

## Commentary

---

# The Early Treatment Phase in Parkinson's Disease: Not a Honeymoon for All, Not a Honeymoon at All?

Araceli Alonso-Canovas<sup>a,b,\*</sup>, Jos Voeten<sup>c</sup>, Larry Gifford<sup>d</sup>, Omotola Thomas<sup>e</sup>, Andrew J. Lees<sup>f</sup> and Bastiaan R. Bloem<sup>g</sup>

<sup>a</sup>*Movement Disorders Unit, Neurology Department, Hospital Universitario Ramón y Cajal, Madrid, Spain*

<sup>b</sup>*Faculty of Medicine, Universidad de Alcalá, Alcalá de Henares, Spain*

<sup>c</sup>*Rijkswaterstaat, Eindhoven, The Netherlands*

<sup>d</sup>*Parkinson's Africa, London, UK*

<sup>e</sup>*PD Avengers, Vancouver, BC, Canada*

<sup>f</sup>*The National Hospital for Neurology and Neurosurgery, London, UK*

<sup>g</sup>*Department of Neurology, Radboud University Medical Center, Donders Institute for Brain and Cognition, Center of Expertise for Parkinson & Movement Disorders, Nijmegen, The Netherlands*

Accepted 6 February 2023

Pre-press 24 February 2023

Published 9 May 2023

**Abstract.** The discovery of levodopa in the late 60s of twentieth century was a 'golden moment' for people with Parkinson's disease (PD). Unfortunately, clinical experience showed that some symptoms escaped from symptomatic control, and long-term complications developed. Back then, neurologists coined the term "honeymoon period" for the early phase of uncomplicated response to levodopa, and it continues to be used in scientific literature. However, medical terms are no longer restricted to professionals, and few people with PD relate to the notion of a "honeymoon". We examine the reasons why this term, once helpful, but inaccurate and inappropriate, should be abandoned.

**Keywords:** Honeymoon, Parkinson's disease, personalized medicine, patient-centeredness

*Honeymoon (Oxford English Dictionary definition):*

*1a. The period immediately following marriage, as characterized by love and happiness. Later also: a period of love and happiness at the beginning of a similar relationship.*

*1b. An initial period of friendly relations, goodwill, or enthusiasm. Frequently in political contexts.*

*2. A holiday taken by a newly-married couple, traditionally immediately after their wedding.*

---

\*Correspondence to: Araceli Alonso-Canovas, Movement Disorders Unit, Neurology Department, Hospital Universitario Ramón y Cajal, Carr. Colmenar km 9.100, 28034 Madrid, Spain. Tel.: +34 913368821; E-mail: aracelialonsocanovas@gmail.com.

## INTRODUCTION

The discovery of levodopa was truly a miracle for people living with Parkinson's disease (PD) [1]. Following its introduction in the late 60s of the previous century, a highly effective symptomatic treatment became available for a very disabling, progressive condition, changing completely the clinical scenario for affected individuals and neurologists. However, clinical experience made it clear that the initially often excellent (and stable) motor response tended to diminish over time, and that the efficacy would begin to fluctuate across the course of the day, making disease management much more complex [2]. These

response fluctuations appeared quite rapidly in particularly those patients who were already severely affected at the time when levodopa was first introduced. Other treatment-related complications also soon became apparent, including psychiatric issues and orthostatic hypotension [2]. Freezing of gait emerged as a new phenomenon after the introduction of levodopa, not witnessed in the pre-levodopa era [3, 4]. This dramatic change from an initially gratifying improvement into a once again very complicated and debilitating condition is beautifully illustrated in the film “Awakenings”, after the book by Oliver Sacks with the same title [5]. This later treatment phase, dominated by a range of adverse effects, was in stark contrast with the initial treatment phase characterized by a robust and stable clinical improvement. Such observations motivated neurologists to introduce the term “honeymoon period”, to describe the first years as opposed to the later, more complicated phase [6]. This vision also persisted after the introduction of dopamine receptor agonists and other forms of dopamine-replacement therapy.

This term “honeymoon period”, that first appeared in scientific papers in the late 1970s, was originally meant to be used within medical circles, as a pragmatic way of separating the different phases of the disease, specifically the first 2–5 years of stable response, before disabling fluctuations and drug refractory complications emerged [7]. In the past four decades, the term has circulated widely in the scientific literature, neurology books and conferences, becoming synonymous with early-stage PD [8–15]. More recently, a “second honeymoon” has been introduced to describe the excellent therapeutic response that many persons with fluctuating PD may experience in the first months after receiving deep brain stimulation [16, 17]. As such, the use of these terms has long served a useful role in the intercollegiate communication between medical professionals, and for educational purposes in the medical curriculum. Referrals to the honeymoon period continue to be used until today (Supplementary Material).

## **THE PERSPECTIVE OF THOSE LIVING WITH PARKINSON'S DISEASE**

Medical information is no longer restricted to medical professionals, but is now readily accessible to the general population as well through, e.g., social media, scientific publications (PubMed), medical conferences, access to professional guidelines (including

lay versions thereof) or educational channels. In discussions with patients in our clinics, we have found that very few persons with PD recall any time that they would refer to as a “honeymoon”. Certainly, the earliest phase of PD is generally characterized by relatively limited disability, with generally an absence of debilitating complications, and with relatively few non-motor symptoms, including absence of dementia or pronounced orthostatic hypotension. And yes, the early years after the introduction of symptomatic dopaminergic treatment are generally characterized by a gratifying reduction in disability, with a concurrent improvement in quality of life [18]. Yet, even the early years of PD can be accompanied by cumbersome symptoms and signs that negatively impact the quality of life, and this is true despite optimal symptomatic treatment.

Indeed, even today, the response to levodopa is variable and unpredictable, due to several potential mechanisms [19, 20]. One example is tremor, which can be partially or even largely resistant to dopaminergic therapy in a subgroup of patients, which may make difficult to forget the disease is still there [21]. Moreover, various non-motor symptoms (e.g., anxiety, gastrointestinal, urinary complaints) are increasingly recognized as early intruders in the clinical constellation of PD, and in general, these do not respond consistently to dopaminergic therapy, yet these symptoms do have an impact in quality of life, in many cases larger even than that of motor symptoms [22, 23]. Moreover, even a dramatically successful response to levodopa does not equate to a “honeymoon” period, because many factors that markedly hamper quality of life are still at play in this early phase immediately after the diagnosis. Many patients find it very complicated to personally adjust to a diagnosis of PD, to change their mindset towards a very different future from what they had expected, to adjust their hopes and perspectives, to envision potential disability, to reconsider their job perspective, and to anticipate some inevitable familial and social adjustments [24].

One should never underestimate the devastating impact the words “You have got Parkinson's disease” can have on an affected individual which—even today—many equate erroneously with a wheelchair existence and a death sentence. Denial, anger, bargaining, and depression are common reactions [25]. Such a worrisome phase of understandable grief is very hard to reconcile with a “honeymoon” feeling, even when the diagnosis is followed by the installment of dopaminergic treatment and the provision of

symptomatic relief. Taken together, it is safe to say that most people experience even the first phase of PD as a very debilitating time in their lives.

We acknowledge that the extent and quality of the acceptance of a chronic disease is highly variable, and that many people are prone to acceptance and commitment, showing remarkable resilience. Some may even find silver linings in these adverse settings (a potential upside to having PD), and to somehow flourish in disability, as we showed in an earlier work [26]. But even in these resilient individuals with the best coping strategies, there is no disappearance of the disease, let alone of its impact. And even those who cope best would probably never volunteer the term honeymoon period themselves. People with PD testimonials of their early experiences with the disease are enlightening, and may help clinicians understand the relevance of adjusting our language to their diverse realities (Table 1).

### **SHOULD THE TERM “HONEYMOON PERIOD” BE ABANDONED ALTOGETHER?**

There are similar experiences outside the field of PD, where certain terms that had been used widely in medical circles were experienced as being counterproductive or offensive by the individuals affected by the disease. A sound example is the work by Stone and colleagues, who used systematic interviews to identify the “number needed to offend” when they presented different wordings commonly used for functional movement disorders to those living with this condition [27]. Their experience clearly shows how differently medical terms may be perceived from each perspective, and how giving a voice to patients can help to identify alternatives that are more palatable to persons living with the disease at hand, and thereby stimulate acceptance of the disease, as a basis for tailored treatment.

The term honeymoon period, although never intended to be offensive, has been considered distasteful and inappropriate by increasingly many people with PD and also by many medical professionals, including one of the authors (AJL) who considered it an inaccurate and unhelpful term even in the early years after levodopa had been introduced (Supplementary Material). We fully acknowledge that initially, the term honeymoon phase clearly served a purpose as a catchy phrase that facilitated intercollegiate communication and professional edu-

cation. And we also agree that, at least in theory, the language used to communicate strictly between professionals does not have to be identical to the language used to communicate with persons living with PD. This is why the term honeymoon period served a purpose for many years. Taken together, we feel that the term honeymoon is no longer a useful term, not even for limited use within medical circles. The very reason for bringing up this issue now is that the world has changed with the advent of modern communication channels, including social media, so that persons with PD now have access to most, if not all, of the interprofessional communications that were once restricted solely to the eyes of medical professionals. And useful or not from educational perspective, persons with PD may be offended by terms such as a honeymoon period, which is why make this plea here to replace such terms by others that may admittedly be less catchy, but that can be used freely in a flat world where medical professionals and persons with PD work together as equals to create a better health. Collectively, we should continue to increase our efforts to adjust our clinical view of the disease to that of those who are best informed: namely individuals living with PD, and there are as many different experiences as there are persons living with the disease [28, 29].

We are not the first to criticize the adequacy of the term “honeymoon” for PD [30]. However, the term continues to be used: in the last two decades alone, 22 articles in PubMed included it among their keywords or abstract, and over 3,150 entries in Google Scholar during the same period reveal an even wider use in manuscripts. The term continues to be used in neurology textbooks and in recent conferences, symposia, as well as educational materials and podcasts (Supplementary Material). This illustrates that the term is still very much alive, and we are feeding it from the academic, scientific, and clinical point of view, despite the many reasons that would discourage its use. Perhaps one explanation for the continued use of the term among professionals is the fact that, if the early phase of PD is to be experienced by anyone as a honeymoon, it is probably not so much by the patient, but rather by the treating physician, who needs to spend less time on making adjustments to complex medication regimes compared to the more later and complicated treatment phase. It is perhaps also because persons with PD may appear to be less debilitated on the outside, but this does no justice to the impact of the underlying nonmotor symptoms, let alone the impact of grief and anxiety.

Table 1  
Examples of testimonials of people with PD regarding the so called "honeymoon period"

---

*My first association with a honeymoon period is a period of celebration and happiness. That is not how I experienced the first period after the diagnosis. The honeymoon phase is the period (long) before the diagnosis of PD when everything is running smooth and easy. The diagnosis is a wake-up call and means trouble in paradise.*

---

*Calling the first period after the diagnosis the honeymoon phase sounds like window dressing and feels like denial. To me PD comes with is a constant process of saying goodbye to things I cannot do anymore. Actually I'm in a constant process of mourning. Besides this constant mourning process, or maybe to cope with this constant process, I try to focus on the things I still can do (and things I can do different or even better).*

Jos Voeten

---

*I have heard that phrase before and it never resonated with me. I remember being more shell shocked the first two years, going to the movement disorders specialist every six months only to get an increase of levodopa and a new medicine or two – all the while thinking – I must really be bad off... and getting worse! [...] In the first two years I also added a neuro physical therapist, a clinical counselor, exercise classes, and a regular support group meeting. For someone who never went to the doctor, didn't regularly exercise and wasn't on any medication for more than a few weeks at a time – this was overwhelming.*

*Rather than a honeymoon phase, the first two years after a Parkinson's diagnosis are more like the tune-up years. Suddenly, your life has been disrupted (destroyed), dreams dashed, plans put on hold and your future loses all certainty. There is, however, an opportunity for transformation (improvement, to be reborn).*

Larry Gifford

---

## TIME FOR AN ALTERNATIVE

Alternative terms are conceivable. Think of, e.g., "early untreated Parkinson's disease" to describe the initial phase after the diagnosis prior to instalment of treatment, to be followed by "the initial treatment phase without response fluctuations" or the briefer version "early treated phase" for the ensuing phase. It may be argued that the use of metaphors such as "honeymoon" or similar catchy phrases such as "drug holiday" may be more helpful for intercollegiate communication among healthcare providers and also for medical educational purposes. We also acknowledge that the proposed alternative terms (which are more descriptive) are less catchy, and appreciate that these may feel more awkward in a colloquial conversation. However, language needs to evolve with time and progress. Conversations between healthcare professionals and persons with PD should not be patronizing, but rather be symmetrical. Using precise and respectful terms to explain, e.g., the course of the disease contributes to a respectful information provision and education of persons with PD, and may thus help to promote a more proactive involvement in their healthcare. All aspects considered, we feel that less catchy is a price that we are more than ready to pay in the interest of respect, broad consensus and collaborative care among professionals and patients alike. Our suggested alternatives are just the start for a broader discussion, and we remain open to further suggestions by the readership.

We acknowledge that simply removing one term from the medical vocabulary will by itself not have a dramatic impact on the way we support people living

with PD. However, we do feel that this is potentially an important step, partially for symbolic reasons towards patients (as a reflection of the fact that we take the voice of persons with PD seriously), but partially also as a signal towards medical colleagues, emphasizing that they should continue to be aware of the terminology they use when discussing medical issues, even when the discussion is intended to be restricted for intercollegiate communication only. But we envision several additional potential benefits as a consequence of abandoning the honeymoon period term. First, this small step may mark a development towards an improved, more respectful and honest communication with patients, and towards an increased preciseness in the way we describe and explain both uncertainties and proven facts about the disease. An explicit ban on the honeymoon concept would also be a reminder for physicians to explore the potential problems and sources of disability for people with PD at an early stage. Language is powerful, and if physicians assume there are no problems to report anyway (after all, who would, while being in a honeymoon?), then they will not proactively investigate them further. In fact, by conveying the honeymoon message, persons with PD may themselves—perhaps even unconsciously—conceal their own problems at this point or fail to relate their experienced symptoms to the disease, which is supposedly "inactive" according to a physician who underscores the honeymoon-like character of the early disease phase. It is well known many persons with PD tend to underreport their symptoms, and even take extra doses of medication to make a better impression on their doctors. We need to work against

this asymmetrical, partially even patronizing relationship in favor of a more symmetrical and consequently satisfying one. Finally, abandoning the honeymoon term would be a contribution to emphasize the considerable heterogeneity of experiences across people with PD, acknowledging that not all people will feel dramatic improvements upon treatment initiation, or that these changes will not suffice to forget the tough personal experience of coming to terms with a chronic and relentlessly progressive disease.

With this viewpoint, we aim to invite the neurological community to now abandon this once useful term, in order to improve the connection between the scientific literature, the medical curriculum and our clinical approach of PD on the one hand, and the actual lived experience of people living with the disease on the other. We cannot make useful and truth-grounded advances in supporting people with PD if we fail to do so.

## ACKNOWLEDGMENTS

There is no financial support for this project to report.

## CONFLICT OF INTEREST

Bas Bloem is a member of the Editorial Board Member of the Journal of Parkinson's Disease but was not involved in the peer-review process nor had access to any information regarding its peer-review.

All other authors have no conflict of interest to report.

## SUPPLEMENTARY MATERIAL

The supplementary material is available in the electronic version of this article: <https://dx.doi.org/10.3233/JPD-225064>.

## REFERENCES

- [1] Lees AJ, Tolosa E, Olanow WC (2015) Four pioneers of L-dopa treatment: Arvid Carlsson, Oleh Hornykiewicz, George Cotzias, and Melvin Yahr. *Mov Disord* **30**, 19-36.
- [2] Cotzias GC, Papavasiliou PS, Gellene R (1969) Modification of Parkinsonism: Chronic treatment with L-dopa. *N Engl J Med* **280**, 337-345.
- [3] Barbeau A (1971) Long-term side-effects of levodopa. *Lancet* **1**, 395.
- [4] Nonnekes J, Bereau M, Bloem BR (2020) Freezing of gait and its levodopa paradox. *JAMA Neurol* **77**, 287-288.
- [5] Sacks O (1973) *Awakenings*. Duckworth & Co. 408 p. ISBN 0-375-70405-1.
- [6] Stern G, Lees A, Shaw K (1978) Ergot derivatives without levodopa in parkinsonism. In Symposium on Dopaminergic Ergot Derivatives and Motor Function, Stockholm. *Wenner-Gren Center International Symposium Series*, Oxford: Pergamon Press **31**, 337-339.
- [7] Lees AJ (1986) L-dopa treatment and Parkinson's disease. *Q J Med* **230**, 535-547.
- [8] Okereke CS (2002) Role of integrative pharmacokinetic and pharmacodynamic optimization strategy in the management of Parkinson's disease patients experiencing motor fluctuations with levodopa. *J Pharm Pharm Sci* **5**, 146-161.
- [9] Lees AJ (2002) Drugs for Parkinson's disease. *J Neurol Neurosurg Psychiatry* **73**, 607-610.
- [10] Rascol O, Payoux P, Ory F, J Ferreira JJ, Brefel-Courbon C, Montastruc JL (2003) Limitations of current Parkinson's disease therapy. *Ann Neurol* **53**, S3-S15.
- [11] Fahn S (2006) Levodopa in the treatment of Parkinson's disease. *J Neural Transm* **71**, 1-15.
- [12] Stocchi F, Jenner P, Obeso JA (2010) When do levodopa motor fluctuations first appear in Parkinson's disease? *Eur Neurol* **63**, 257-266.
- [13] Cesaro P, Dedefvire L (2014) Drug treatment of early-stage (de novo and "honeymoon") Parkinson disease. *Rev Neurol (Paris)* **170**, 237-246.
- [14] Castrioto A, Thobois S, Anheim M, Quesada JL, Lhommée E, Klinger H, Bichon A, Schmitt E, Durif F, Azulay JP, Houeto JL, Longato N, Philipps C, Pelissier P, Broussolle E, Moro E, Tranchant C, Fraix V, Krack P; Honeymoon study group (2020) A randomized controlled double-blind study of rotigotine on neuropsychiatric symptoms in de novo PD. *NPJ Parkinsons Dis* **6**, 41.
- [15] Meira B, Lhommée E, Schmitt E, Klinger H, Bichon A, Pélissier P, Anheim M, Tranchant C, Fraix V, Meoni S, Durif F, Houeto JL, Azulay JP, Moro E, Thobois S, Krack P, Castrioto A; Honeymoon study group (2022) Early Parkinson's disease phenotypes tailored by personality, behavior, and motor symptoms. *J Parkinsons Dis* **12**, 1665-1676.
- [16] Tanner CM (2013) A second honeymoon for Parkinson's disease? *N Engl J Med* **368**, 675-676.
- [17] Rodriguez-Oroz MC, Moro E, Krack P (2012) Long-term outcomes of surgical therapies for Parkinson's disease. *Mov Disord* **27**, 1718-1728.
- [18] Verschuur CVM, Suwijn SR, Boel JA, Post B, Bloem BR, van Hilten JJ, van Laar T, Tissingh G, Munts AG, Deuschl G, Lang AE, Dijkgraaf MGW, de Haan RJ, de Bie RMA, LEAP Study Group (2019) Randomized delayed-start trial of levodopa in Parkinson's disease. *N Engl J Med* **380**, 315-324.
- [19] Martin WRW, Miles M, Zhong Q, Hartlein J, Racette BA, Norris SA, Ushe M, Maiti B, Criswell S, Davis AA, Kotzbauer PT, Cairns NJ, Perrin RJ, Perlmutter JS (2021) Is levodopa response a valid indicator of Parkinson's disease? *Mov Disord* **36**, 948-954.
- [20] Beckers M, Bloem BR, Verbeek MM (2022) Mechanisms of peripheral levodopa resistance in Parkinson's disease. *NPJ Parkinsons Dis* **11**, 8:56.
- [21] Zach H, Dirx MF, Roth D, Pasman JW, Bloem BR, Helmich RC (2020) Dopamine-responsive and dopamine-resistant resting tremor in Parkinson disease. *Neurology* **95**, e1461-e1470.
- [22] Hely MA, Morris JG, Reid WG, Trafficante R (2005) Sydney Multicenter Study of Parkinson's disease: Non-Ldopa-responsive problems dominate at 15 years. *Mov Disord* **20**, 190-199.

- [23] Erro R, Picillo M, Vitale C, Amboni M, Moccia M, Santangelo G, Pellecchia MT, Barone P (2016) The non-motor side of the honeymoon period of Parkinson's disease and its relationship with quality of life: A 4-year longitudinal study. *Eur J Neurol* **23**, 1673-1679.
- [24] MacCarthy B, Brown R (1989) Psychosocial factors in Parkinson's disease. *Br J Clin Psychol* **28**, 41-52.
- [25] Corr CA (2021) Should we incorporate the work of Elisabeth Kübler-Ross in our current teaching and practice and, if so, how? *Omega (Westport)* **83**, 706-728.
- [26] Alonso-Canovas A, Voeten J, Thomas O, Gifford L, Stamford JA, Bloem BR (2022) The silver linings of Parkinson's disease. *NPJ Parkinsons Dis* **8**, 21.
- [27] Stone J, Wojcik W, Durrance D, Carson A, Lewis S, MacKenzie L, Warlow CP, Sharpe M (2002) What should we say to patients with symptoms unexplained by disease? The "number needed to offend" *BMJ* **21**, 325:1449-1450.
- [28] Armstrong MJ, Okun MS (2020) Time for a new image of Parkinson disease. *JAMA Neurol* **77**, 1345-1346.
- [29] Bloem BR, Okun MS, Klein C (2021) Parkinson's disease. *Lancet* **397**, 2284-2303.
- [30] Colosimo C, Bhidayasiri R (2016) Nonmotor symptoms in Parkinson's disease: Are we still waiting for the honeymoon? *Eur J Neurol* **23**, 1595-1596.