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Oscillatory Head Movements in Cervical Dystonia: Dystonia, Tremor, or Both?

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Abstract

Cervical dystonia is characterized by abnormal posturing of the head, often combined with tremor-like oscillatory head movements. The nature and source of these oscillatory head movements is controversial, so they were quantified to delineate their characteristics and develop a hypothetical model for their genesis. A magnetic search coil system was used to measure head movements in 14 subjects with cervical dystonia. Two distinct types of oscillatory head movements were detected for most subjects, even when they were not clinically evident. One type had a relatively large amplitude and jerky irregular pattern, **and** the other had smaller amplitude with a more regular and sinusoidal pattern. The kinematic properties of these two types of oscillatory head movements were distinct, although both were often combined in the same subject. Both had features suggestive **of** a defect in a central neural integrator. The combination of different types of oscillatory head movements in cervical dystonia helps to clarify some of the current debates regarding whether they should be considered as manifestations of dystonia or tremor and provides novel insights into their potential pathogenesis.

Keywords

torticollis; neural integrator; cerebellum; midbrain; basal ganglia

Cervical dystonia is the most common adult-onset focal dystonia.[1] In addition to abnormal head postures, 28 **to** 68% of patients have additional abnormal head movements often described as tremors.[2–9] Because the nature of these additional movements is a matter of current debate, we use the term "oscillation" here to avoid confusion.[10–12] Clinically **one can** discern two different types of oscillatory head movements. One is a relatively regular oscillation with a frequency of 3 **to** 9 Hz.[4,13] Another is irregular and jerky**,** with a frequency typically between 0.1 **and** 0.5 Hz.[13] Despite many studies, the nature and pathogenesis of these oscillatory head movements remain uncertain.

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Most prior studies have focused on the regular head oscillations in cervical dystonia. Some investigators have viewed them as a tremor analogous to essential tremor.[3–5] Evidence in support of this view includes several phenomenological similarities with essential tremor, including regularity, sinusoidal appearance, relatively small amplitude, and frequency. Additional evidence includes a high prevalence of limb tremor in cervical dystonia patients, a high frequency of isolated tremor in family members, and therapeutic responses to anti-tremor medications. Other investigators, however, have taken the view that these oscillatory head movements are a manifestation of dystonia.[7,8,14–17] The evidence supporting this view includes observations that they can precede the appearance of overt dystonia, they often are accompanied by signs of dystonia, and they sometimes respond to anti-dystonic medications.

Fewer studies have focused on the jerky head oscillations or spasmodic movements. Some investigators view the jerky head oscillations as dystonic tremor, noting irregular amplitudes and varying frequencies. [14,15] Other investigators designate the jerky or spasmodic movements as “head jerks” or “spasms” rather than tremor, despite their somewhat rhythmic tempo.[2,3]

Many factors have contributed to the different views of oscillatory head movements in cervical dystonia. The first is that some studies included relatively small or nonrepresentative patient populations.[7] For example, one study described an unusually high frequency of tremor in 30 patients with cervical dystonia, but the occurrence of parkinsonism in 10 of them suggests an atypical population.[18] Other studies were larger but included subjects with broader segmental and generalized patterns of idiopathic dystonia, secondary dystonias due to drugs or trauma, and psychogenic dystonias.[5] Thus, different conclusions may result from heterogeneity in the study population.

A second factor contributing to the different views of oscillatory head movements is that most studies relied on clinical assessments, often from retrospective review of charts or databases. These methods may be influenced by investigators’ preconceived notions, and they lack sensitivity. More importantly, discriminating components of a mixed disorder by clinical examination alone can be challenging. For example, one study found that head tremors above 10 Hz could be detected with electromygraphy but were not clinically visible,[14] and another documented distinct bursting patterns that did not correspond to clinical diagnoses of essential or dystonic tremors.[4] Thus, variations in the frequency and nature of the oscillatory head movements in cervical dystonia reflect the methods used to evaluate them.

A third factor contributing to different views of oscillatory head movements has been varied and evolving usage of the term “tremor” in dystonia.[4,14] Several investigators have used the term “dystonic tremor” to designate only the jerky head oscillations, in keeping with original descriptions for this term.[19] Others have used the same term to refer to any oscillatory head movements in cervical dystonia. In recognition of this inconsistent terminology, a committee of the Movement Disorders Society proposed dystonic tremor to be redefined as any oscillatory movement in a dystonic body part.[20] This definition provides an easily applicable terminology for clinical use. However, it does not accommodate mixed disorders and conflicts with prior studies suggesting **that** the oscillatory head movements of cervical dystonia may reflect a combination of different disorders.[3–5,21–24] Because of these limitations, the newer definition of "dystonic tremor" has not been uniformly adopted. The proper nosological classification of the oscillatory head movements in cervical dystonia is more than an academic pursuit, **because** it has direct implications for pathophysiology and treatment.[15]

We recently began to evaluate more closely the nature of oscillatory head movements in patients with cervical dystonia. Our results shed light on the 20-year-old debate by demonstrating at least two overlapping subtypes of head oscillations.[13] One subtype has greater amplitude and lower frequency; it appears jerky, with a sawtooth-shaped waveform corresponding to early definitions of dystonic tremor. Its kinematic features suggested that it is not really a tremor, but instead it has properties analogous to gaze-evoked nystagmus of the eyes. These results help to explain why it may not behave like other tremors.[13] Another subtype seen in some of the same patients had sinusoidal waveforms.[13] The sinusoidal head oscillations had significantly smaller amplitude and higher frequency as compared **with** jerky head oscillations.[13] Importantly, these distinct types of oscillations could not be discriminated by typical clinical evaluations. Here we scrutinize these sinusoidal head oscillations, compare their kinematic properties with the jerky oscillatory head movements, and provide a hypothetical framework for their pathogenesis.

Methods

The study was approved by the Johns Hopkins University Institutional Review Board, and all subjects signed informed consent before participating. Fourteen subjects with idiopathic isolated cervical dystonia were evaluated, **regardless of** whether head oscillations were clinically apparent. All patients routinely received botulinum toxin for the treatment of cervical dystonia. Our studies were performed approximately 3 months **after** their last injections, to ensure **that** dystonic symptoms were present. We excluded subjects who had **a** known or presumed cause for dystonia, broader involvement suggestive of multifocal, segmental, or generalized dystonia, parkinsonism, essential tremor, and those with features suggestive of a more widespread neurodegenerative disorder. All 14 subjects had head oscillations; **five** had only the irregular and jerky oscillations**, and nine** had both irregular and regular oscillations.

Head movements were recorded using a dual search coil (Skalar, Delft, The Netherlands) mounted on the forehead. Subjects sat in the magnetic coil frame such that the center of the inter-pupillary line coincided with the center of the frame. The orientation of the search coil with respect to the magnetic coil frame was sampled at 1000 Hz, and the data w**ere** processed to compute head positions in three dimensions.[25]

The subjects wore a laser pointer mounted on a headband and turned their head to align the projection of the laser with light-emitting diode targets located 2 m ahead of the subject at 0 **degrees**, and to the right or left at 10 **degrees**, 20 **degrees**, and 30 **degrees**. Subjects were asked to keep their head steady at each orientation, and we recorded horizontal, vertical, and torsional head positions. Three-dimensional head positions were analyzed using Matlab (The

Mathworks, Natick, MA). Head velocity was computed from mathematical derivations of head position. Noise inherent to the signal acquisition and mathematical derivations (Matlab statistics toolbox) was removed by a Savitzky-Golay filter.

The head position signal was de-trended to assess the properties of sinusoidal head oscillations. We separately processed data from each axis and their composite vector (square root of the sum of the squared position signal from the three planes).

A cycle-by-cycle analysis was performed on smoothed three-dimensional composite vectors. The X-coordinates of the intersection of the trace with the abscissa (moving from the negative value to the positive value) were recorded. The X-coordinate of the first data point that crossed the abscissa marked the beginning and the subsequent data point marked the end of a cycle. The cycle width was computed by measuring the difference between two crossings. The inverse of the cycle width yielded the cycle frequency**,** and the difference between the peak and trough yielded the amplitude (Fig. 1).

Results

Figure 1A illustrates a subject with cervical dystonia who attempted to hold the head straight ahead. The head position traces show two types of oscillatory head movements. One type has a low frequency, high amplitude**,** and jerky (sawtooth) waveform (Fig. 1A, B). Superimposed is another type that is regular, sinusoidal, and with higher frequency but smaller amplitude (Fig. 1A, C). These two types of oscillatory head movements were separately studied. The jerky head oscillations were isolated by applying a high-frequency filter to remove the more rapid oscillations, and the sinusoidal head oscillations were isolated by detrending the larger waveforms.

Amplitude of Sinusoidal Head Oscillations

Our previous studies showed that the jerky head oscillations are dependent on the position of the head relative to the torso.[13] Here we show that the sinusoidal head oscillations also depend on the orientation of the head. In the subject shown in Figure 2, the amplitude is smaller when the head is turned 30 **degrees** to the right. Conversely, the amplitude increases when the head is turned to the left. This effect of head position on oscillation amplitude was consistently seen in all **nine** subjects. Figure 3 summarizes the relationship of mean amplitude of sinusoidal head oscillations measured during 20-s epochs at various head orientations for all **nine** subjects who had them. For all subjects**,** the amplitude of head oscillations depended systematically on head position. The amplitude increased while turning the head to the right and decreased while turning left for subjects 2, 3, and 5. The opposite trend was seen for subjects 1, 3, 4, 5, 7, 8, and 9. The maximal amplitude varied between 0.4 **degrees and** 10.7 **degrees**, but **it** was less than 2 **degrees** in all except subject 1.

We asked subjects to let their head drift into its most preferred orientation to determine the clinical null (Fig. 4, dashed black line). Although the clinically determined null positions correlated strongly with head orientations **in which** the jerky head oscillations were minimal**,**[13] they did not correlate with the head orientations **in which** the sinusoidal head oscillations were minimal (correlation coefficient=0.22; P=0.56). These differences suggest that jerky and sinusoidal head oscillations have distinct physiological mechanisms.

Frequency of Sinusoidal Head Oscillations

Although the amplitudes of the sinusoidal head oscillations depended on the orientation of the head on the body, their frequencies did not (Fig. 2). Figure 4 summarizes the relationship of the mean frequency of sinusoidal head oscillations measured during 20-s epochs of various head orientations. The frequency of sinusoidal head oscillations remained relatively constant despite changing head-on-trunk orientations, with an overall average of 4.4±0.8 Hz (mean±**standard deviation**).

We recently showed that jerky head oscillations in cervical dystonia had kinematic properties that resemble gaze-evoked nystagmus of the eyes, findings that could be predicted by impairment in a neural integrator for head motor control.[13] These findings raise **a** question regarding whether the sinusoidal head oscillations also originate from a defective neural integrator. A key feature of sinusoidal eye oscillations resulting from a defective neural integrator is that just after rapid movements and when the movement ends, the oscillations return at a different phase; hence there is a phase reset.[26] Figure 5 illustrates a subject with cervical dystonia **in which** the phase of horizontal oscillations resets from −18.2 **degrees** to 0.03 **degrees** after voluntary horizontal head movements (Fig. 5A, B). Similar phase changes were noted in vertical head oscillations from 39.6 **degrees** to 160.0 **degrees** after a rapid horizontal head movement (Fig. 5C, D).

Figure 5E, F summarizes the phase resets after voluntary rapid head movements for all **nine** subjects as a polar histogram. Phase resets were observed for all cases. The mean phase change was 177.0±109.9 **degrees** for horizontal head oscillations (Fig. 5E) and 159.4±112.6 **degrees** for vertical head oscillations (Fig. 5F).

Discussion

Consistent with clinical impressions, our measurements indicate that head oscillations in cervical dystonia comprise at least two distinct subtypes. One subtype is jerky and irregular**,** with features that correspond to early definitions of “dystonic tremor.” The other is sinusoidal and regular, resembling more closely the tremor of “essential tremor.” The results provide important insights into current debates regarding the nosological relationships between dystonia and tremor.

Sinusoidal Head Oscillations in Cervical Dystonia and Essential Tremor

Several kinematic features of the sinusoidal head oscillations in cervical dystonia resemble essential tremor of the limbs**,** including their sinusoidal pattern, regularity, relatively small amplitude, and frequency. These findings may not be surprising, **because** many patients with cervical dystonia often have limb tremors that clinically resemble essential tremor.[2,3,7,17,21] In many patients, tremor is not limited to the limbs but may affect other body regions, such as the head. Many authorities have questioned the concept of essential head tremor based on the clinical phenomenology and co-existence of dystonia.[8] Our studies provide strong support for a mixed disorder, combining sinusoidal oscillatory head movements that resemble the tremor of essential tremor with jerky coarse head oscillations corresponding to early definitions of "dystonic tremor." If this is the case, the more recent definition of "dystonic tremor" as any oscillatory movement in a dystonic body part erroneously combines two very different types of movement as if they are the same.

These two types of oscillatory head movements in cervical dystonia cannot be discriminated on routine clinical examination, but they were readily evident on quantitative head movement measurements. In our subjects, the sinusoidal head oscillations had a frequency ranging from 4 **to** 6 Hz (Fig. 4), which falls in the range of frequencies reported for essential tremor of the limbs (4–10 Hz).[27] Larger body parts with heavier weight and bigger inertia, such as **the** head, necessarily oscillate at lower frequencies than smaller and lighter body parts, such as the fingers or the hand. For example, the resonance frequency of the fingers is 25 Hz, **and that of** the hands is 6 **to** 8 Hz.[27]

Head Orientation Dependence of Sinusoidal Head Oscillations

Head orientation modulated the amplitude of sinusoidal head oscillations, but its frequency remained unaltered. Selective attenuation of amplitude but not frequency may result from mechanical exaggeration of oscillations **because of** muscle activation at certain head-on-trunk orientations, while dampening by passive muscle stretch at the head orientation in the opposite direction. This phenomenon could be analogous to dampening of the amplitude of essential tremor of the hands with weight loading without influencing its frequency.[28,29] Alternatively, the head position dependence of the sinusoidal oscillations might reflect changes in the processing of proprioceptive or efference copy signals of head position by the neural networks that normally hold the head still.

Neural Correlates of Sinusoidal Head Oscillations

Contemporary theories view dystonic disorders as system-level circuit disorders rather than disorders linked to a single brain region.[30–32] We recently proposed that jerky head oscillations corresponding to dystonic tremor result from a defect in the circuit involving a neural integrator for head position.[13] Prior studies in nonhuman primates have suggested that this integrator is likely to be located within or near the interstitial nucleus of Cajal and nearby nucleus of Darkschewitsch.[33,34] The results of the current studies show that the neural integrator hypothesis **also** can explain the regular sinusoidal head oscillations.

Normal neural integration relies on cerebellar, visual, proprioceptive, and efference copy feedback. Disruption of such feedback results in drifts in head position in humans or nonhuman primates.[13,33,34] Neural integrators are usually bilateral but must communicate.[35] Abnormal feedback to the ocular motor neural integrator leads to sinusoidal oscillations of the eyes.[26] The phase of these oscillations is vulnerable to the bursts of excitatory or inhibitory stimulation, being reset after eye saccades.[26] We predicted that instability in the head neural integrator, in presence of abnormal feedback, causes sinusoidal head oscillations. The reset in the phase of sinusoidal oscillations after rapid head movements supports the idea that the head neural integrator in cervical dystonia has abnormal feedback (Fig. 5). Alteration in the frequency of head oscillations **also** can explain the change in their phase. However, the head movement did not affect the oscillation frequency in our patients (Fig. 4).

Proposals regarding the interstitial nucleus of Cajal or surrounding areas as neural integrators for head position do not necessarily imply that pathology in cervical dystonia is intrinsic to these regions. Abnormal afferent inputs to bilaterally symmetric integrators may lead to functional asymmetry and subsequent instability leading to sinusoidal head oscillations. Anatomical studies have shown that the major inputs to the interstitial nucleus of Cajal arise from several regions previously implicated in cervical dystonia**,** including the cerebellum.[36–39] Furthermore, the nucleus of Darkschewitsch, an area around the interstitial nucleus of Cajal, receives projections from substantia nigra and zona incerta.[40] The nucleus of Darkschewitsch then sends projections to the cervical spinal cord for head movements.[41]

In summary, these results reveal two distinct forms of oscillatory head movements in patients with cervical dystonia. One with sinusoidal trajectories resembles the tremor of essential tremor**, and** the other**,** traditionally called "dystonic tremor**,**" has kinematic features typical for head nystagmus.[13] Both types of oscillatory head movements may result from impaired function of the neural integrator controlling head movements.

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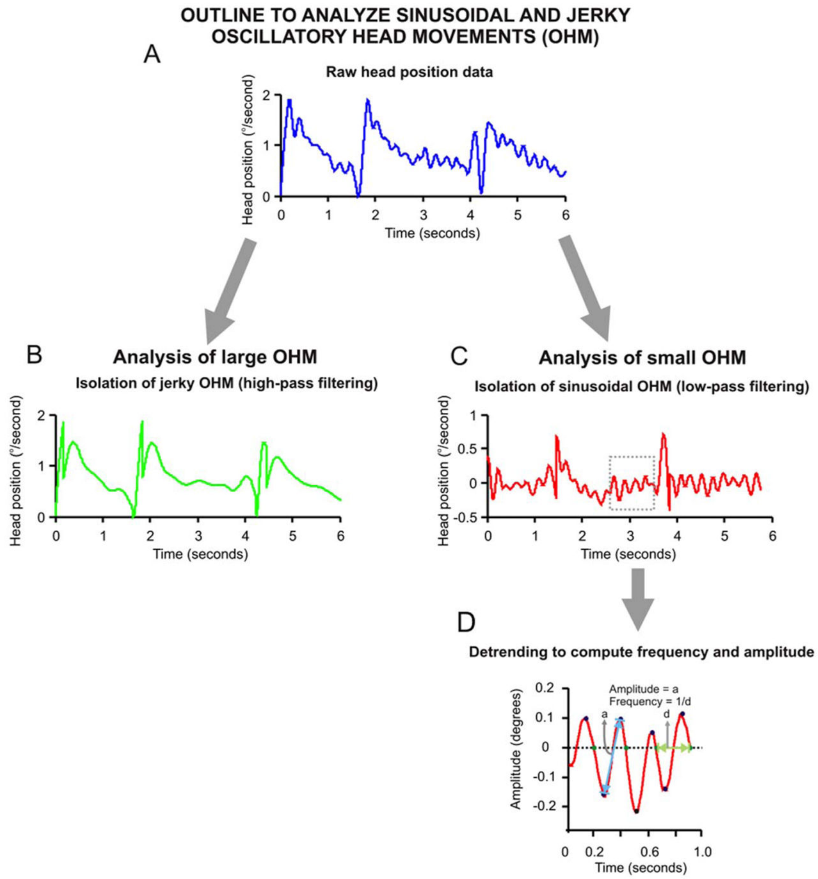

FIG. 1.

An example of oscillatory head movements from a subject with cervical dystonia attempting to hold the head steady. Head positions are plotted on the *y*-axis, and time is plotted on the *x*-axis. (A) The raw trace of head position shows two types, with small regular oscillatory head movements superimposed on larger irregular oscillatory head movements. (B) Sinusoidal oscillatory head movements was separated from jerky oscillatory head movements by using low-pass filtering. Green trace illustrates low-pass filtered waveform that characterizes jerky oscillatory head movements. (C) Epochs of high-pass filtered small oscillatory head movements separated from the same epoch showed in this panel. (D) Detrended signal was aligned to zero by de-trending and offsetting by its mean value. The *x*-coordinate of the intercept between composite vector (red trace) moving from high to low and zero-line (black dashed line) is acquired (zero-crossing, green symbols in the figure). The difference between such zero-crossing assessed cycle width (or period) and the inverse of the period is frequency of the given cycle. The amplitude of the cycle was computed by measuring the difference between peak to trough (ie, difference between blue symbols in the figure). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com]

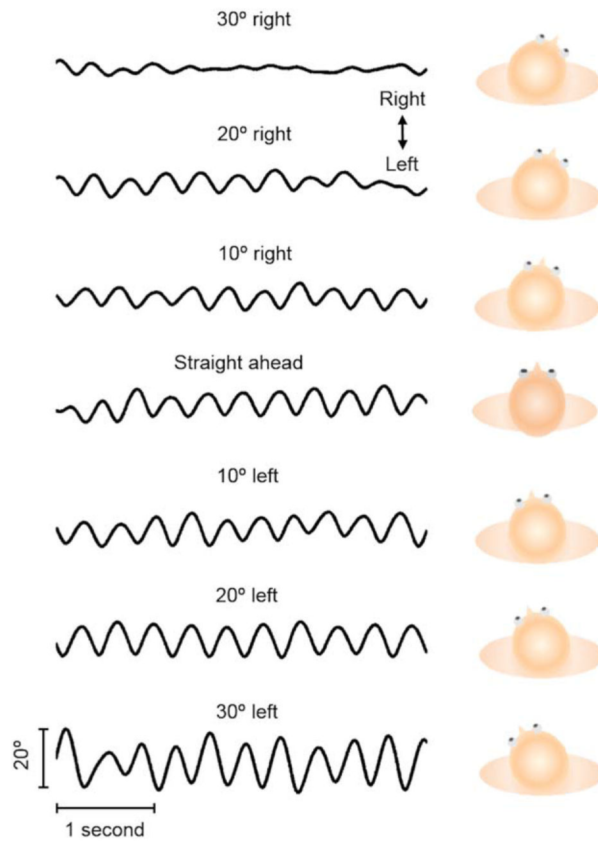

FIG. 2.

An example from a subject with cervical dystonia aiming the head in different positions to show the effect of different head positions on the amplitude of the small sinusoidal oscillatory head movements. Traces depict head position versus corresponding time. Positive deflections are rightward movements, whereas negative deflections are leftward movements. Caricatures next to trace depict the degree of head turn on the trunk. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com]

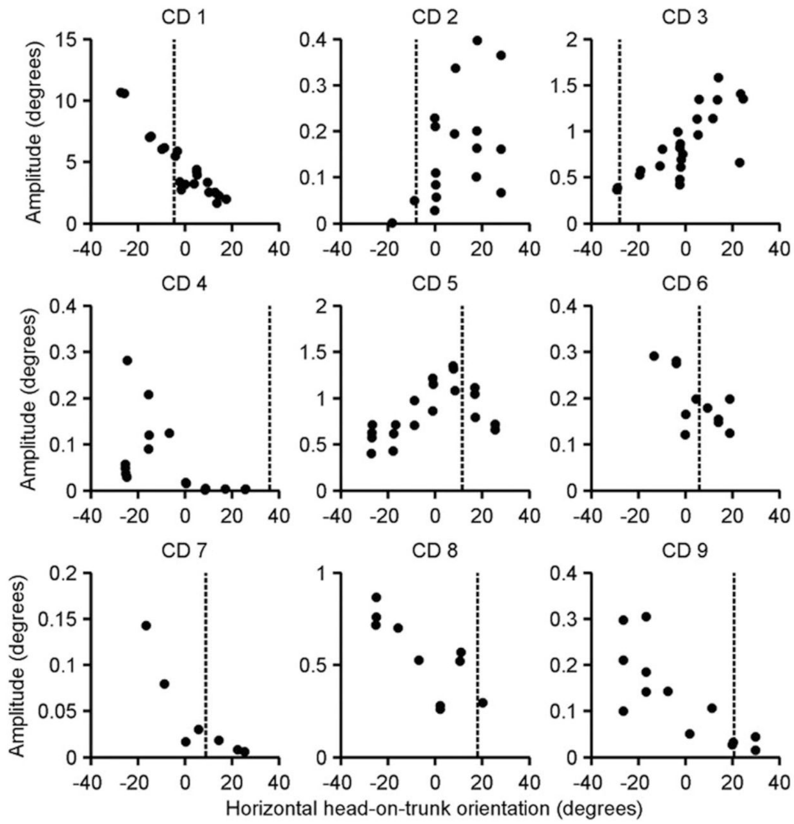

FIG. 3.

Position-dependent amplitudes of sinusoidal oscillatory head movements for all nine cervical dystonia subjects. The mean amplitudes of oscillatory head movements during 20-s epochs are plotted on the *y*-axis, whereas head orientations are plotted on the *x*-axis. Each data point depicts one observation over 20 s, and each panel illustrates one subject. The amplitude of oscillations changes with the head-on-trunk orientation. The intercept of the linear fit through the data depicts the "null" position for a given patient. The dashed vertical line depicts the location of the head on trunk at the time of maximal attenuation of dystonic tremor.

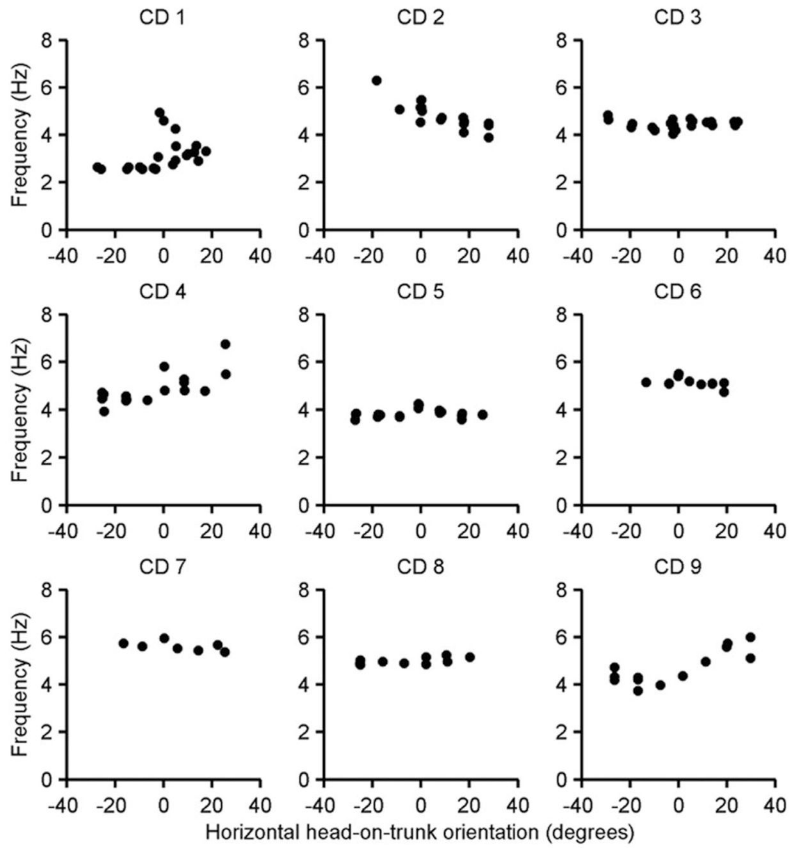

FIG. 4.

Example of head-on-trunk orientation dependence of the frequency of sinusoidal oscillatory head movements. Mean frequency 20-s epochs of eccentric head-on-trunk orientation is plotted on the *y*-axis, whereas corresponding head orientation is plotted on the *x*-axis. Each data point depicts one observation over 20 s, and each panel illustrates one subject. The frequency of oscillations remains insensitive to the head-on-trunk orientation.

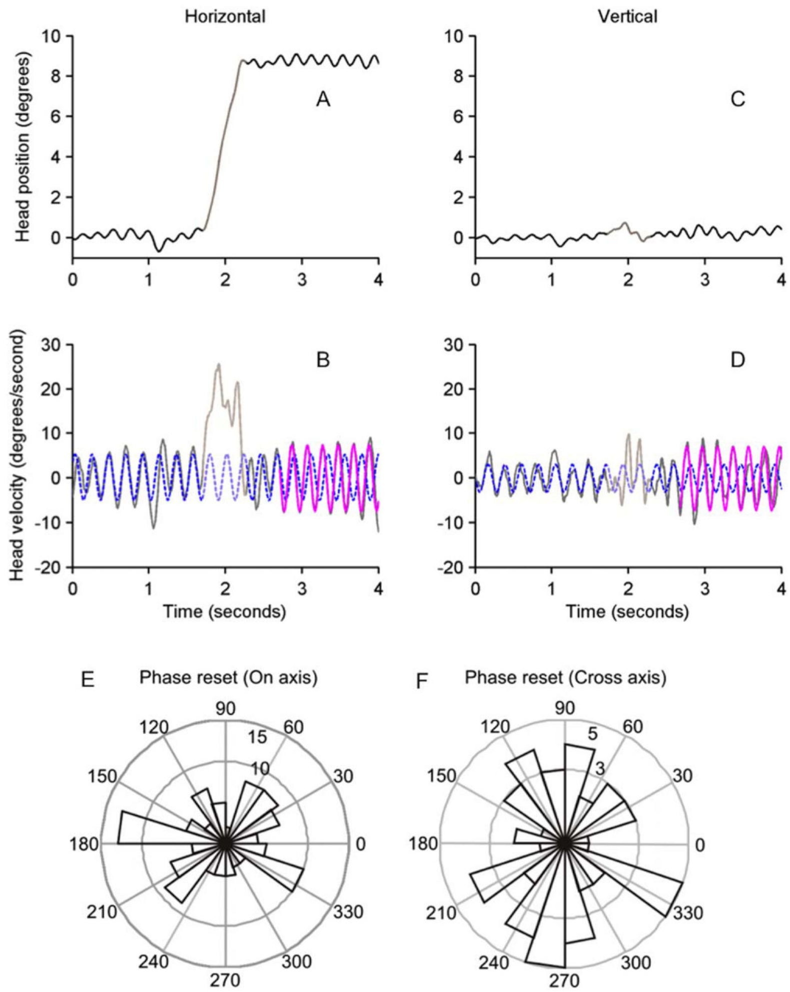

FIG. 5.

Influence of rapid voluntary horizontal head movement on oscillatory head movements in subjects with cervical dystonia. Panels A and C depict horizontal and vertical head positions, respectively, whereas panels B and D depict corresponding head velocities. Head positions and velocities are plotted on the *y*-axis, and the *x*-axis depicts corresponding time in seconds. Panels A and B depict the effects of voluntary horizontal head movement on the phase of oscillations. The phase was computed by determining the shift in the phase of sinusoidal fit in head velocity trace before voluntary head movement (blue dashed line) and after the voluntary head movement (magenta line). The same analysis is done for the effect of horizontal head movement on vertical head oscillations. Thus, phase shift after rapid horizontal head movement is measured for (on-axis) horizontal and (cross-axis) vertical head oscillations. Polar histograms show that in all instances there was a phase shift. Bins of the phase shift are plotted on the perimeter of the circle, and the bars at the spokes of the circle depict the number of instances that fall in a range of phase shift depicted by a given bin. D represents the summary of the phase shift of horizontal oscillations, whereas E is a phase shift of vertical oscillations. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com]