Changes induced by levodopa and subthalamic nucleus stimulation on parkinsonian speech

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Changes Induced by Levodopa and Subthalamic Nucleus Stimulation on Parkinsonian Speech

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Abstract: Levodopa (l-dopa) and subthalamic nucleus (STN) stimulation treatments have been associated with both improvement and exacerbation of dysarthria in Parkinson’s disease (PD). We report four cases illustrating variant responses of dysarthria to dopaminergic and STN stimulation therapies. Patients’ motor disability and dysarthria were perceptually rated by the United Parkinson’s Disease Rating Scale (UPDRS) in four conditions according to medication and STN stimulation. Dedicated software packages allowed acquisition and analysis of acoustic recordings. Case 1, who had a severe off period aphonia, experienced improvement of speech induced by both levodopa and STN stimulation. In Case 2, both treatments worsened speech due to the appearance of dyskinasias. Case 3 had a dysarthria exacerbation induced by STN stimulation with parameters above optimal levels, interpreted as current diffusion from the STN to corticobulbar fibers. In Case 4, dysarthria exacerbation occurred with stimulation at an electrode contact located caudally to the target, also arguing for current diffusion as a potential mechanism of speech worsening. The presented cases demonstrated variant effects in relation to l-dopa and STN stimulation on speech. It seems that motor speech subcomponents can be improved like other limb motor aspect, but that complex coordination of all speech anatomical substrates is not responsive to STN stimulation. These hypotheses may be helpful for better understanding and management of STN stimulation effects on motor speech and skeleton–motor subsystems. © 2005 Movement Disorder Society

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Dysarthria in Parkinson’s disease (PD) can frequently appear in the later stages of the disease, which is often concomitant with the appearance of motor fluctuations induced by levodopa (L-dopa). Axial signs such as dysarthria are known to be less responsive to L-dopa administration than the other symptoms. After 10 or years or longer of dopatherapy, axial signs including dysarthria, freezing of gait, and postural reflexes for most of the PD patients worsen, unlike the limb tremor, rigidity, or akinesia, which can still be improved by dopamine replacement therapy. Regarding dysarthria, L-dopa has been associated with improvements and exacerbations of speech. These variable effects could be related to the partial involvement of the dopaminergic system and basal ganglia in speech production, as well as degeneration of nondopaminergic structures. Functional neuroimaging studies have revealed an underactivation of the main motor cerebral regions (primary motor cortex, cerebellum) and an overactivation of premotor and prefrontal cortices to represent the cerebral basis of parkinsonian dysarthria.

The results of surgery in the basal ganglia for the treatment of PD depend on the structure targeted and the surgical technique employed. It has been recognized that lesions of the ventral intermediate nucleus of the thalamus (VIM), the internal globus pallidus (GPi), or subthalamic nucleus (STN), which alleviate PD symptoms, can induce a worsening of speech, especially if surgery is performed bilaterally. This is most likely because of the proximity of all three targets to the corticobulbar fibers. Deep brain stimulation (DBS) of the thalamus was introduced to avoid the side effects induced by the lesion, but VIM stimulation has also been shown to induce a worsening of speech. As stimulation parameters can be adjusted, exacerbation of dysarthria following VIM stimulation would generally not be severe. However, some speech impairment might be accepted by patients as a compromise for a better tremor control. Ventroposterolateral pallidotomy, dorsal subthalamotomy, and stimulation of both targets have been proposed more recently in parkinsonian patients to improve not only tremor, but also akinesia. If akinesia is improved, then parkinsonian dysarthria might also be expected to improve. However, neither ablative surgeries nor stimulation of the pallidum result in any significant improvement in terms of speech. Regarding stimulation of the STN, beneficial effects on specific speech components have been observed, such as phonation and articulation. No beneficial effect of STN stimulation has been reported on intelligibility.

Thus, even if the use of pharmacological or surgical therapies is generally beneficial for the treatment of akinesia, rigidity, and tremor of the limbs, this effect is not always observed on parkinsonian speech. In particular, it is not well understood why the response of speech to STN stimulation differs from that of other parkinsonian signs. In this study, we report four illustrative cases that demonstrate variable, including oppositional, speech effects in response to L-dopa therapy and STN stimulation. Hypotheses pertaining to responsible underlying neural mechanisms have been discussed.

**PATIENTS AND METHODS**

Preoperatively, the patients’ global motor disability was rated using part 3 (maximal score, 108) of the Unified Parkinson’s Disease Rating Scale (UPDRS) in on and off L-dopa conditions. In this scale, dysarthria was rated perceptually by item 18, and speech impairment was scored from 0 (normal) to 4 (unintelligible). Clinical characteristics of the patients have been reported in Table 1. All four patients had electrodes implanted for STN

**TABLE 1. Clinical and perceptual assessments of global motor state and speech by means of the UPDRS**

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (yr)</th>
<th>PD duration (yr)</th>
<th>Presurgery</th>
<th>Postsurgery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Off medication</td>
<td>On medication</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>UPDRS Speech</td>
<td>UPDRS Speech</td>
</tr>
<tr>
<td>1</td>
<td>43</td>
<td>14</td>
<td>52</td>
<td>4</td>
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<tr>
<td>3</td>
<td>47</td>
<td>8</td>
<td>63</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>60</td>
<td>12</td>
<td>37</td>
<td>1</td>
</tr>
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</table>

Clinical assessments and acoustic recordings were made at 3, 5, 5, and 3 years after the surgery for Patients 1, 2, 3, and 4, respectively. The age of the patients and the PD duration correspond to those at the time of surgery. The maximal score of the global motor UPDRS is 108, and the maximal score of item 18 is 4. On medication refers to a state reached using a suprathreshold dose of L-dopa, and ON stimulation state refers to optimal electrical parameters allowing beneficial therapeutic effects based on limb motor assessment.

**Key words:** Parkinson’s disease; dysarthria; speech; L-dopa; subthalamic nucleus stimulation

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stimulation according to the surgical procedure previously described. Postoperatively, patients’ global motor disability and dysarthria were perceptually rated utilizing the UPDRS in the four following conditions: off medication/OFF stimulation, off medication/ON stimulation, on medication/ON stimulation, and on medication/OFF stimulation (Table 1). The on medication conditions corresponded to states reached with a suprathreshold dose of L-dopa, and the ON stimulation conditions referred to the chronic optimal parameter settings (Table 2). These assessments were conducted 3, 5, 5, and 3 years post-surgery for Patients 1, 2, 3, and 4, respectively.

Acoustic recordings were obtained for each patient with a head-worn microphone (ATM 71; Audio Technica, Stow, OH). Voice was recorded at a 16 kHz sample frequency using a computerized acquisition technique (Phone´dit; SQ Lab, Aix-en-Provence, France) and analyzed by means of dedicated software (CSL 4150; Kay Elemetrics, Lincoln Park, NJ). The patients were asked to sustain the vowel /a/ for as long as possible on a single deep breath. This task provided the data for further analysis of relative speech intensity and phonation time during the different examination conditions. In the absence of absolute sound pressure level measurements, which is the case in this study, the relationship between the vertical scale of the displayed signal on the one hand, and sound intensity (or loudness) on the other hand, is ambiguous. However, the same mouth–microphone distance and recording levels were used across measurements, and the signals could thus be compared with each other, allowing for the evaluation of intraindividual improvement or deterioration of relative speech intensity. Patients 1, 2, and 3, native French speakers, were also asked to repeat during 30 s the sentence “Le petit chat joue avec la balle” (the little cat plays with the ball) at a conversational rate. Patient 4 was a native English speaker and was asked to repeat during 30 s the sentence “Buy Bobby a puppy.” This second task (repetition of sentences) allowed us to assess particularly changes in speech rate during the different examination conditions. These acoustic recordings were conducted at the same time as the clinical assessments, established as 3, 5, 5, and 3 years postsurgery for Patients 1, 2, 3, and 4, respectively. These recordings were obtained during the classical drug and STN stimulation postoperative adjustment period.

**Case 1: Improvement Induced by L-Dopa and/or STN Stimulation**

Preoperatively, Patient 1 suffered from a severe off period dysarthria, up to complete aphonia, which responded well to L-dopa. The complete aphonia in this patient was possibly linked to laryngeal dystonia. Dysarthria was rated 4/4 and 3/4 by item 18 of the UPDRS in the off and on medication conditions. After the surgery, dysarthria of Patient 1 remained severe in the off medication/OFF stimulation condition (Table 1). In this state, acoustic analysis revealed aphonic speech: no sustained phonation of the vowel could be produced (Fig. 1A). For the same task, an improvement was observed either ON stimulation or on medication conditions. Stability and amplitude of loudness were two parameters that demonstrated improvement following STN stimulation despite a short phonation time (Fig. 1B). An improvement of speech intensity induced by a suprathreshold dose of L-dopa was observed (Fig. 1C) but was not as effective as those changes observed in loudness stability following STN stimulation. No further improvement was observed in the combined on medication/ON stimulation condition (Fig. 1D) compared to the two previous conditions.

In this case, STN stimulation mimics the effect of L-dopa, which was effective for the off period aphonia.

**Case 2: Impairment Related to L-Dopa-Induced Dyskinesias**

For Patient 2, acoustic recordings in the off medication/OFF stimulation condition (Fig. 2A) revealed a dysarthria mainly characterized by a reduced vocal loudness

### Table 2. Therapeutic parameters of STN stimulation

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Voltage (V)</th>
<th>Frequency (Hz)</th>
<th>Pulse width (µs)</th>
<th>Contact</th>
<th>Voltage (V)</th>
<th>Frequency (Hz)</th>
<th>Pulse width (µs)</th>
<th>Contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left side of the brain</td>
<td>Right side of the brain</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3.6</td>
<td>145</td>
<td>60</td>
<td>3</td>
<td>3.6</td>
<td>130</td>
<td>90</td>
<td>2</td>
</tr>
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<td>3</td>
</tr>
<tr>
<td>3</td>
<td>3.3</td>
<td>170</td>
<td>60</td>
<td>0</td>
<td>3.3</td>
<td>185</td>
<td>60</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>3.6</td>
<td>185</td>
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<td>3</td>
<td>3.6</td>
<td>185</td>
<td>60</td>
<td>3</td>
</tr>
</tbody>
</table>

These parameters were adjusted in order to reach optimal effects in terms of limb motor control. The contact (negative; the case was positive) refers to the localization of the stimulation, chosen among the four possibilities offered by the quadripolar electrode (type 3387 for Patient 3 and type 3389 for Patients 1, 2, and 4; Medtronic, Minneapolis, MN).
and relatively preserved articulation (rated 3/4 by item 18 of the UPDRS; Table 1). Dysarthria was exacerbated by STN stimulation, characterized by increased variability in both rate and loudness (Fig. 2B). Following a suprathreshold L-dopa administration, the acoustic analysis in the on medication/OFF stimulation condition revealed a mild worsening of speech compared to the OFF state.

FIG. 1. Acoustic signal obtained during sustained phonation of the vowel /a/ by Patient 1 during the off medication/OFF stimulation (A), off medication/ON stimulation (B), on medication/OFF stimulation (C), and on medication/ON stimulation (D) conditions. A illustrates the off period aphonia of the patient whose noisy breathiness was the only production possible. With STN stimulation (B), improvement of speech was notably observed in vowel relative intensity, which reached normal values in this state. With L-dopa (C), speech was improved compared to the off/OFF state, but the improvement was not as significant as the one reached with STN stimulation in terms of relative intensity stability. Combination of the two treatments (D) did not reveal any better improvement than the OFF state. On the left side of the figure, the amplitude of the waveform data illustrates the speech recording signal; the related measure of speech loudness (relative intensity) is shown on the right. On medication refers to a peak-dose state after administration of a suprathreshold dose of L-dopa; ON stimulation parameters were the following: 3.6 V, 145 Hz, 60 μs, contact 3 (negative; case, positive) for the left side of the brain, and 3.6 V, 130 Hz, 90 μs, contact 2 (negative; case, positive) for the right side of the brain. i and e: inspiration and expiration related to a phonation attempt in the off/OFF state.

FIG. 2. Acoustic signal obtained during repetition of a short simple sentence by Patient 2 during the off medication/OFF stimulation (A), off medication/ON stimulation (B), on medication/OFF stimulation (C), and on medication/ON stimulation conditions (D). Compared to the off/OFF state (A), voice quality was impaired by both treatments: (1) number of sentences produced decreased following STN stimulation (13 sentences during state A vs. 10 sentences during state B) but the voice amplitude was relatively conserved; (2) no change on the produced sentence number was observed following L-dopa administration (13 sentences in both states A and C), but the voice amplitude was more affected and a fatigability of the production was noticed at the end of the task. In the on/ON state (D), with seven sentences produced and a marked impairment of voice quality, a greater speech difficulty was demonstrated when L-dopa and STN stimulation were combined. The amplitude of the waveform data illustrates the speech recording signal. On medication refers to a peak-dose state after administration of a suprathreshold dose of L-dopa; ON stimulation parameters were bilaterally the following: 4 V, 130 Hz (right), 160 Hz (left), 60 μs, contacts 3 (negative; case, positive; right), 2 (negative; case, positive; left).
medication/OFF stimulation state. This slight aggravation was mostly due to the appearance of dyskinesias that affected speech production, especially in the last four sentences of the task (Fig. 2C). A more severe exacerbation of dysarthria was observed during the on medication/ON stimulation condition: even if speech loudness could achieve an acceptable level, speech rate decreased drastically, reflecting greater speech difficulty (Fig. 2D).

In this patient, both 1-dopa and STN stimulation exacerbated dysarthria, possibly associated with the evocation of dyskinesias.

Case 3: Impairment Induced With STN Stimulation Above Optimal Level

Patient 3 suffered from a mild 1-dopa–responsive dysarthria, rated 1/4 and 0/4 by item 18 of the UPDRS in the preoperative off and on medication conditions (Table 1). Following 5 years of surgery, dysarthria worsened in the off medication/OFF stimulation condition (Fig. 3A), characterized by a reduction of speech loudness and inspiratory volume and a high degree of fatigability. Dysarthria responded well to the STN stimulation (Fig. 3B): vocal loudness increased and pauses during sentence production disappeared. A dysarthria exacerbation (marked decrease in loudness, long pauses between sentences, alteration of articulatory quality), however, appeared to be induced subsequent to administration of a suprathreshold dose of 1-dopa (Fig. 3C), as well as when voltage and pulse width stimulation parameters were raised to above optimal parameters (from 3.3 V/60 μs to 3.6 V/90 μs; Fig. 3D).

For this patient, exacerbation of dysarthria when using parameters above the optimal level could be explained by current diffusion outside the target.

Case 4: Impairment Corresponding to Stimulation of a Contact Located Outside Target

Patient 4 suffered from a mild dysarthria preoperatively, rated 1/4 and 2/4 in the preoperative off and on medication conditions (Table 1). Following the surgery, speech was stable in the off medication/OFF stimulation condition, although Patient 4 had severe generalized akinesia (Fig. 4A). In the ON stimulation condition, using adequate electrode contact (located at the dorsal border of the STN and the zona incerta) and optimal parameters (Table 2), a mild exacerbation of dysarthria was observed. Coordination between respiration and phonation was more difficult in this state, leading to an altered stability of speech loudness during the sustained phonation and an increased fatigue (Fig. 4B). Indeed, speech worsening represented a subjective complaint from the patient, which was reportedly more obvious with increasing voltage levels. Speech remained impaired in the same way when 1-dopa was administered.
With the patient off medication, bilaterally altering stimulation contacts to the more caudal ones (contacts H11005, whose centers are located 6 mm more caudally than contacts 3, which means below the target) led to a severe exacerbation of dysarthria (Fig. 4D). Speech became almost inaudible and a tremor of the limbs and voice was also observed. This case illustrated a worsening of speech related to stimulation outside the target, underlining that exacerbation of parkinsonian dysarthria may be related to current application outside the STN.

**DISCUSSION**

The four cases we reported illustrated variable changes in dysarthria following L-dopa and STN stimulation treatments for PD. In Patient 1, STN stimulation mimicked the effect of L-dopa. In Patient 2, both L-dopa and STN stimulation induced an exacerbation of dysarthria that can be explained by the generation of dyskinesias induced by both treatments. For Patients 3 and 4, a worsening of speech has been observed with STN stimulation when using above-optimal voltage and pulse width levels relative to limb control (Case 3) or when stimulating a contact electrode outside the STN (Case 4). These exacerbations were interpreted to represent the effects of possible current diffusion outside the target, to neighboring structures such as the corticobulbar fibers. It is noteworthy that frequent discrepancies occurred between clinical ratings and acoustic data, underlying the inconsistent conclusions that assessment of intelligibility and speech subsystems may lead to.

Dopaminergic deprivation induced by the nigrostriatal denervation leads to development of parkinsonian signs, including speech impairment. However, dysarthria and other axial signs are symptoms that might also be linked to the nondopaminergic lesions that characterize disease progression. This is the most commonly accepted explanation as to why dysarthria only partly responds to L-dopa, and much less so than parkinsonism of the limbs. On the other hand, akinesia affects complex motor programs such as speech and handwriting to a greater extent than simple motor tasks. Speech is indeed probably the most complex motor task that we routinely use. It implies coordination of many muscle groups, face, jaw, tongue, pharynx, larynx, and respiratory muscles. This complexity requires various cerebral activations that, compared to hand movements, seem to be differently altered in PD. This therefore may also explain the less effective response of speech to L-dopa and STN stimulation compared to less complex limb movement. L-dopa–induced dyskinesias can also have deleterious effects on speech, so too may STN stimulation as illustrated by Case 2.

It is commonly accepted that functional neurosurgical procedures that involve lesioning of subcortical structures typically leads to a worsening of speech in PD patients. This side effect has been observed following lesions of the thalamus, the pallidum, and the STN. In these cases, worsening of speech may be explained by the proximity of the corticobulbar fibers to surgical targets. Lesions that are too large or misplaced would lead to a pseudobulbar syndrome, especially in bilateral surgery. Some studies have shown, how-

**FIG. 4.** Acoustic signal obtained during the sustained phonation of the vowel /a/ by Patient 4 during the off medication/OFF stimulation (A), off medication/ON stimulation (B), and on medication/OFF stimulation (C) conditions when using an adequate electrode contact location and off medication/ON stimulation (D) condition when using an inadequate electrode contact location. Compared to off/ON state (A), voice quality was improved (B) when the optimal electrode contact was chosen for stimulation [3.6 V, 185 Hz, 60 μs, contacts 3 (negative; case, positive)]. Improved speech was observed when stimulation was coupled with l-dopa (C). Speech worsened (D), however, when a more caudal contact was selected [3.6 V, 185 Hz, 60 μs, contacts 0 (negative; case, positive)]; both vocal loudness and stability decreased. On the left side of the figure, the amplitude of the waveform data illustrates the speech recording signal; the related measure of speech loudness (relative intensity) is shown on the right. On medication refers to a peak-dose state after administration of a suprathreshold dose of l-dopa.
ever, improvements in speech following ablative neurosurgical procedures. With DBS, current diffusion to the corticobulbar and corticospinal fibers can lead to contractions of facial, tongue, pharyngeal, laryngeal, or respiratory muscles, also resulting in dysarthria. For that reason, as opposed to DBS-induced improvement of limb akinesia, improvement of speech is still debated. STN is generally considered the most efficient target for PD treatment, and beneficial effects on speech components have been observed following STN stimulation. By contrast, some studies using perceptual scales such as the UPDRS generally reveal either no significant speech improvement or even worsening of speech. In order to understand these seemingly conflicting results, the different mechanisms illustrated in our case reports need to be considered: (1) respiratory, phonatory, and articulatory components of speech can be improved like other limb motor function (speech subcomponents are improved); (2) complex coordination of all anatomical substrates involved in speech might not be responsive to STN stimulation (intelligibility is not improved); and (3) current diffusion outside the target or target-related dyskinesias may lead to a worsening of speech intelligibility and seems to be a frequent fact (intelligibility can worsen). In other words, item 18 of the UPDRS does not adequately evaluate the often complex speech changes that may result from l-dopa treatment or STN stimulation.

Thus, assessment and treatment of dysarthria in PD is still a challenge for the clinician. First, the UPDRS is insufficient to characterize the dysarthria of PD. Alternative perceptual scales may be used to allow a more accurate description of the presenting dysarthria, including the examination of individual speech subsystems. Second, self-evaluation of patients’ speech must be taken into account, since the patient’s perception of voice seems to reveal more details that can be heard by the clinician. Third, acoustic recording might be a helpful tool to assess changes of phonatory and respiratory subcomponents of speech following treatment. Improvement of speech should not be systematically expected with introduction of l-dopa due to the partial involvement of the dopaminergic system and the basal ganglia in speech function. If STN stimulation is then proposed to the patient, multiple contradictory effects would make it difficult to predict the outcome of the treatment’s impact on speech. In the postoperative management of patients, it is important to determine the stimulation threshold that induces an exacerbation of the presenting dysarthria and to stay, if possible, underneath this threshold. In some patients, a compromise between optimal antiparkinsonian effect and acceptable worsening of speech may have to be chosen.

To conclude, we should say that l-dopa therapy and STN stimulation have similar effects on parkinsonian dysarthria: (1) variable improvement probably inherent to the nature, location, and degree of the denervation; (2) less improvement for dysarthria compared to simpler motor tasks; (3) possible worsening resulting from the appearance of dyskinesias induced by l-dopa or STN stimulation; and (4) STN stimulation may worsen speech related to diffusion outside the target. In that case, ceasing stimulation may reverse these exacerbations, which may be accepted as a therapeutic compromise.

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REFERENCES


Abstract: We report on two cases of sporadic idiopathic Parkinson's disease and motor neuron disease co-occurring in the same individuals. Pathological analysis revealed the presence of Lewy bodies in brainstem nuclei and basal forebrain consistent with Lewy body disease (LBD), as well as motor neuron degeneration and argyrophilic grain disease. We compared our two cases to all previously published pathological cases of combined LBD and motor neuron degeneration. © 2005 Movement Disorder Society

Key words: sporadic idiopathic Parkinson’s disease; motor neuron disease; Lewy bodies; argyrophilic grain disease

Most neurodegenerative diseases are characterized by the predominance of clinical features that result in an identifying syndrome. Personality change, language dysfunction, and behavioral dyscontrol suggest frontotemporal degeneration (FTD), muscle weakness and atrophy with prominent fasciculations suggest a diagnosis of motor neuron disease (MND), and resting tremor, bradykinesia, postural instability, and rigidity suggest a diagnosis of idiopathic Parkinson's disease (iPD). However, there are neurodegenerative diseases in which combined syndromes coexist and even though they are relatively rare they can be recognized by specific features. Parkinsonism, frontotemporal dementia, and MND co-occurring are features suggestive of frontotemporal dementia and Parkinsonism linked to chromosome 17q (FTDP-17) or amyotrophic lateral sclerosis/parkinsonism dementia complex of Guam (ALS/PDC). Frontotemporal dementia and MND (FTD–MND) also coexist and is relatively easily recognized.

The pathological findings in these diseases are known and can be predicted from the presenting clinical features. The deposition of abnormally phosphorylated τ protein characterizes FTDP-17 and ALS/PDC, while the nonspecific protein ubiquitin characterizes FTD–MND. FTDP-17 and ALS/PDC are pathologically characterized by τ-positive intracellular inclusions affecting cortical and subcortical regions. FTD–MND is characterized by the presence of ubiquitin-positive intraneuronal inclusions affecting motor neurons and extramotor neurons in neocortical and hippocampal dentate granular cells.

In this report, we describe the clinical and pathological features of two cases with mixed clinical syndromes that came to autopsy and did not have τ or ubiquitin pathology but were noted to have Lewy bodies and motor neuron degeneration.

PATIENTS AND METHODS

The two cases were seen in our Neurology Department by movement disorders and neuromuscular disease specialists. In both patients, parkinsonism and motor neuron disease were identified on clinical examination. The clinical, laboratory, and imaging data were reviewed.

Neuropathology

At postmortem, the brains of both cases were fixed in 10% formalin for 2 weeks before dissection; 7 µm sections from wet sections were taken from mid-frontal, superior-temporal, and motor cortices, hippocampus, amygdala, medulla, pons, midbrain, cerebral and thoracic spinal cord, and cerebellum. Each section underwent routine histopathological studies, including staining with hematoxylin and eosin (H&E), glial fibrillary acid protein (GFAP), and Gallyas and Bielschowsky silver

Alpha-Synuclein

Immunohistochemistry in Two Cases of Co-occurring Idiopathic Parkinson’s Disease and Motor Neuron Disease

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Alpha-Synuclein

Immunohistochemistry in Two Cases of Co-occurring Idiopathic Parkinson’s Disease and Motor Neuron Disease