of PD patients present normal DAT imaging findings,[4,10] recent evidence suggests that these patients probably do not have PD,[13] indicating that normal DAT SPECT probably rules out neurodegenerative Parkinsonism. Conversely, it is important to keep in mind that DAT imaging is also normal in nondegenerative Parkinsonism such as L-dopa–responsive dystonia,[14] drug–induced Parkinsonism,[4] or vascular Parkinsonism,[15] disorders that should be considered before PsyP diagnosis.

Prognosis of PsyP is far from benign, and symptoms and signs frequently persist despite an adequate treatment.[1,2] Thus, only 1 of our patients recovered from PsyP. Although prognosis of psychogenic movement disorder may depend greatly upon the underlying psychiatric disturbance, several reports indicated that those patients with shorter duration of psychogenic movement disorder seem more likely to recover.[1] DAT imaging can support the clinician's suspicion of PsyP and, consequently, could be useful in advancing its diagnosis and enhancing the chances of recovery.

In conclusion, DAT imaging is useful as a supportive diagnostic tool in the evaluation of suspected PsyP. In cases of suspected PsyP with a high degree of certainty, DAT imaging is usually normal, supporting its diagnosis. In patients for whom the diagnosis of PsyP is less certain, DAT imaging is probably more useful. In this setting, DAT imaging can sometimes show decreased striatal tracer uptake, suggesting an underlying neurodegenerative Parkinsonism and should encourage the search for additional causes for the syndrome. Appropriate prospective studies need to be conducted to demonstrate if DAT SPECT helps at all in advanced PsyP diagnosis, and, therefore, improves the outcome of these patients.

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Open-Label Pilot Study of Levetiracetam (Keppra) for the Treatment of Chorea in Huntington's Disease

Theresa A. Zesiewicz, MD, FAAN,[1–3]*
Kelly L. Sullivan, MSPH,[1,3]
Robert A. Hauser, MD, FAAN,[1,3,4]
and Juan Sanchez-Ramos, MD, PhD[1–3]

[1]Parkinson's Disease and Movement Disorders Center and Department of Neurology, University of South Florida, Tampa, Florida, USA; [2]James A. Haley Veterans Administration Hospital, University of South Florida, Tampa, Florida, USA; [3]National Parkinson Foundation Center of Excellence, University of South Florida, Tampa, Florida, USA; [4]Department of Pharmacology and Experimental Therapeutics, University of South Florida, Tampa, Florida, USA

Abstract: **The objective of this study is to evaluate the tolerability and preliminary efficacy of levetiracetam (LEV) in reducing chorea in Huntington's disease (HD) patients in**

*Correspondence to: Dr. Theresa A. Zesiewicz, University of South Florida, 12901 Bruce B. Downs Blvd., MDC Box 55, Tampa, Florida 33612. E-mail: tzesiewi@hsc.usf.edu

Received 21 November 2005; Revised 15 February 2006; Accepted 18 April 2006

Published online 28 August 2006 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/mds.21061

a prospective open-label pilot study. Nine HD patients with chorea were treated with LEV in doses up to 3,000 mg/day for up to 48 days. The primary endpoint measure was the Unified Huntington's Disease Rating Scale (UHDRS) chorea subscore. The mean dose (±SD) of LEV at endpoint was 2,583.3 ± 1,020.6 mg/day. Mean UHDRS chorea score decreased from 12.6 ± 3.0 at baseline to 6.7 ± 4.3 at endpoint ($P = 0.01$). There was no significant change in UHDRS total motor scores (38.8 ± 11.4 at baseline and 33.6 ± 26.7 at endpoint; $P = 0.24$). Somnolence contributed to a 33% drop-out rate, and 3 patients developed Parkinsonism. Results of this open label study suggest that LEV may be efficacious in reducing chorea in HD patients. © 2006 Movement Disorder Society

Key words: **levetiracetam; Keppra; chorea; Huntington's disease**

Huntington's disease (HD) is a hereditary neurodegenerative disorder characterized by the progressive loss of neurons in many regions of brain with early loss of medium-sized spiny neurons of the striatum.[1] Clinical signs include chorea, dementia, behavioral disturbances, and balance impairment.[2] Chorea, when moderate to severe, can cause major disability and can have a significant negative impact on day-to-day function.[3] Currently, no drug is approved for the treatment of chorea. Drugs that block dopamine transmission (neuroleptics) or prevent vesicular storage of cathecholamines (reserpine) may be effective but have side effects such as postural hypotension and diarrhea that limit their use.[4,5]

Levetiracetam (LEV; (*S*)-alpha-ethyl-2-oxo-1-pyrrolidine acetamide; Keppra) is an antiepileptic drug that can inhibit hypersynchronization of abnormal neuronal firing in experimental models of epilepsy. LEV is a pyrrolidine derivative with strong specific binding to cerebellar receptors. It has been approved by the Food and Drug Administration as add-on therapy in partial-onset seizures and is chemically related to piracetam, which is used in the treatment of myoclonus.[6,7] We sought to evaluate the tolerability and preliminary efficacy of LEV in reducing chorea in HD patients in a prospective open-label pilot study.

PATIENTS AND METHODS

Patients with HD who were followed at a university movement disorders center were invited to participate in the study. Patients were eligible for inclusion in the study if they had HD confirmed by HD CAG analysis and a Unified Huntington's Disease Rating Scale (UHDRS) chorea subscore of 10 or higher. Additional inclusion criteria included a Hamilton Depression (Ham-D) Scale score less than or equal to 15, UHDRS dysphagia score less than 2, UHDRS dysarthria score less than 3, and independent ambulation. Patients were required to remain on stable doses of all medications for 4 weeks before study entry and for the duration of the study. Exclusion criteria included pregnancy or lactation; the presence of severe renal disease, or blood urea nitrogen 50% greater than normal; and major neurological, psychiatric, or medical disorders that were judged by the principal investigator to disqualify a patient from entering the study. Patients who met inclusion and exclusion criteria provided informed consent to enter the study. Institutional review board approval for the study was granted through the University of South Florida.

Patients who entered the study were administered oral LEV in tablet form, beginning at a dose of 250 mg/day and increasing by 250 mg every 4 days to a maximum of 3,000 mg/day. Study medication was titrated upward using a four times a day (q.i.d.) schedule to reduce the likelihood of somnolence from higher individual doses. Patients underwent evaluations at baseline and biweekly thereafter for 48 days. Dose adjustments were permitted at each office visit, and further LEV titration could be halted with a patient report of satisfactory chorea control or emergence of side effects. The primary endpoint measure was the UHDRS chorea subscore. Patients were also evaluated using the Clinical Global Improvement Scale and Epworth Sleepiness Scale.

Data were analyzed using nonparametric paired samples analysis. Last observation carried forward was used for patients who prematurely withdrew from the study.

RESULTS

A total of 5 women and 4 men with HD were enrolled in the study (mean age, 51.9 ± 9.3 years; mean UHDRS motor score, 38.8 ± 11.4). All patients were included in the analysis, and 6 patients completed 48 days of treatment. There were 3 patients (33%) who discontinued the study prematurely (2 patients on day 1 taking LEV 250 mg/day, and 1 patient on day 9 taking LEV 750 mg/day) due to somnolence.

The mean dose of LEV at endpoint was 2,583.3 ± 1,020.6 mg/day. Mean UHDRS chorea score decreased from 12.6 ± 3.0 at baseline to 6.7 ± 4.3 at endpoint in the intention-to-treat (ITT) group ($P = 0.01$; Table 1). For the 6 patients who completed the study, mean UHDRS chorea scores decreased from 13.2 ± 3.3 at baseline to 5.8 ± 4.0 at endpoint ($P = 0.003$). There was no significant change in UHDRS total motor scores in the ITT group (38.8 ± 11.4 at baseline and 33.6 ± 26.7 at endpoint, $P = 0.24$) or the completers group (39.83 ± 17.13 at baseline and 33.33 ± 29.26 at endpoint, $P = 0.40$). Of the 7 patients who completed at least 1 week of the study, 6 (86%) reported minimal to marked improve-

TABLE 1. *Changes from baseline to endpoint with LEV treatment*

	Baseline	Post-LEV (day 48 completers only)	Post-LEV LOCF
Mean age	51.89 ± 9.25	–	–
Male sex, n (%)	4 (44)	–	–
UHDRS (motor) (mean ± SD)	38.75 ± 17.35	33.33 ± 29.26	33.57 ± 26.71
UHDRS (chorea)(mean ± SD)	12.63 ± 2.97	5.83 ± 3.97[a]	6.71 ± 4.30[a]
UHDRS (dystonia)(mean ± SD)	2.75 ± 4.62	4.80 ± 8.67	4.00 ± 8.00
ESS score (mean ± SD)	3.83 ± 5.64	6.00 ± 8.94	4.43 ± 7.79

[a]$P < 0.01$ compared to baseline.

LEV, levetiracetam; LOCF, last observation carried forward; UHDRS, Unified Huntington's Disease Rating Scale; ESS, Epworth Sleepiness Scale.

ment in chorea and 3 reported improvement in HD symptoms.

Two patients developed Parkinsonism: one at day 41 (dose = 500 mg/day) and one 4 months after completing the study (dose = 3,000 mg/day). Symptoms included rest tremor in the extremities, increased rigidity, bradykinesia, and imbalance, stooped axial posture, and hypophonia. In both cases, symptoms of Parkinsonism resolved after discontinuation of LEV, and chorea increased to baseline. Concurrent medications at the time Parkinsonism developed were, for the first patient, olanzapine 5 mg/day, donepezil 10 mg/day, paroxetine 30 mg/day, trazodone 100 mg/day, furosemide 80 mg/day, oxybutynin 15 mg/day, and Neurontin 900 mg/day and for the second patient, alprazolam 0.75 mg/day, Risperdal 1.5 mg/day, and Celebrex 200 mg/day for the second patient.

DISCUSSION

In this open-label pilot study, LEV significantly reduced chorea in HD patients. UHDRS motor scores decreased, but not significantly. Somnolence contributed to a 33% drop-out rate, and prohibited remaining patients from reaching maximum allowable LEV dose. These preliminary study results suggest that LEV is efficacious in reducing chorea in HD patients. However, the study is limited by its small sample size, and the changes seen could be due to placebo effect.

Recent studies have suggested that LEV can reduce established levodopa-induced dyskinesia in animal models of PD.[8,9] In a study by Hill and colleagues, LEV (60 mg/kg) significantly reduced L-dopa–induced dyskinesia in methyl-phenyl-tetrahydropyridine *N*-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-lesioned marmosets.[10]

Two patients developed Parkinsonism during the study. Although both patients experienced a reduction in chorea with LEV, they also developed rest tremor, increased bradykinesia and rigidity, stooped axial posture, imbalance, and hypophonia. These signs resolved within 7 days of discontinuation of LEV in both patients. The mechanism by which LEV induces Parkinsonism is not clear. The clinical observation of Parkinsonism suggests the possibility that it may have an antidopaminergic effect, although interactions with concomitant medications cannot be excluded. One patient took donepezil, a reversible acetylcholinesterase inhibitor, in addition to LEV, and a possible interaction between LEV and donepezil might theoretically cause Parkinsonism. Animal models indicate that LEV facilitates cholinergic function, and Parkinsonism due to enhancement of cholinergic function has been reported.[11,12] It is also possible that additional interactions between LEV and other medications taken by the patients (olanzapine, paroxetine, trazodone, oxybutynin, furosemide, gabapentin, risperdidone) contributed to the observed side effects. For example, olanzapine is a dopamine receptor antagonist with an affinity for muscarinic receptors,[13] and LEV might have increased the absorption or decreased the metabolism of olanzapine.

Our open-label pilot study indicates that LEV may be effective in treating chorea in HD. There is a need for further tolerability and efficacy studies using LEV in patients with HD.

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Intention Tremor of the Head in Patients With Essential Tremor

Julie Leegwater-Kim, MD, PhD,[1]
Elan D. Louis, MS, MD,[1–3]* Seth L. Pullman, MD,[1]
Alicia G. Floyd, BS,[1] Sarah Borden, BA,[2]
Carol B. Moskowitz, MS,[1]
and Lawrence S. Honig, MD, PhD[1–3]

[1]Department of Neurology, College of Physicians and Surgeons, Columbia University, New York, New York, USA; [2]G.H. Sergievsky Center, College of Physicians and Surgeons, Columbia University, New York, New York, USA; [3]Taub Institute for Research on Alzheimer's Disease and the Aging Brain, College of Physicians and Surgeons, Columbia University, New York, New York, USA

Video 

Abstract: **Patients with essential tremor (ET) have kinetic arm tremor; this tremor can also have an intentional component. We are unaware of reports of intention tremor of the head in ET. Our aims were to describe, provide electrophysiological data and video documentation of, and estimate the prevalence of intention tremor of the head in our sample. Ten (9.0%; 95% confidence interval = 4.7%–14.3%) of 111 patients had intention tremor of the head; in 7 it involved the neck and in 3 the chin. These patients trended toward having more severe kinetic arm tremor and they had more severe intention tremor of the arms. These observations provide further support for the evolving view that the cerebellum may be involved in ET.**

Key words: essential tremor; intention tremor; head tremor; cerebellum

The predominant clinical finding in patients with essential tremor (ET) is arm tremor.[1,2] This tremor is primarily a kinetic tremor but patients may also exhibit a postural tremor.[1,2] ET patients with longstanding disease may also develop a tremor at rest in their arms.[3,4] Finally, there is an intentional or terminal component to arm tremor in many ET patients (i.e., the tremor increases in amplitude at the endpoint of goal-directed movement such as finger-to-nose testing).[5] The presence of intention tremor provides additional evidence, along with imaging studies,[6–8] electrophysiological studies,[5,9–12] and case reports,[13] for the evolving view that the cerebellum may be involved in the pathogenesis of ET.

Tremor commonly affects other body regions besides the arms in ET patients, and postural tremor (tremor while seated or standing) may occur in the head in 34% to 53% of patients.[14–18] We report another type of head tremor, intention tremor of the head, which is phenomenologically distinct from postural head tremor and, to our knowledge, has not been described previously. We used the term "head tremor" to refer to tremor involving structures (e.g., the chin) that are part of the head or are connected to the head (e.g., the neck). Our two primary aims are to describe and provide video and electrophysiological documentation of intention tremor of the head in patients with ET, and to estimate the prevalence of this tremor in our sample of ET patients. A secondary aim is to begin to explore some of the possible clinical correlates of this type of tremor. Our overarching goal is to provide further support for the accumulating literature that suggests that the cerebellum is involved in ET.[5,9–12]

PATIENTS AND METHODS

ET patients are being recruited as potential brain donors to the Essential Tremor Centralized Brain Repository at Columbia University.[19] Participation in the program entails completion of demographic and medical questionnaires and creation of a videotaped tremor ex-

This article includes Supplementary Video, available online at http://www.interscience.wiley.com/jpages/0885-3185/suppmat

*Correspondence to: Dr. Elan D. Louis, Unit 198, Neurological Institute, 710 West 168th Street, New York, NY 10032.
E-mail: edl2@columbia.edu

Received 29 March 2005; Revised 15 March 2006; Accepted 18 April 2006

Published online 7 September 2006 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/mds.21079