CASE REPORT

Self-Medication with *Ganoderma lucidum* ("Reishi") to Combat Parkinson's Disease Symptoms: A Single Case Study

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ABSTRACT   Parkinson's disease (PD) is a prevalent neurodegenerative disease for which only symptomatic treatments, mainly focused on motor symptoms. In contrast, conventional pharmacological treatments do not address cognitive impairment and emotional dysfunction. Together with potential treatment side effects, these can cause distress, lower the quality of life, and increase motor impairment in patients. Preclinical research suggests that the Traditional Chinese Medicine *Ganoderma lucidum* ("Reishi") can alleviate symptoms in neurological disorders like PD. However, no clinical research to date has addressed this. An (unmedicated) patient, 50 years of age and diagnosed with PD for 5 years, approached the author as he decided to initiate self-treatment with Reishi, lasting 3 months. He wanted to evaluate the effects and decide to continue self-treatment or not. He agreed to be followed during this period, using questionnaires asking him about his (non-)motor symptoms. The most notable finding was the increase in Mindfulness, 3 months after self-treatment started. The motor symptoms stayed stable, there were no extreme changes in quality of life, and emotion regulation seemed to deteriorate over time while slightly improving at the 3-month assessment. While the findings do not allow firm conclusions seen the nature ($N=1$) of this study, the small positive changes in some facets of affective behavior and the patient's experience, combined with the evidence from preclinical research, warrant clinical studies in this patient population.

KEYWORDS: ● *case report* ● **Ganoderma lucidum** ● *Parkinson's disease* ● *Reishi* ● *Self-medication*

INTRODUCTION

PARKINSON'S DISEASE (PD) is a neurodegenerative disease with an estimated 2–3% prevalence in the population above 65 years of age.[1] In general, the prevalence increases with age, from 1% at age 45–55 to 4% (men) and 2% (women) at age 85.[2] Typical are the motor symptoms related to (nonreversible) loss of dopaminergic cells in the substantia nigra.[3] Patients also suffer from nonmotor problems of physical (constipation), physiological (sleep problems), cognitive (disturbed memory), and affective (depression, anxiety) nature. These are supposedly related to disturbances in the cholinergic, serotonergic, and norepinephrine neurotransmitter system.[1] Substances like carbidopa/levodopa, substituting for dopamine, are used as a symptomatic treatment to manage motor symptoms; substances that address the cholinergic and serotonergic system aid with cognitive and affective problems.[3,4] The downside of treatment, especially with these dopaminergic substances, is that they can lead to (severe) side effects, including abnormal muscle movements, nausea, and psychosis, that reduce the quality of life.[4,5] Notably, (emotional) stress can transiently increase motor symptoms or accelerate the neural degeneration.[6,7] The need for alternative medicines without or with less adverse effects, which might also enhance emotional and cognitive processes, is clear.[8]

Ganoderma lucidum (*GL*) is a popular Traditional Chinese Medicine (TCM), known as "Ling-Zhi" in China and "Reishi" in Japan.[9] This medicinal fungus is the most widely used for promoting health and longevity in Asian countries and studied in TCM.[9] Based on the color, there are different subtypes, of which *GL* is the most widely used.[9] It includes several active ingredients of which polysaccharide is the most studied. Preclinical research uses a water-soluble extract from the culture medium of the fungus MAK.[10] The extract MAK, also labeled as a functional food, contains various types of constituents such as polysaccharides, including beta-glucans, triterpenes, and lignin derived from the culture medium and its digestion products by the mycelia.[10]

Preclinical research demonstrated a reduction in the duration of immobility in the forced swimming test in mice and rats orally treated with 100–400 mg/kg and 1 g/kg, respectively, of MAK.[10,11] Notably, these findings are similar to those after the administration of serotonergic (5-HT) antidepressants.[12] Of note, head-twitch responses that signal 5-HT2A receptor activation were reduced by MAK, suggesting the involvement of this receptor in MAK's antidepressant actions.[10] Next to effects on affective processes, preclinical research has also shown that the extract reduced MPTP-induced Parkinsonism in an animal model[13] and protected dopaminergic neurodegeneration in rat brains.[14] These effects lead to suggest that *GL* could play a role in the treatment of PD.[9] However, this has not yet been demonstrated in humans.[15] Importantly, preclinical research has also shown the absence of toxic, anxiolytic-like, or sedative effects in mice, after treatment with MAK, in doses up to 2500 mg/kg, for some parameters.[11] Also, clinical trials seem to support this safety profile of *GL*, or fractions (polysaccharides) of *GL*, as it is generally well tolerated after repeated administrations, for several months.[16,17]

A patient with PD who just started using *Ganoderma lucidum* contacted the author. He decided to self-medicate for 2–3 months with this substance to test whether it would bring him the "enlightenment" experienced by another patient. This unique opportunity to understand the effects of treatment with *GL* on (non-)motor symptoms in humans resulted in a case study described in this article. The focus of the current study was on nonmotor symptoms based on several facts and reasons. First, treatments addressing nonmotor symptoms are highly needed.[8] Second, in other neurological disorders, interventions aimed at increasing self-compassion alleviate psychological distress[18] something important in PD, as stress increases the severity of motor symptoms.[6,7] Third, the quality of life is associated with the severity of motor symptoms.[19] Therefore, in this study, questionnaires focusing on the quality of life, self-compassion, and emotion regulation were chosen next to a questionnaire assessing (non-)motor Parkinson's symptoms.

METHODS

Case presentation

This single case study describes the motor and nonmotor symptoms of a male person ("the patient") 50 years of age and diagnosed with PD since April 2014, at the age of 45. The patient contacted the author because he was starting with self-medication with "Reishi" (*GL*) to combat his symptoms. During these 3 months, he and his daughter ("other") filled out questionnaires about his motor and nonmotor symptoms at baseline and 1 and 3 months following the start of the self-medication.

Questionnaires were the Movement Disorder Society Unified PD Rating Scale (MDS-UPDRS IA and IB, assessing nonmotor aspects of daily living and Part II, assessing motor aspects of daily living)[20]; the PD Quality of Life Questionnaire (PDQ-39)[21]; the Difficulties in Emotion

Regulation Scale (DERS)[22]; and the Neff's Self-Compassion Scale (Neff's SCS).[23,24] Additionally, a daily diary, including types of positive mood,[25] sleep quantity and quality, the Bristol Stool Chart (Stool type, bowel movement),[26] and an optional open-ended question asking about remarkable events during the day. The patient and the other gave informed consent before filling out the questionnaires presented using the online platform Qualtrics XM. Demographic information was collected in a telephonic interview with the patient.

The Ethics Review Committee Psychology and Neuroscience of the Faculty of Psychology and Neuroscience at Maastricht University gave ethics approval for this observational study (Number: ERCPN 207_08_04_2019).

Movement disorder society-unified Parkinson's disease rating scale

The revised version of the MDS-UPDRS is an instrument to measure motor and behavioral aspects of the disease.[27] It consists of four parts: Part I (nonmotor experiences of everyday life), Part II (motor experiences of daily life), Part III (motor examination) and, Part IV (motor complications). Seen the nature of the present study (online), only parts I and II were included. Part I consists of two parts with 13 items in total. The first part (IA) includes six questions, typically scored by the researcher, based on the remarks of the patient and the caretakers; It concerns the behavioral aspects of the patient. Due to the online nature of the study, the patient and his daughter filled out this part (IA), and not the researcher. The second part (IB), including seven questions, is completed by the patient independently of the researcher. Part II is a self-administered 13-item questionnaire, much like Part IB. Items in scales I and II employed a 5-point scale (0–4), where higher scores indicate more severe impairment compared with lower scores; maximal scores are 24 (IA) and 52 (IB and II), respectively.[20]

Dutch PD quality of life questionnaire

The Dutch PD Quality of Life Questionnaires (PDQ-39) is a disease-specific measuring questionnaire to assess relevant aspects of health status (quality of life) of patients with PD. It consists of 39 five-point scale items, with never and always as descriptive anchors. It has eight subcategories (mobility, everyday life, emotional wellbeing, stigma, social support, cognitive impairment, communication, and physical discomfort), and a Single Index Score ("PDQ-SI"), calculated from these subcategories. The minimum–maximum of all scales is 0–100, where a lower score means better-perceived health status. Higher scores are associated with more severe symptoms of the disease, such as tremor and rigidity. The profile of scores can be used to determine the impact of treatment upon particular aspects of functioning and wellbeing in patients with PD.[21]

Neff's self-compassion questionnaire

The 12-item version of Neff's self-compassion questionnaire is a measure of self-compassion. Items have a

five-point response scale ranging from one (Never) to five (Always). Six subscales can be derived: (1) Self-kindness, (2) Self-judgment, (3) Common humanity, (4) Isolation, (5) Mindfulness, and (6) Over-identified. The subscale scores are computed by adding item scores, and a total self-compassion score[28] is computed by reversing the negative subscale items and then adding all subscale scores.[24] As a rough guide, average scores for the SCS are around 3.0 on the 1–5 Likert scale, a score of 1–2.5 indicates low self-compassion, 2.5–3.5 indicates moderate, and 3.5–5.0 is an indication of high self-compassion.[23]

Difficulties in emotion regulation scale

The DERS is a 36-item self-report questionnaire designed to assess multiple aspects of emotional dysregulation. The items have a five-point scale going from one (Seldomly) to five (Almost always). The sum of scores on all items is the total score; also, six subscales are calculated: (1) Non-acceptance of Emotional Responses, (2) Difficulties Engaging in Goal-Directed Behavior, (3) Impulse Control Difficulties, (4) Lack of Emotional Awareness, (5) Limited Access to Emotion Regulation Strategies, and (6) Lack of Emotional Clarity. Higher scores suggest more significant problems with emotion regulation.[22]

Diary

The patient diary included the Types of Positive Affect Scale, which has 18 items (''feeling'' words), rated on a six-point scale from 0 (not) to 5 (the whole day). The scale assesses the degree to which people experience different positive emotions. The scores of three subscales, Activating Positive Affect (e.g., excited, dynamic, active), Relaxed Positive Affect (relaxed, calm, peaceful), and Safeness/Contentment Positive Affect (e.g., safe, secure, warm) are calculated afterward.[25] Next to that, there was a question about sleep quality, which was rated on a scale from 0 (very bad) to 5 (excellent), and sleep quantity (number of hours sleep). Then there was a question asking to typify the stool using the Bristol stool chart, where Type 1–2 indicates hard stool or constipation, Type 3–5 are normal stools, and Type 6–7 indicates loose stool or diarrhea.[26] It is known that PD patients can have bowel movement problems,[29] but also that medication can have an effect on bowel movements; therefore, this question was included. Recently, scientific attention for the influence of the gut on the individual's mental wellbeing increased.[30]

A final open-ended question asked whether the patient wanted to share things that happened that day (Do you want to share something else about your day? Was there something different from usual, for example: eating something special or going out to eat, drinking alcohol, taking medication, taking physical activity (e.g., walking)?).

Statistical analyses

Questionnaire scores are according to instruction presented as a sum score, or a percentage, following the description in the methods section. Given the nature of the present study ($N=1$), no statistical comparisons were performed. Where possible, scores are interpreted against norm scores or cut-offs provided by questionnaire developers. The scores are visually compared between the different time points. Additionally, whenever possible, the scores are compared with scores of Parkinson's patients in clinical trials.

RESULTS

Case description

In 2014, the patients' daughter noticed that the patient had trembling fingers. The patient attributed this to him being busy, tensed, and stressed. He waited a couple of months before going to his general practitioner, who referred him to a neurologist to exclude PD. The patient wanted to wait 2 months before going to self-evaluate, and then in March 2014, he received two brain scans, including a dopamine transporter scan. In April 2014, he received the diagnosis of PD. He never took conventional medicine, although he founded a Facebook Page where patients can exchange experiences about alternative or additional therapies.

The patient has a healthy lifestyle, partly driven by the knowledge that several factors influence the severity of symptoms. Stress reduction, exercising, and healthy food play an important role. He started 2.5 months ago with ''Parkinson boxing'' with a punching ball. He notices that his ''bad side'' is improving, but he cannot box for 3 months now because he overloaded his shoulder. He also takes walks in nature, where he can walk easily and fast. He does have a dragging leg that he sometimes needs to steer consciously. He also practices yoga and notices that his stiffening side is now almost as flexible as the other side. Also, he meditates when he has a stressed feeling, and he does this a couple of times a week. Lastly, next to Reishi (GL), he was already taking multivitamins and Q10 in the morning, and Mucuna Pruriens, two 500 mg capsules in the morning and in the evening, which comes from a plant that contains levodopa in varying amounts.[31] In April 2019, the patient decided to start self-medicating with Reishi for 3 months, after which he would make up the balance. He took one capsule of Reishi (300 mg) (Fig. 1) each day, usually before noon, and reported on his (non)-motor symptoms in a diary. The patient filled out questionnaires at baseline and 1 month and 3 months after the initiation with self-medication.

Treatment satisfaction questionnaire for medication

At the end of the 3 months, the author had an interview with the patient, which included a questionnaire (Treatment Satisfaction Questionnaire for Medication, Version 1.4) to assess the satisfaction with the treatment. It covers four domains: Effectiveness; Side Effects; Convenience; and Global Satisfaction; scores are expressed as a percentage.[32] The scores of the patient were 60% (Effectiveness), 100% (Convenience), 85% (Global Satisfaction), and the Side Effects were not applicable.
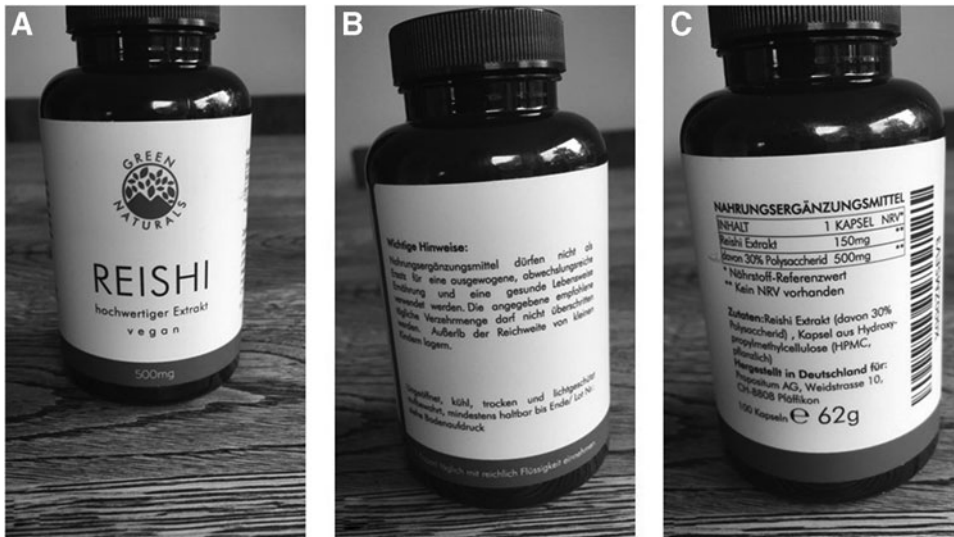
FIG. 1. Bottle with capsules that was used to self-medicate. In **(A)** the front of the bottle is shown, in **(B)** the instructions on how to use it, and in **(C)** the ingredients. Source: Pictures made by the patient of whom permission to use them was obtained.

The patient's perspective

The patient was motivated to start with *GL* as he wanted to test whether he could also gain clarity in his brain, as his source stated: ''I regained my brain''; This is also what he experienced, not immediately but approximately after 2 weeks of self-treatment. The patient stated to be less panicked, although he acknowledged that this could be due to the self-medication or the increased calmness in his life. He did not experience motor changes but stated that the time to conclude that something is not working went faster. For example, he states: ''When eating with a fork is difficult, the solution to take the fork in the other hand, comes quickly to mind.'' When asking about the expectations he had when starting with medicating, he stated to have been curious, and thought: ''There is no harm in trying.''

Questionnaires filled out at baseline and after initiation with self-treatment

The scores on the scales are partly presented in Figure 2 and described below. After 1 and 3 months of self-dosing, the scores are visually compared with baseline, and when applicable to cutoff scores provided by the scale developers.

Movement disorder society-unified Parkinson's disease rating scale

Nonmotor experiences of everyday life were questioned in Part I, where the patient and the other completed section A, and only the patient completed section B. Part IA revealed a discrepancy between the patient and the other's judgments. The former remained stable over time (9-10-9), whereas the latter was higher (15-15-12) than the former, and showed a decrease at the 3-month assessment. Part IB showed a decrease in ratings at 1-month follow-up (9) compared with baseline (14), with an increase just above baseline scores at the 3-month follow-up (16). These findings on Part IA indicate that the ''other'' rates nonmotor

symptoms as more severe, with almost maximal scores, whereas the patient did not seem to experience it as that severe. The latter is also reflected in Part IB, where the scores were less than 50% of the maximal scores. The patient-total score for Part I (23-19-25) indicates the presence of ''mild'' nonmotor symptoms. Part II dealt with motor experiences of daily life. Stable scores over time (19-20-19) that were less than 50% of the maximal score indicate slight-to-moderate motor problems.

Dutch PD quality of life questionnaire

The overall wellbeing index (PDQ-SI) showed, compared with baseline, a slight decrease in the first and third months after self-treatment initiation, with the lowest (''best'' health) value in the third month. Despite this seemingly positive pattern, life quality can generally be regarded as stable, likewise six of the eight subscales, Mobility, Activities of Daily Living, Emotional Wellbeing, Stigma, Cognitive Impairment, and Communication. Of interest are the two aspects that did show a more pronounced change, Social Support and Bodily Discomfort. The latter was rated the best at the 1-month follow-up, and the former the best at the 3-month follow-up. The enhancement in Social Support might be attributable to the patient's relational status, who was exploring a new relationship (Fig. 2A).

Neff's self-compassion questionnaire

The Total Self-Compassion score was relatively stable over the 3 months, and using the guidelines of Neff, this is considered ''moderate.''[23] In that same line, the subscales Self-Judgement, Common Humanity, Isolation, and Over-Identification were all relatively stable and labeled as ''moderate''. Self-Kindness was high in general. Interestingly, Mindfulness increased from ''moderate'' at baseline to ''high'' (with a maximal rating) at a 3-month follow-up (Fig. 2B).
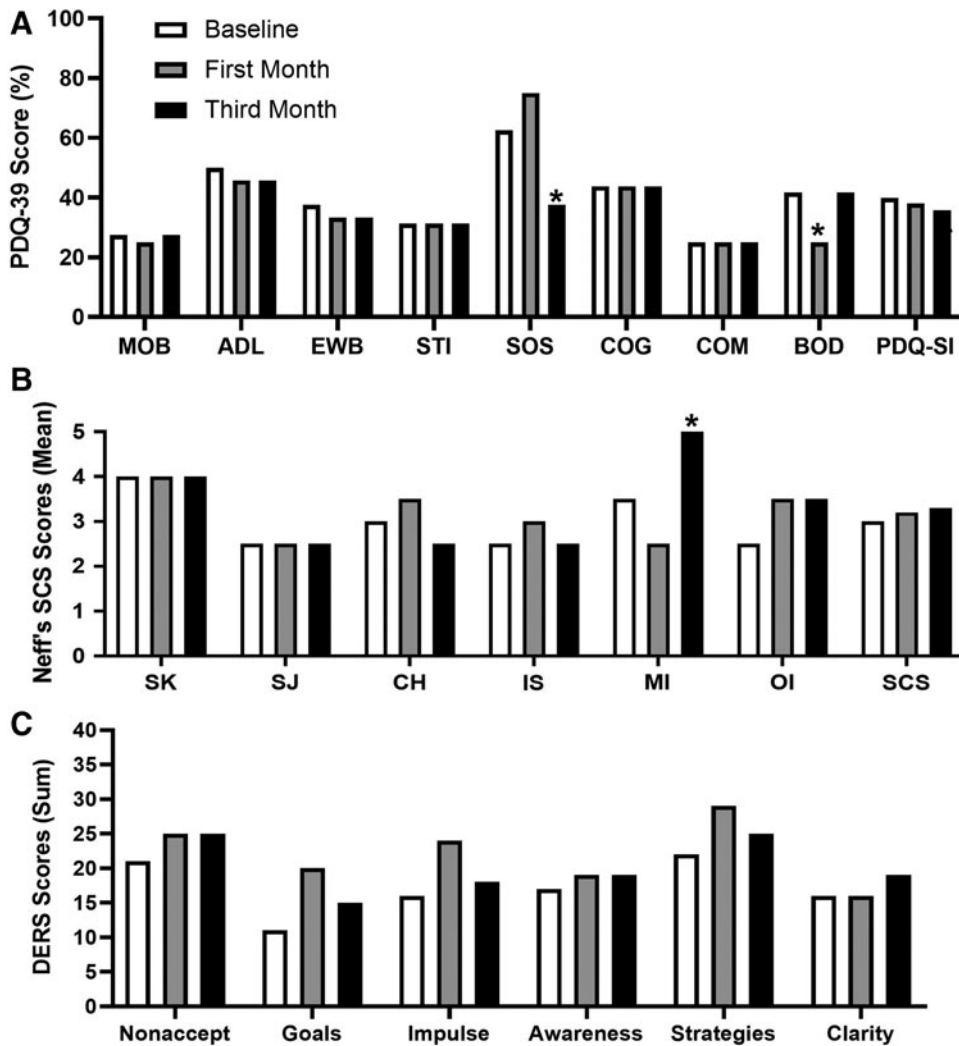
FIG. 2. Scores on **(A)** the Parkinson's Disease Questionnaire (PDQ-39), **(B)** the Neff's SCS, and **(C)** the DERS, rated by the patient at baseline, and after one month and three months of self-medication with GL. *Indicates a change in scoring category, not a statistically significant difference. MOB, mobility; ADL, activities of daily life; EWB, emotional wellbeing; STI, stigma; SOS, social support; COG, cognitive impairment; COM, communication; BOD, bodily discomfort; SK, self kindness; SJ, self judgment; CH, common humanity; IS, isolation; MI, mindfulness; OI, overidentification; SCS, Self Compassion Scale; DERS, Difficulties In Emotion Regulation Scale.

Difficulties in emotion regulation scale

The Total Emotion Regulation score showed an increase at 1 (133) and 3 months (121) after self-medication initiation, compared with baseline (103). This Total score seems to suggest that emotion regulation deteriorates with time. While it looks like self-treatment with *GL* slightly reverses this decline after 3 months, it is not possible to confirm this due to this study's nature. Three other emotion regulation facets, Difficulties in Engaging in Goal-Directed Behavior, Impulse-Control Difficulties, and Limited Access to Emotion Regulation, showed the same pattern as the Total score. Ratings of Nonacceptance of Emotional Responses and Lack of Emotional Awareness were the same at 1 and 3-month follow-up, and higher than baseline. Lack of Emotional Clarity only increased at a 3-month follow-up compared with baseline. These three facets also show that emotion regulation deteriorated over time; in the case of Emotional Clarity, it is clear that self-treatment with *GL* did not prevent the decline in this facet (Fig. 2C).

The patient filled out the diary on 58 days in 3 months (from April 6 until July 8). Throughout the study, the compliance to fill out the diary decreased, and therefore, there are fewer data points in the third month of assessment. The individual data are shown in the violin plots to be transparent on the number of collected data points per month (Fig. 3).

Types of positive affect

The mood pattern in the 3 months of self-medication was relatively stable for the three affect types with some differences in the second month of self-medication compared with the other months. For Active, there was less variation in responses. However, for Relaxed, there were also some outliers in the second month, and for Safe, the responses became somewhat more variable over time. There were also some outliers in the second month of self-medication. All the outliers were a decrease in positive affect.

Interestingly, the ratings by the other showed an increasing trend in all the positive affect scales over time: Active (20-30-36), Relaxed (17-23-33), Safe (16-19-23), whereas the average ratings per month by the patient showed a decreasing tendency Active (24.8, 20.6, 17.9), Relaxed (21.8, 20.2, 18.4), and Safe (15.3, 14.4, 13.7).
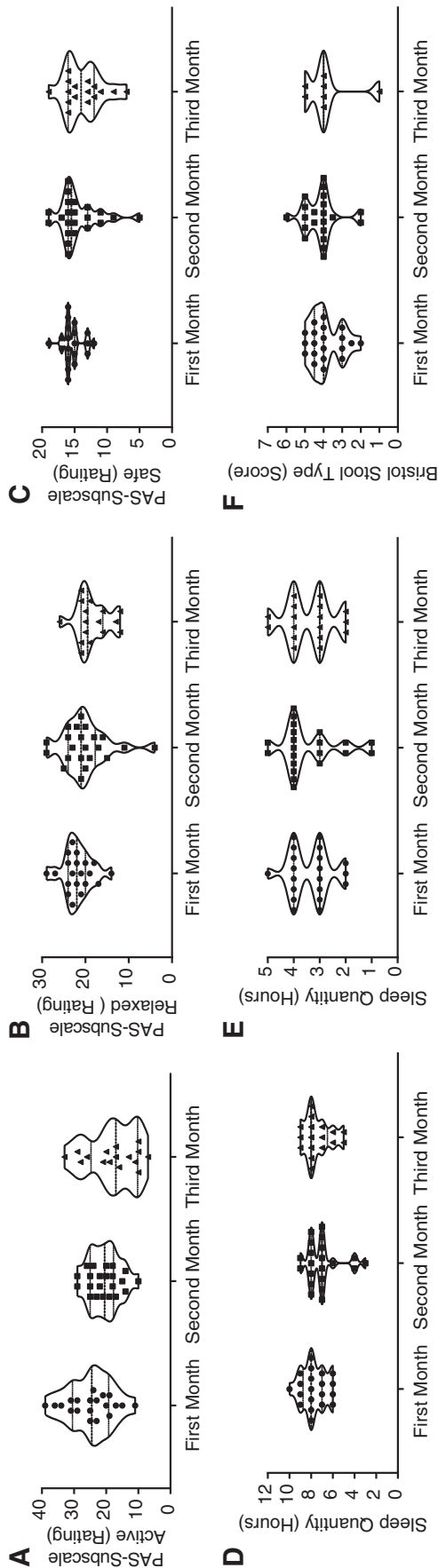
FIG. 3. (A–C) Show the positive affect scales Active, Relaxed, and Safe, (D, E) show the self-rated sleep quantity and quality, and (F) shows the stool type, all rated over a three-month period during which the patient self-medicated with GL.

Sleep

In general, the patient slept between 6 and 10 h per night during the 3 months of self-treatment, and the quality was around 3–4 on average. In the second month, there were some outliers in sleep quality and quantity, the patient slept less on several occasions, and the sleep was of less quality.

Stool type

Figure 3F shows that, on average, the stool type was typical over the three assessment moments suggesting no remarkable changes throughout self-medication.

DISCUSSION

This study aimed to investigate by following a PD patient who initiated self-medication with *GL* whether (non-)motor symptoms improved. The emphasis of this study was the nonmotor dimension, to that end, including measures of self-compassion, emotion regulation, and quality of life. The most notable finding was the increase in one facet of self-compassion, Mindfulness, 3 months after self-treatment started. Other than that, motor symptoms stayed stable. There were no pronounced changes in quality of life, and emotion regulation seemed to deteriorate over time while slightly improving at the 3-month assessment. The other rated the motor symptoms as more severe than the patient, although with a slight improvement at the 3-month follow-up. In the second month, outliers in mood and sleep (quality and quantity) were observed, most likely associated. There were no remarkable findings concerning mood, sleep, or stool that would indicate an effect of self-treatment with *GL* on these parameters. The differences in average mood ratings by the patient and by the other show the need always to include ratings by other people. An additional step could be to confront the patient with the other's scores and discuss apparent discrepancies. Nonetheless, the other's scores represent an overall impression of a month, based on one rating. At the same time, the patient continuously rated his mood, something that might explain differences in self-other ratings.

The scores on the PD symptom questionnaire (MDS-UPDRS) were slightly higher than those of a sample of PD patients, of whom most categorized as two on the scale of Hoehn and Yahr. The latter means having bilateral involvement without impairment of balance. The majority received some pharmacotherapy and had a mean PD duration of 8.3 years (SD: 6.7; range: 0–40 years).[20] The patient in the present study did not receive pharmacotherapy and had the diagnosis for 5 years. The patient's average score on Part I (22) was beyond one standard deviation of the patient sample who scored 11.5 on average (SD: 7.0); the average score on Part II (19) was higher than the average of the PD sample, although within one standard deviation of that score [16.0 (SD: 10.0)].[20]

Overall, quality of life scored as relatively good with no significant changes. Compared with other patients, 66 years of age on average, and with an average diagnosis "age" of 6.7 years, the patient's overall wellbeing was in between

that of patients with a Hoehn and Yahr staging score of one (unilateral impairment) and two (bilateral impairment).[21] The self-compassion was generally relatively stable over the 3 months, labeled as ''moderate'', and comparable to that of a community sample, except for two scales, Self-Kindness and Mindfulness.[33] Self-Kindness (*e.g.*, ''I am disapproving and judgmental about my flaws and inadequacies''[33]) was high at baseline and did not change throughout the self-medication. Mindfulness (*e.g.*, ''When something painful happens I try to take a balanced view of the situation''[33]) increased from ''moderate'' at baseline to ''high'' at a 3-month follow-up. The ratings on these two scales were comparable to that of a meditator sample (with a similar age as the PD patient).[33] The increase in Mindfulness suggests something changed in this facet of self-compassion, during the self-medication, without changing the ''overall'' self-compassion.

Findings showed that all facets of emotion regulation diminished over time. At least for three facets (Goal-Directed Behavior, Impulse Control, and Limited Access to Emotion Regulation), self-treatment with *GL* seemed to push back this deterioration, although only when treated for three months. Nonetheless, three other facets, Nonacceptance of Emotional Responses, Emotional Awareness, and Emotional Clarity, did not seem to be influenced by self-treatment with *GL*. The patient's scores were, in general, similar to the mean (plus one standard deviation) scores of two samples of healthy adults 23 and 36 years of age on average, respectively.[22,34] Of note, the Nonacceptance, and the Total score of the patient, seemed to be higher compared with the youngest sample described in Gratz and Roemer.[22] This finding is remarkable as Staples and Mohlman (2012)[35] showed that scores are lower in ''older'' people as they are more able to cope with situations or have more effective coping strategies.

In Conclusion, The findings suggest some improvements after self-treatment for three months with *GL* in an unmedicated patient with PD. However, these changes were *observed* on a *selection* of nonmotor and emotional facets, and these were not statistically tested. Of note, before initiation of *GL* use, the patient was already using vitamin supplements. Given that the only newly introduced factor at the time of these assessments was *GL*, the observed changes can, with some certainty, be attributed to *GL* and not to other supplements. The demonstration that due to unmet needs, patients are self-medicating to keep the living standards is an important message. The patient experienced positive effects of self-medication without experiencing adverse effects. Next to additional preclinical research, placebo-controlled clinical trials in Parkinson patients with *GL* treatment is warranted to conclude whether this substance is safe to use and beneficial in the betterment of (non-)motor symptoms, as suggested by animal research, and as suggested by the current case study.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethics approval for this observational study was obtained from the Ethics Review Committee Psychology and Neuroscience of the Faculty of Psychology and Neuroscience at Maastricht University (Number: ERCPN 207_08_04_2019).

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

AVAILABILITY OF DATA AND MATERIALS

Due to the nature of this research, participants of this study did not agree for their data to be shared publicly, so supporting data are not available.

AUTHORS' CONTRIBUTIONS

K.P.C.K. conceptualized, collected, and analyzed the data, and wrote the article.

AUTHOR DISCLOSURE STATEMENT

The author declares to have no conflict of interest.

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