

Light and Shade in Patrick Lewis et al's Paper on the First Photographs of Parkinson's Disease

Patrick Lewis et al's article, "Pierre D. and the First Photographs of Parkinson's Disease,"¹ discusses the case of a patient first reported by Albert Boucher (Observation IX) in his MD thesis of 1877,² which was later extended by Paul de Saint-Léger (Observation VII) in his thesis of 1879.³ Pierre D.'s severe bilateral tremor began days after he was lined up against a wall with others to be executed during the Paris Commune; he was spared only because an alert caused the insurgents to flee "leaving behind more dead than alive" (p 54).² A severe, acute-onset postural and action tremor of the hands and head prevented Pierre D. from working as a master mason and made it impossible for him to drink a glass of wine without spilling the contents. This symptom remained

prominent for 6 years until 1877, when after a hospital admission and treatment with sulfurous baths, the tremor improved markedly, becoming limited to a mild quiver of the hands at rest. Considerable improvement in Pierre's stiffness, gait, and speed of movement was also observed, which led Boucher to comment:

"État du malade en janvier 1877. — Son état s'est singulièrement amélioré depuis son entrée à l'hôpital; l'amélioration s'est faite lentement, insensiblement, mais l'état actuel est, sur bien des points, complètement différent de ce qu'il était en septembre 1876" (p 61).²

We interpret this by speculating that Pierre D. either had a nonparkinsonian tremor that disappeared over the years as his parkinsonian stiffness and bradykinesia evolved, or he had a functional tremor in addition to incipient parkinsonism as a consequence of the acute emotional shock. In this regard, there is very little difference between the 2 snippets of Pierre D.'s handwriting taken in 1876 and 1879, both of which showed some tremulousness but no micrographia (although micrographia may have become evident if longer samples of his writing had been recorded). Both Charcot and Gowers were impressed by acute severe stress as a trigger for the emergence of parkinsonian signs,^{4,5,6} and Boucher mentioned another predisposition to its onset favored by Charcot: that Pierre D. had been exposed to a cold, damp environment in his apartment in Auteuil (pp 4–6).² What is more surprising is the apparent sustained moderate improvement in Pierre D.'s rigidity and bradykinesia after his second hospital admission, which, according to St-Léger, had persisted during his 2-year stay in l'Hôpital Bicêtre.

Much of the clinical detail of Pierre D.'s medical history before 1877 — including a snippet of his handwriting dated 1876 — was provided by Dr LTJ Landouzy (who subsequently became Professor of Therapeutics and Dean of the Medical Faculty in Paris), who looked after Pierre on the ward during his first admission to La Charité Hospital, and arranged for Pierre to be photographed.

Lewis et al mistakenly claimed that these images of Pierre D., which were simply dropped into Saint-Léger's thesis and attracted no comment from the author concerning their striking visual features, are the first photographs of the disease (p 1).¹ However, the photograph of Anne-Marie Gavr, taken by Paul Regnard 4 years earlier, appeared in the first volume of *L'Iconographie de la Salpêtrière* in 1875 (p 92),⁷ see Figure 1; Paul Richer's iconic drawing of Gavr followed, which both Boucher (p 52)² and Saint-Léger (pp 96–102)³ refer to in their theses.

In Observation XV, Saint-Léger, who was a pupil of Ernest-Charles Lasègue (not of Charcot's, as stated by Lewis et al), noted that Gavr had come under the care of Charcot at the Salpêtrière in December 1873; Saint-Léger recorded the evolution of her condition covering an 11-year period and thanked M. Bourneville for permission to publish Richer's drawings of her in his thesis (p 96).³ The case descriptions of Gavr demonstrated a clear appreciation of the long-term

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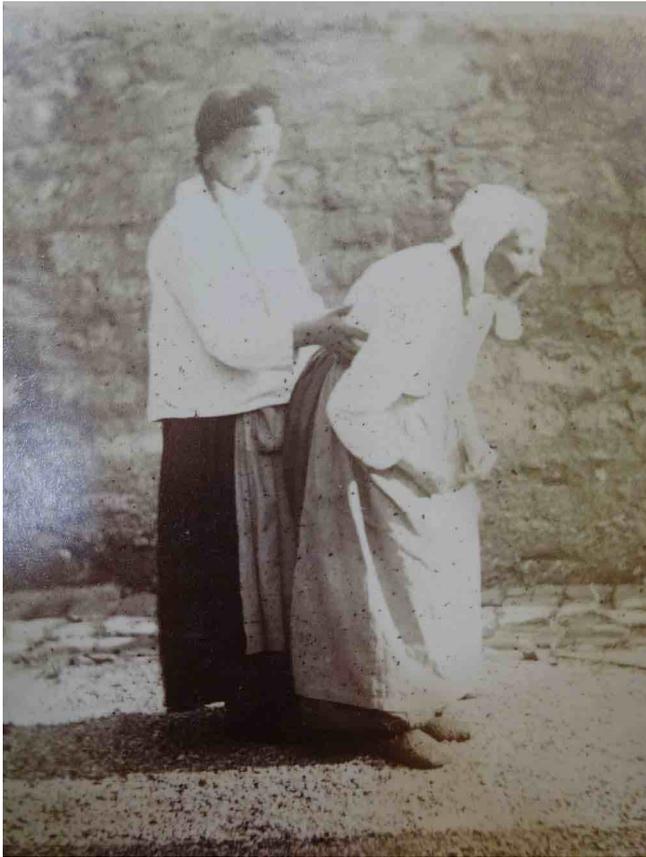


FIG. 1. Anne-Marie Gavr, the first known photograph of a person with Parkinson's disease, photographed by Paul Regnard (volume one of *L'Iconographie de la Salpêtrière*, 1875 (7 planche 92). [Color figure can be viewed at wileyonlinelibrary.com]

nature of her condition, which gives precedence to Regnard's earlier photograph of her over those of Pierre D.

Lewis et al further claim that the clinical descriptions of Pierre D., which spans an 8-year period, provide “a detailed longitudinal aspect to the case that was lacking from James Parkinson's original description of the shaking palsy” (p 1).¹ The authors have underplayed Parkinson's contribution in an attempt to over-egg the significance of their own report. In the Preface to his essay on the shaking palsy, Parkinson wrote:

“The disease is of long duration: to connect, therefore, the symptoms which occur in its later stages with those which mark its commencement, requires a continuance of observation of the same case, or at least a correct history of its symptoms, even for several years” (pii).⁸

His sixth clinical case concerned a 72-year-old man whom Parkinson noted had suffered from the condition for “[a]bout eleven or twelve, or perhaps more, years” (p 15).⁸ In recounting the case Parkinson first summarized its trajectory and divided it into 3 triennial periods and reported that in year 11 the patient suffered a stroke from which he “nearly lost the use of the right side”:

“During the time of their having remained in this state, neither the arm nor the leg of the paralytic side was in the least affected with the tremulous agitation; but as their paralysed state was removed, the shaking returned” (p 16).⁸

Parkinson's sixth case is a detailed and closely observed account whose “longitudinal aspect” is a prominent aspect of the description and confutes Lewis et al's assertion that Parkinson's exemplars were described only “in passing” (p 2).¹ Parkinson's appreciation of the course of the malady is exemplified in relation to a man whose shaking he noticed had completely ceased after 10 years, whom he concluded did not suffer from the shaking palsy. Its “longitudinal aspect” is also apparent in his generic account of the condition, set out in chapter 1 of the essay, which developed a detailed chronological clinical picture of the condition, from onset to death (p 498).⁹ Increasing disability over the years was a constitutive aspect of Parkinson's belief that he had recognized a new syndrome.

The photographs of Pierre D. are striking visual illustrations of the postural abnormalities characteristic of the later stages of Parkinson's disease, but a still photograph can only hint at the changes of facial expression described by Charcot and cannot reliably demonstrate the cardinal features of rigidity, bradykinesia, or tremor found by inspection and neurological examination. For Lewis et al to cast light on the photographs of Pierre D. by placing Parkinson's contribution in the shade goes counter to the historical record. ■

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Reply to: “Light and Shade in Patrick Lewis et al's Paper on the First Photographs of Parkinson's Disease”

We extend our thanks to Profs. Hurwitz, Lees, and Walusinski for their detailed and insightful commentary on our article relating to Pierre D., in particular for bringing to our attention to the photograph of Anne-Marie Gavr, of which we were unaware. ■

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Spinal Cord Stimulation for Parkinson's Disease: Dynamic Habituation as a Mechanism of Failure?

We read with great interest the study from Prasad and colleagues¹ on the effects of spinal cord stimulation on gait in patients with advanced Parkinson's disease (PD), in which no

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Key Words: cycling stimulation, habituation, Parkinson's disease, spinal cord stimulation, noninvasive stimulation

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clinically relevant influence was found over the 12 months of follow-up. We share the authors' view that the variety of stimulation parameters and heterogeneity of the studied population throughout spinal cord stimulation (SCS) trials makes a robust consensus unattainable at present.

We would like to contribute to the discussion with another current delivery strategy. Some PD patients from our practice have had a good initial response to SCS that evolves with a disappointing loss of benefit days to weeks following parameters adjustment. Considering the possibility of habituation, we implemented cycling stimulation as part of our SCS protocol. Surprisingly, this led to some benefit in patients unresponsive to tonic stimulation. To illustrate, we present the case of a 55-year-old male patient with PD and 5 years of STN DBS, with advanced gait problems. Thoracic SCS was performed, and no clear sustained effect was observed despite the various parameter tests at tonic stimulation. We compared cycling stimulation (alternating 15 minutes on-SCS, 15 minutes off-SCS – arbitrary paradigm) to best continuous on-SCS and off stimulation (off-stim); evaluations were made 4 weeks apart from each scenario during on-medication. The patient improved from 17 seconds off-stim to 15 seconds continuous on-stim and 10 seconds cycling on-stim during the 10-m walk test. In addition, he scored 12 on New Freezing of Gait Questionnaire (NFOG-Q) during off and continuous on-stim situations and 9 under the cycling protocol. Although the results were modest and from this single report, we ask whether some of the lack of sustained effect seen could derive from a “short habituation.”

Assuming that motor improvement after SCS in monkeys was strongly associated with desynchronization of aberrant low-frequency corticostriatal oscillations,² SCS could work by replacing pathologically rhythmic in the gait network. The question is: are we efficiently delivering the current to do that? We hypothesize that delivering intermittent trains (ie, varying the interpulse interval [IPI]) could more powerfully break the pathologically disordered neuronal activity into the gait network³ and prevent a possibly “quick habituation” of the stimulated circuitry. A more “chaotic” IPI could minimize the tolerance by avoiding phase-coupling (“adaptation”) of the pathological oscillation with the SCS current.³ Phase resetting is fundamental for the synchronization of different neurons, which might be better generated by reshaping IPI. Notably, chronic SCS in a parkinsonian model of rats applied the current only twice per week (30 minutes per session) and led to significant improvement in symptoms.⁴

Last, despite the negative results reported by Prasad et al, the individual analysis showed different responses – one patient improved freezing by around 50% 1 month after SCS. We wonder whether predictive response for epidural SCS through trans-spinal magnetic stimulation applied before the surgery would be useful. This is an emerging method that activates similar target neural structures noninvasively and has recently been explored in the treatment of spasticity after spinal cord injury.⁵ A pilot trial on PD is ongoing (clinicaltrial: NCT04171076). ■

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