a vector of Gaussian random errors of zero mean and fixed (unknown) variance and the pseudovariable \(D\) equals one and zero when \(t < t_p\) and \(t > t_p\) respectively.

The slopes of the phase I and phase II were approximated by straight line fits in order to obtain torque measures and the time of slope change with respect to stimulus onset (referred to as ‘duration of phase I’) for statistical purposes. The same procedure was applied to the responses of the patients where the torque responses were more variable and the slopes change showed, in most cases, only a reduction rather than a reversal.
of a voluntary head control system (see Discussion) and were used to derive estimates of model parameters. The curve fits were made using a constrained nonlinear optimization algorithm ('fmincon' from the Matlab Optimization Toolbox) that adjusted model parameters to minimize the weighted error value given by

$$E = \sum_{t=1}^{T} \frac{M(t) - H(t)}{M(t) + H(t)}$$

where $M(t)$ and $H(t)$ represent the values of the model and experimental torque responses, respectively, at the time instant $t$.

The error magnitude at each instant was summed across the 3 stimulus peak velocities (2.3, 4.6, and 18.4°/s) and the two stimuli used for the fitting (trunk-only and head-only rotations). Extensive simulations were performed to validate the data analysis and parameter estimation procedures. Simultaneous curve fits were made to all average torque response curves, separately for the two subject groups. To limit the number of unconstrained fit parameters, we made the assumption that passive stiffness and damping amount to 10% of active stiffness and damping (compare Maurer et al., 2006).

The curve fits described in Discussion reliably converged to single solutions.

Fig. 2. Average torque response data. Mean responses of PD patients (bold curves) and of normal controls over time (thin). Leftward and rightward data are lumped together. Grey areas give ±1SD ranges of normals and dashed curves +1SD ranges of patients. Rows: Stimulus trunk-only (A), head-only (B), and head + trunk (C; insets, subject from above). Columns: Peak velocities (a, 2.3°/s; b, 4.6°/s; c, 18.4°/s). Negative sign of torques indicates that they are resistive. HS, TS, HT: head-space, trunk-space, and head-trunk rotation (see Fig. 1). Inset in panel Aa shows correlation between PD patients’ peak torques and values of UPDRS rigidity score ($r$, correlation coefficient; see also text).
Results

Fig. 1 illustrates the experimental paradigm and gives representative examples of the resistive torque exerted by a normal subject (thin curve) and a PD patient (bold) in response to trunk-only rotation with peak velocity of 4.6°/s (5 s duration stimulus). Here, the trunk-space rotation is to the left (downward), while the head-trunk rotation is to the right, so that the head remains stationary in space. Resistive leftward torque is presented as deflection downward, meaning that torque was directed counter to the head-trunk excursion. The response starts with a steep slope (phase I; see Methods). Approximately 700 ms later, the torque curve of the normal subject levels off and starts to decline (phase II). The response of the patient also shows an initial sharp rise, with a similar slope to that of the normal subjects, but it continues to rise almost till the end of the rotation, before it starts to decline.

The grand average data obtained for the three stimulus combinations and the three peak stimulus velocities are given in analogous form in Figs. 2A–C, superimposing the mean torque responses of the PD patients (bold curves; dashed lines, patients’ ±1SD ranges) on those of the normal controls (thin; grey shaded areas, normals’ ±1SD ranges).

Normal subjects

Trunk-only rotation

The averaged torque response to the 4.6°/s trunk-only stimulus in Fig. 2Ab essentially resembles the above described representative example of the normal subject in Fig. 1. Qualitative similar responses were obtained with the 2.3°/s and 18.4°/s stimuli with the following exceptions. With increasing stimulus speed (decreasing duration, from 10 s and 5 s to 1.25 s) the initial torque slope increased essentially linearly (0.09 ± 0.05, 0.22 ± 0.12, to 0.86 ± 0.32 Nm/s, respectively; Fig. 3A), while the duration of phase I decreased correspondingly (Fig. 3B). The corresponding mean peak torque values, attained at variable time intervals after stimulus onset for each subject (and therefore not standing out in average curves), amounted to 0.24 ± 0.24, 0.20 ± 0.18, and 0.39 ± 0.18 Nm, respectively. Thereafter, the torque decreased towards baseline, first sharply and then more gradually, approximately reaching the baseline within the following 20 s.

The data are re-plotted in Fig. 4A in terms of so-called tension-length diagrams (here torque–angle diagrams) with an indication of the torque at phase I end (mean and ±1SD of normals and patients, large and small vertical dashed lines and circles, respectively). In these diagrams, the slopes give a measure of stiffness (Nm/°). Note that phase I is characterized by high stiffness and that the phase I stiffness slopes are similar across all three stimulus speeds. Thereafter, the curves level off, first more abruptly and then gradually, indicating that stiffness is increasingly replaced by compliance. This applies similarly with the three different peak velocity stimuli. Note, however, that the leveling off was clearly less pronounced and that the average torque magnitude reached was considerably higher with the 18.4°/s stimulus than with the 2.3°/s and 4.6°/s stimuli.

Head-only rotation

The results were very similar to those obtained upon the trunk-only stimuli. This applied to the average responses (Fig. 2B, a–c) and the initial slopes of torque increase over time (Fig. 3A) as well as to phase I duration (not shown). Peak torque values were somewhat lower with head-only rotation, however, as can be seen from the torque–angle curves in Fig. 4B. The mean values amounted to 0.13 ± 0.13, 0.13 ± 0.10, and 0.35 ± 0.17 Nm upon the 2.3, 4.6, and 18.4°/s stimuli, respectively. The peak values were attained earlier during the course of stimulus application with the head-only than the trunk-only rotation, especially with the 18.4°/s stimulus, after which torque magnitude decreased before peak displacement was reached. Thus, normals followed the “relax the neck” instruction more successfully with the head-only than the trunk-only stimulus.

Head + trunk rotation

Upon the en-block head and trunk rotations, no considerable torque responses were obtained for the 2.3°/s and 4.6°/s stimuli. In contrast, the 18.4°/s stimulus evoked a transient biphasic response (Fig. 2C) that we could attribute essentially to head inertia (see Discussion and Fig. 6C).

PD patients

Trunk-only rotation

As shown above for the representative patient (Fig. 1), the initial rise in torque was normal in the patients (Fig. 2A, a–c). The corresponding torque velocity values obtained for the 2.3°/s, 4.6°/s, and 18.4°/s stimuli amounted to 0.08 ± 0.06, 0.26 ± 0.66, and 0.88 ± 0.52 Nm/s, respectively (Fig. 3A). But leveling off started later than in normals and a shallow rise of torque continued essentially until the end of the stimuli (see Fig. 2A, a–c). Averaging the individual peak torque values with the 2.3, 4.6, and 18.4°/s stimuli yielded values of 0.5 ± 0.18, 0.47 ± 0.46, and 0.52 ± 0.41 Nm, respectively. Note that these values are similar across the three stimuli. After the peak, the torque decreased, first sharply and then more gradually, staying well above baseline during the following 20 s, unlike in normal subjects.

In the torque–angle re-plots of the data (Fig. 4A), the initial stiffness essentially coincide with those of normals, similarly for the 2.3, 4.6, and 18.4°/s (i.e. 10, 5, and 1.25 s duration) stimuli. The significant decrease in slope, taken as change from phase I to phase II,
occurs later than in normals (Fig. 3B; duration values of phase I are lumped together across the trunk-only and head-only stimuli in both normals and patients, as the effect of the factor condition was insignificant; cf. below, statistics). In the torque–angle presentations shown in Fig. 4A, the following decrease in slope stands out more clearly than in the torque–time presentations (Fig. 2A). It demonstrates that also patients, tried to follow the instruction to relax the neck muscle, but did so less effectively than normal subjects. Inspection of the individual responses revealed that also in patients the change in slope tended to occur abruptly, but its timing showed considerable variation.

**Head–only rotation**

The responses to the head–only rotations resembled those of the trunk–only rotations. A slight difference was that the mean across the individual peak torque values declined somewhat with increasing stimulus peak velocity (0.57 ± 0.65, 0.45 ± 0.50, and 0.38 ± 0.23 Nm upon the 2.3, 4.6, and 18.4°/s stimulus, respectively, Fig. 2B). And, the leveling off upon the 18.4°/s stimulus was earlier and stronger than with trunk–only rotation (Fig. 4Bc).

Note furthermore that upon both the head–only and trunk–only rotations, the leveling off during the 18.4°/s stimulus was more effective than during the slower stimuli. This was different from normals’ responses where it was less effective during the fastest stimulus. As a consequence, the difference in peak torque between normals and patients was smallest with the fastest stimulus.

**Head + trunk rotation**

The rotation evoked a biphasic response upon the 18.4°/s stimulus, which closely resembled that of the normal subjects. No considerable response was obtained upon the 2.3 and 4.6°/s stimuli in patients either.

**Statistics**

It was performed using a 3×2×2 repeated measures ANOVA, with stimulus peak velocity and condition, i.e. trunk–only and head–only rotation, as within–subject repeated measures factors and group as the between groups factor: Initial torque slope in patients was statistically not different from that in controls (F = 0.09, p = 0.77). Stimulus peak velocity proved highly significant (F = 174.5, p < 0.0001), reflecting the fact that the initial slope increased with increasing peak velocity. Also, there was a significant interaction of the factors peak velocity×condition (F = 10.8, p = 0.0001), which reflects the fact that the rate of torque increase with the 18.4°/s head–only rotation was higher than with trunk–only rotation. Slopes upon the 2.3°/s and 4.6°/s stimuli were not different between the two conditions (Fig. 3A).

**Phase I duration.** The time until the initial slope started to level off amounted to 0.76 ± 0.66 s in normals (average across the three stimulus velocities and the head–only and trunk–only conditions) and was significantly longer and more variable in patients (1.49 ± 1.50 s). Stimulus peak velocity proved to be a statistically significant factor (F = 83.1, p < 0.0001; reflecting the fact that phase I duration decreased with increasing stimulus peak velocity; Fig. 3B). Both the interactions stimulus peak velocity×group and stimulus condition×group proved to be significant as well (F = 15.7, p = 0.0001 and F = 8.7, p = 0.006, respectively). Thus, phase I duration was more prolonged in the patient group when (i) stimulus speed was low (Fig. 3B) and (ii) head–only was compared with trunk–only stimulation.
Peak torque. This value was significantly higher in patients than in controls \(F = 19.8, p = 0.0001\). There was a significant interaction with stimulus velocity. Testing with post hoc Scheffe showed a significant difference for the 2.3°/s stimulus \((p = 0.0008)\) and the 4.6°/s stimulus \((p = 0.0002)\), whereas the peak torque values upon the 18.4°/s stimulus were not significantly different. As shown in the inset of Fig. 2Aa, patients' peak torque correlated with the UPDRS rigidity score (Table 1). This applied to the stimuli with 2.3°/s and 4.6°/s \((p = 0.045)\) and not with the 18.4°/s stimuli \((p = 0.28)\).

Discussion

Passive head rotation in our subjects led to an initial steep rise in resistive neck torque, similarly in normals and PD patients. The rise was followed by a pronounced attenuation in normal subjects, which was clearly less so in the patients. These observations suggested to us that the responses may stem from reflexive head stabilization, which normals are able to suppress, whereas the patients show difficulties in doing so. These findings are compatible with the hypothesis put forward by Mink and Thach (1991), which suggests that suppression of postural reactions is a main basal ganglia function (see Introduction).

In the following, we first compare our findings to previous ones in the literature. Then, we address our hypothesis using an engineering approach. We present a dynamic model of reflexive head stabilization and add to it a mechanism that allows for voluntarily suppression of reflexive neck stabilization. The experimental findings are then used for parameter fitting to the model, which allows us to make inferences on the cause of PD rigidity. Finally, we test whether the model describes and predicts present, as well as, previous findings.

Comparison with earlier torque measurements in PD

Phase I (initial transient) torque response

Comparable previous studies on PD rigidity addressed mainly steady state responses during periodic stimulation and paid little, if any attention to the initial transient torque response. The transient response can be found, however, in previous studies of axial rigidity (normals: Gurfinke et al., 2006, see their Fig. 2; normals and PD patients: Wright et al., 2007, their Figs. 2B, D; also Mak et al., 2007) and limb rigidity (e.g. Xia and Rymer, 2004). Gurfinke et al. (2006; normal subjects) briefly addressed the initial transient response, attributing it to a passive muscular resistance that is found in contracting muscles upon rapid stretch (‘short-range stiffness’, Rack and Westbury, 1974). Neither rapid stretch nor considerable background muscles contraction were given in our experiments, however. We therefore assume that this short-range stiffness played no considerable role in our experiments. Instead, we attribute it foremost to reflexive stiffness.

In phase I, torque velocity essentially followed stimulus velocity (Fig. 3A). A particular finding in normals was that torque velocity with the 18.4°/s stimulus was higher during head-only than during trunk-only rotation. This can be explained mainly by a head inertia effect stemming from head rotation (Fig. 2C). This notion was confirmed by our simulations (compare Fig. 6C). A minor contribution from the vestibulo–collic reflex cannot be excluded, though. The torque–angle plots shed a different light on the data. They show that the stiffness slopes of phase I are similar across all trunk-only and head-only responses, amounting to approximately \(-0.1\) Nm/° (see oblique comparison lines in Figs. 4A, B). Only with the 18.4°/s stimulus was the initial stiffness slightly higher.

Whereas torque velocity and stiffness of phase I were similar across subject groups, the parameters related to its end differed. A qualitative feature common to both groups was that the higher peak velocity of the stimuli was, the earlier phase I ended. Quantitatively, the duration values in normals were shorter than in patients, and their variability was smaller (Fig. 3B). As a consequence of the duration effects, the torque magnitude reached at the end of phase I was largest with the fastest stimulus, again qualitatively similar and quantitatively different in both groups (Figs. 4A, B). Interestingly, the parameter fit procedure in our simulations (see below) suggested that phase I end is related to both, a time consuming process (delay time) and an amplitude dependent process (magnitude threshold and gain) of the presumed suppression mechanism, with clear differences in the parameters between the two subject groups.

The present data did not allow us to directly measure the onset latency of the phase I response because our stimuli showed a gradual rise, as did the torque responses. We therefore refer to data from a study that applied a more appropriate method (abrupt stimulus onset, EMG measurements). The work of Ito et al. (1995) distinguishes between subjects with functioning vestibular system and vestibular loss, observing EMG onset latencies of \(\approx 20\) ms and \(\approx 55\) ms after abrupt head drops, respectively. In our study, vestibular head stabilization can largely be neglected, since vestibular stimulation during head + trunk rotation yielded no responses upon the 2.3°/s and 4.6°/s stimuli and only a transient response upon the 18.4°/s stimulus. The latter could be explained by head inertia (see above). We therefore assume that the torque responses stemmed mainly from a proprioceptive loop and that this has a delay of 55 ms (this loop was used in our simulations, see below).

A latency of 55 ms is considerably longer than the 20 ms onset latency of the short-latency reflexes known for passive arm movements (see Introduction). We therefore consider the 55 ms response a medium to long-latency reflex. The absence of a short-latency neck reflex can possibly be related to previous findings of a relatively weak direct excitatory connection of muscle spindles to neck motoneurons in the cat (Abrahams and Richmond, 1988; Richmond and Loeb, 1992). At any rate, since the phase I end of our subjects' torque responses occurred clearly later than 55 ms, we feel rather safe in assuming that the torque suppression involves supra-spinal mechanisms.

Phase II torque response

The most outstanding difference between normal controls and PD patients concerned the ability to level off further rise in torque after phase I. This led us to suggest that PD rigidity results from insufficient suppression of the reactive resistive torque that is evoked upon passive joint rotation. In the following, we focus on the per-rotatory part of phase II (response till rotation end, i.e. until final stimulus position was reached). The subsequent slow post-rotatory torque decay will be considered in the modeling part (‘adaptation time constant’).

If we consider, by comparison, previous studies, the leveling off corresponds to a ‘flattening’ of the torque–time or torque–angle curves after the stimulus onset transient (to be distinguished from transients occurring at the turning points during periodic stimuli with triangular waveform, for instance). The leveling off can be seen in qualitative similar manner in figures of the afore mentioned studies, despite differences in the joint tested as well as in stimulus wave form and velocity (axial: Wright et al., 2007; \(1°/s\) periodic triangular horizontal rotations; Mak et al., 2007, 60–105°/s hip flexions and extensions; limb: Xia and Rymer, 2004; 50°/s triangular periodic wrist flexions–extensions). In our stiffness data, the leveling off can best be appreciated by the deviations of the torque slopes from the 0.1 Nm°/s comparison lines in Figs. 4A, B. Interestingly, when increasing peak stimulus velocity from 2.3°/s and 4.6°/s to 18.4°/s, it became less pronounced in normals and more pronounced in the patients. As a result, the differences between the two subject groups became less with the 18.4°/s stimulus. This suggests that fast stimuli are less suited for parameter estimation in normals vs. patients with the 18.4°/s stimulus to be accounted for? Considering first the effect in normals, their weaker leveling off with the high stimulus velocity can be explained by a delay in the suppression mechanism, as suggested by our simulations (distinct from the 55 ms proprioceptive loop delay). The delay is even longer in patients. However, how is then the
slightly improved suppression in patients with the 18.4°/s stimulus to be explained? We tend to explain it with a signal-to-noise effect. Assuming that the torque suppression involves a higher processing level, we expect that patients profited from the 18.4°/s stimulus in that this provides them with better sensory input than the slower stimuli (e.g. via the bite boards, through dental shear forces). An analogous assumption might explain why patients showed a more efficient torque suppression with the head-only as compared to the trunk-only 18.4°/s stimulus. The former, unlike the latter, adds a further stimulus modality (vestibular; strongest with 18.4°/s stimulus, since the horizontal canals provide a velocity signal). An additional point is that the head-only stimulus is likely perceptually better identified than the trunk-only stimulus, since one is more familiar with head on trunk rotations than with trunk rotations under a stationary head.

How does our hypothesis of an impaired voluntary suppression of reflexive muscle tone in PD relate to other proprioceptive impairments of these patients previously reported in the literature (see Introduction)? We like to speculate that there is a common underlying problem in the proprioceptive sensorimotor integration of PD patients, caused by abnormally large internal noise and unwanted oscillations (compare Moran et al., 2008). Our own previous work on stance control in PD patients revealed an abnormal tendency for high frequency/velocity body oscillations (Maurer et al., 2003). Using a dynamic stance control model, parameter fitting suggested noise to be a relevant factor (Maurer et al., 2004). It remains to be seen whether and to what extent the main findings in the present simulations (see below): changes in threshold, gain, and delay times, represent primary deficits or secondary attempts of patients to compensate for the noise and oscillations (compare Janson et al., 2004).

Our hypothesis of rigidity resulting from insufficient voluntary control of reflexive proprioceptive joint stabilization would explain a number of earlier observations. For instance, it would explain why PD patients show reduced leg swinging during the pendulum leg test (Le Cavaizin et al., 2003) and reduced head oscillations during pseudorandom back-forth oscillations of the trunk (Gresty, 1989).

Previous literature gives a hint as to the suppression mechanism itself. Xia and Rymer (2004), investigating fast passive wrist exten-
sion–flexion cycles, related the “lead-pipe” character of PD rigidity to flattening in the torque–angle relation. They attributed the flattening to so-called “shortening reactions” they observed in the EMG of the corresponding muscles. Such shortening (as well as lengthening) reactions have originally been described in animal preparations and humans with brain damage (see Tatton et al., 1984, and Gurfinke1 et al., 2006, for literature). They consist of an active muscle shortening that can be observed to occur upon, and along with passive shortening. According to Gurfinke1 et al. (2006), however, they represent a physiological mechanism. These authors investigated passive axial rotations in healthy normal subjects and found shortening reactions in about half of them. In PD patients, the reactions appear not to be enhanced or more frequent (Wright et al., 2007). How are intermittent active contractions during passive muscle shortenings to be interpreted? We interpret them as evidence for a stiffness servo control mechanism that levels off reflexive joint stabilization, i.e. for the presumed voluntary torque suppression mechanism (details below).

We assume a supra-spinial loop for the suppression mechanism, since normal subjects are able to voluntarily titrate the resistive torque upon passive movements (making it larger or smaller, or even reverse it). And, in PD patients, it is a common clinical experience that rigidity is related to the perceptual awareness of the passive joint stimulus. When one is testing a wrist joint, for instance, rigidity becomes enhanced if one succeeds to shift the patient’s perceptual awareness away from the tested hand. This may be achieved, for instance, by having her or him perform a demanding finger-to-thumb tapping sequence with the other hand. In contrast, a simple tapping task that can be performed automatically has no such effect. We conceive that the perceptual awareness effect may also be responsible for the “activated rigor” phenomenon, where the patient is asked to actively contract the contra-lateral limb (Webster, 1960).

Model of voluntary control of reflexive joint stabilization

Our model of proprioceptive head stabilization is shown in Fig. 5. Unlike in previous head control models (see Introduction), a vestibular feedback is omitted and the relevant proprioceptive

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**Fig. 5.** Dynamic control model of reflexive proprioceptive head stabilization and its voluntary suppression (details in Supplementary Materials). The model contains two proprioceptive negative feedback loops for head stabilization: PROP, autogenic short-latency spinal reflex (dashed; not relevant in neck; see text), PROP′: supra-spinial long-latency reflex loop. Box Biom. (for biomechanics) contains passive viscous-elastic elements, considered to be relatively weak. Box High Level Proprioceptive-Motor Integration contains mechanism of voluntary suppression. When switched on (Switch 2), it derives a tracking signal from PROP′ (box TR) and adds it after some delay with positive sign to the Set Point Signal. This partially neutralizes the negative PROP′ feedback, leading to leveling off of resistive torque. In our experiments, Switch 1 was open: torque and head inertia effect, measured before switch, did not evoke head movements, because head was strongly fixed via bite board to head rotation device. Stimuli affecting loop are head-space and head–trunk rotations (obtained through turntable and head gear rotations).
feedback loop PROP′ is given a 55 ms latency (for reasons, see above). For simplicity, PROP′ is given ideal transfer characteristics (unity). Details of the model are given in Supplementary Materials (SM) together with parameter lists and additional simulation results that we will mention, but not show in the following.

Using automatic parameter fits to determine the parameter of our model, we first considered the phase I response of normals and patients. We determined the proportional, P, and derivative, D, factors of the controller for proprioceptive joint stabilization. Simulations showed that they are also well suited for voluntary head movement control (see SM). In a subsequent step, we implemented the voluntary suppression of the reflexive joint stabilization. As already considered by Houk (1979), there are basically two possibilities. One would be a direct attenuation of the proprioceptive negative feedback loop. The other possibility is to neutralize the negative feedback by feeding a similar signal, but with a positive sign, into the set point input of the control (for early concepts of such a supra-spinal servo-regulatory control of stiffness, see Houk, 1979). We chose this solution and refer to it in the following as ‘set point servoing’. We implemented it into the model by obtaining a tracking signal from PROP′ (TR in box High Level Proprioceptive–Motor Integration of Fig. 5). This is then passed through a threshold, a gain element, and a delay time, before adding an adaptive decay and feeding it into the set point input. If the mechanism is switched on once (Switch 2), it neutralizes the negative feedback in a gradable way.

One reason why we preferred the set point servoing solution is that it preserves the PROP′ loop. Consider the situation where a subject is suppressing reflexive resistance to a slow passive head movement, while suddenly a rapid inertial force is acting on the head. Preserving the PROP′ loop protects against the rapid force, since the torque suppression via the high-level mechanism has a considerable additional delay. If, instead, we used a high-level mechanism that directly weakens PROP′, the additional delay would not allow for immediate protection. A further factor to be mentioned in this context is that the suppression becomes less effective with fast movements (see normals’ responses to 18.4°/s stimuli; effect is well mimicked in our simulations). Admittedly, there exists also a passive (viscous-elastic)

![Fig. 6. Simulated torque–time curves of normals and PD patients using the model of Fig. 5 (presentation as in Figs. 2A–C).](image-url)
resistance from muscle and joint elements (box Biom. in Fig. 5), but we consider it to be relatively weak (compare Maurer et al., 2006).

Applying the parameter fitting to the elements of the serving mechanism in the model, we considered all torque responses obtained with the trunk-only and head-only rotations, comparing patients with normals. Patients showed higher gain, G = 0.93 vs. G = 0.70, slightly higher position threshold, T = 0.7° vs. T = 0.6°, and prolonged delay time, Δτ = 161 ms vs. Δτ = 103 ms. The mean square fitting error across all responses indicated a good correspondence between simulated and experimental data for patients and normal subjects (0.012 and 0.011, respectively; a value of zero/unity error refers to zero/unity gain when expressing the difference between experimental and simulated responses in terms of gain). The simulated torque-time curves are shown in Figs. 6A–C. They closely resemble the experimental ones (Figs. 2A–C).

Conclusion

We take the experimental and model findings as support for our hypothesis that PD rigidity represents incomplete suppression of proprioceptive head stabilization. We relate the impairment in the patients mainly to an increased delay time, enlarged threshold, and reduced gain of the set point serving signal that they use for the suppression.

Acknowledgments

DFG Ma 2543/3-1; Me 715/5-3; ELKE, University of Athens.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.expneurol.2009.03.010.

References


