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ORIGINAL ARTICLE

Compassionate mind training for people with Parkinson's disease: A pilot study and predictors of response

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Abstract

Introduction: People with Parkinson's disease (PD) often present with disabling neuropsychiatric symptoms. Compassionate mind training (CMT) is a psychological approach effective in reducing stress and promoting psychological well-being. Heart rate variability (HRV), a measure reflecting sympathovagal balance, has been associated with psychological well-being and a compassionate attitude.

Aim: To assess the feasibility and effectiveness of CMT in enhancing the quality of life and psychological well-being in PD patients. Additionally, we evaluated HRV as a physiomarker for assessing the CMT outcomes.

Methods: Twenty-four PD patients participated in the study. A 6-week online CMT intervention was delivered on a weekly basis. At baseline and post-intervention patients completed questionnaires assessing depression, anxiety and quality of life. In a subsample of 11 patients, HRV was measured at baseline and post-intervention in three conditions: at rest, during stress and after 3 min of deep breathing.

Results: The attendance rate was 94.3%. Quality of life and perceived stigma improved post-intervention as compared with baseline ($p = 0.02$ and $p = 0.03$ for PD Questionnaire-39 total score and Stigma subscore, respectively). After CMT, patients presented better physiological regulation to stress, as measured by higher HRV as compared with baseline ($p = 0.005$). Notably, patients who were more resilient to stress at baseline (less decrease in HRV during stress) experienced a more substantial reduction in anxiety and depression following CMT.

Conclusions: CMT is feasible and can improve quality of life and stigma in PD patients. HRV emerges as a promising physiomarker for predicting and measuring the outcomes of psychological interventions in PD.

KEYWORDS
compassion, heart rate variability, neuropsychiatric symptoms, Parkinson's disease, stigma

Elena Makovac and Lucia Ricciardi share senior authorship.

INTRODUCTION

Neuropsychiatric symptoms are highly prevalent in individuals with Parkinson's disease (PD), causing considerable distress for both patients and their families [1, 2]. The treatment of neuropsychiatric disturbances, particularly anxiety and depression in PD, remains a significant unmet need, and there is a lack of evidence-based guidelines for their management [3]. Medications employed to treat primary mood and anxiety disorders in non-parkinsonian people are often not effective in treating PD-associated depression and anxiety [4] and whilst cognitive behavioural therapy has been reported to be effective for depression in PD [5], little evidence exists on non-pharmacological treatment of anxiety disorders in PD.

Mindfulness-based interventions and other psychological treatments have been shown to be feasible and effective in reducing neuropsychiatric symptoms and improving quality of life in healthy and clinical populations [6, 7]. Pioneer studies suggest that these therapies may also be beneficial for people with PD [8, 9]. However, components and mechanisms of potential action are poorly understood.

Compassionate mind training (CMT), inspired by compassion-focused therapy, is a mindfulness-based therapy that holds promise for individuals with PD. This approach integrates both compassion and mindfulness practices to alleviate stress and enhance overall well-being [10, 11]. Mindfulness can be defined as a core element of self-compassion, where the attention, recognition and acceptance that one is suffering is the foundation [12]. Self-compassion is the ability to show compassion towards oneself during difficult times, by means of self-kindness, recognition of common humanity and mindful awareness [12]. Compassion-focused therapy is based on the premise that there are three main emotional systems: the threat and self-protection system, the drive and excitement system, and the contentment and social safeness system [13]. The threat and self-protection system is responsible for detecting and responding to threats and is associated with emotions such as anxiety, anger and disgust. The drive and excitement system is related to the pursuit of resources, achievements and goals. It is associated with feelings of joy, anticipation and excitement. Lastly, the contentment and social safeness system is related to feelings of calm, contentment and connection and is activated when we feel safe, content and connected to others [13]. CMT aims to cultivate a compassionate mind which encompasses the three interactive flows of compassion: compassion toward the self, compassion toward others, and receiving compassion from others. CMT improves general well-being [14] and its effectiveness as a psychotherapy has been shown in a range of medical conditions and healthy populations [15, 16]. It has been shown to have moderate effect sizes for reducing depression, anxiety and stress, as well as increasing one's levels of compassion, mindfulness and well-being [15]. Interestingly, it has been reported that self-compassion might serve as a protective factor against the detrimental impact of stigma on psychological distress in people with PD [17], pointing to a potential benefit of CMT in PD.

Recent studies have confirmed that CMT is effective in activating the soothing affect system which is connected with parasympathetic nervous system activity influencing heart rate variability (HRV) [18]. HRV, which evaluates the variability in the interval between consecutive heart beats, is a marker of autonomic nervous system function, and more specifically of the parasympathetic regulation of the heart (via the vagus nerve) [19]. Changes in HRV have been associated with fluctuations in mood and anxiety in healthy and clinical populations [20, 21]. A reduction in HRV is usually observed during emotional [22] or mental stress [23], and it may therefore serve as a potential biomarker of current anxiety [24], indicating a decrease in sympatho-parasympathetic balance.

To date, no study has employed CMT as an intervention in people with PD.

The objective of this study was threefold. First, we aimed to assess the feasibility of an online CMT programme in people with PD. Second, we aimed to investigate its effectiveness in improving quality of life and neuropsychiatric symptoms in the same group of patients. Third, we aimed to evaluate whether HRV can be used as a potential physiomarker of CMT outcome. We hypothesised that CMT is feasible in PD and that it is effective in improving quality of life. Furthermore, we hypothesise that HRV increases after CMT in PD, and this predicts the changes in anxiety and depression and quality of life after the intervention.

METHODS

Participants and recruitment

In January/February 2022 participants were recruited via ParkinZone, a no-profit patients' association based in Rome, Italy. A 1-hour online informative recruitment session was held by the research team and included a brief description of the study aims and procedures. The study was advertised through the ParkinZone newsletter addressed to its members.

The study was approved by the Medical Ethics Committees of Neuromed Institute in Italy and registered on clinicaltrials.gov (registration number NCT05410769). The study conformed with the World Medical Association Declaration of Helsinki.

Inclusion criteria were having a diagnosis of PD established by a neurologist; and the ability to use online resources to take part in the intervention. Exclusion criteria were a clinical diagnosis of dementia and/or a score < 24 on the Montreal Cognitive Assessment (MoCA), any respiratory or cardiac disease, any major medical condition, and inability to give consent.

People with a clinical diagnosis of PD who were interested in participating in the study contacted the research team via email. They completed an online pre-screening interview to assess preliminary

inclusion criteria and they were required to provide written informed consent to participate.

Those who chose to participate, and who provided signed consent, underwent an online semi-structured screening interview which included gathering information on current medications, medical history, year of PD diagnosis and past psychiatric history. Additional screening procedures included the MoCA telemedicine version (available at www.mocatest.com). Participants who were considered eligible after screening were invited to join the study.

General overview of the study

Patients were tested on two different occasions: at baseline (T0) and at follow-up (T1) following a 6-week period of CMT (Figure 1). Before and after the CMT, patients completed questionnaires assessing depression, anxiety and quality of life (outcome measures are described below). In a subgroup of 11 patients, who agreed to be tested in person, we also collected physiological measures of autonomic function including HRV in a resting condition, during a trigger interview and during a deep breathing exercise (Figure 1).

Intervention

The intervention consisted of CMT, a compassion-focused intervention tailored for people with PD. The intervention was delivered online, in a group format across 6 weeks, once a week for approximately 2 h for each session. The group was led by a psychotherapist (SDM) expert in CMT and in PD. The programme started with a psychoeducational explanation of the rationale of the intervention and each session focused on a specific topic (see Table S1 for details on the intervention).

Assessments

Questionnaires

Patients completed questionnaires accessing sociodemographic, clinical and lifestyle (nicotine, alcohol and caffeine consumption, physical activity) information.

Feasibility measures

This was assessed using programme attendance and dropout rate as well as acceptability [25] (defined as willingness to continue practising as per feedback questionnaire at the end of the intervention, when participants were asked: "Do you think it would be helpful for you to continue training your compassionate mind?").

Clinical outcome measures

Primary outcome measure: The Parkinson's Disease Questionnaire (PDQ-39) [26] is a 39-item, self-report questionnaire, which assesses PD-specific health status and quality of life over the last month. It has eight subscales evaluating eight different dimensions of daily living. Each item is rated on a five-point scale

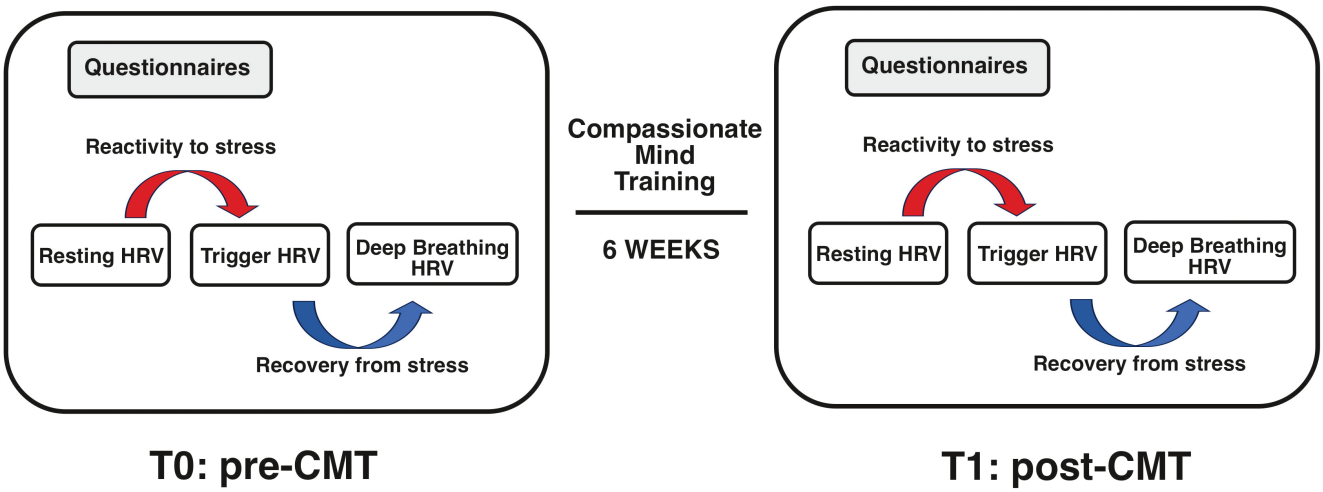

FIGURE 1 General overview of the study and experimental conditions. Psychological and physiological variables were tested at baseline (T0) and following a 6-week compassionate mind training (CMT) period (T1). Heart rate variability (HRV) measures were collected at rest (Resting HRV), in response to a stress-inducing interview (Trigger HRV) and following a deep breathing exercise (Deep Breathing HRV). The change in HRV from the Resting to the Trigger condition was used as a measure of physiological reactivity to stress. Similarly, the change in HRV from the Trigger to the Deep Breathing condition was used as a measure of Recovery from stress.

ranging from 0 (never) to 5 (almost always). The PDQ-39 summary index is derived by the sum of the eight subdomain scores divided by eight (the number of domains), giving a final score between 0 and 100.

Secondary outcome measures

The Spielberger State-Trait Anxiety Inventory (STAI) was employed to measure anxiety [27]. STAI is a 40-item, self-administered scale assessing state anxiety (i.e., STAI-Y1, how one feels at the moment) and trait anxiety (i.e., STAI-Y2, how one generally feels) using a four-point Likert scale (from 0 to 3 points) for each item.

The Beck Depression Inventory (BDI) [28] was used to measure self-reported depression. This is a 21-item, multiple-choice inventory rating the severity of the symptoms on a four-point scale, ranging from the absence to an intense level of a symptom. A score >17 indicates clinical depression.

The Self-Compassion Scale (SCS) [29]: This is a 26-item, validated scale of self-compassion, consisting of six subscales: self-kindness, self-judgment, common humanity, isolation, mindfulness and over-identification. Subscale scores are computed by calculating the mean of subscale item responses. The total self-compassion score is computed reversing scores of the negative subscale items (self-judgement, isolation and over-identification) and then computing a total mean; the total score ranges from 1 to 5, with higher scores indicating greater self-compassion.

Self-monitoring questions

Participants completed self-monitoring questions on their perceived compassion flows and effectiveness of the treatment (details in Material S1).

Physiological outcome measures

Eleven participants agreed to be tested in person and were included in the physiological substudy. Heart rate was recorded using a sensor incorporated in a belt that was tied around the chest of the patients (H10/H7 Heart Rate Sensor; Polar Electro Oy, Kempele, Finland). Participants' HRV was recorded at T0 (before the CMT) and at T1 (at the end of the 6-week intervention) in three different conditions. Two-minute epochs were recorded for each condition. In the first condition, patients were asked to sit quietly and breathe normally ('Resting'). For the second condition, patients participated in a 'Triggering interview', during which clinicians posed questions aimed at eliciting personal experiences and emotional reactions concerning the diagnosis ("How is it for you to live with Parkinson's disease?") ('Trigger'). People had 5 min to respond before the HRV measurement was taken. In the third condition, participants engaged in a 3-min-long deep breathing exercise aimed at improving focus and inducing relaxation (referred to as 'Deep breathing').

Statistical analysis

All data are expressed as means and standard deviations. Normality of the variables was examined using Shapiro–Wilk tests. Non-normally distributed variables were logarithmically transformed before proceeding with further analyses. If normality was achieved, parametric tests were performed. Otherwise, nonparametric tests were selected. Non-normal variables are summarised with medians and percentiles. Age and gender were used as covariates of no-interest in all of the performed analyses. Differences at $p < 0.05$ were regarded as significant. Data analysis was performed with SPSS 23.0 for Windows (SPSS Inc., Chicago, IL, USA). Pre- and post-treatment questionnaires scores were compared by means of paired sample - test or Wilcoxon test according to normality of data distribution. To facilitate correlational analyses, delta scores were computed for clinical measures, by subtracting T1 scores from T0 scores. These scores reflected the change in the measure following the CMT intervention, with negative scores indicating a decrease in the scale score following CMT, whereas positive scores indicated an increase in score. Consequently, delta PDQ-39, delta STAI and delta BDI reflected the change in quality of life, anxiety and depression following CMT.

Analysis of HRV data

HRV values were extracted from the Polar Belt software. The time–domain analysis was used for the determination of the root mean square of successive differences between consecutive heartbeats (RMSSD). RMSSD reflects vagal tone [30] and, compared with other HRV measures, is relatively less affected by respiratory rate [31, 32].

To facilitate correlational analyses and interpretation, we computed delta RMSSD scores, to measure the relative change in RMSSD during the trigger interview in comparison with the resting condition (Stress Reactivity = RMSSD Trigger – RMSSD Resting; Figure 1, red arrow), and during the deep breathing in comparison to the trigger (Stress Recovery = RMSSD Deep Breathing – RMSSD Trigger; Figure 1, blue arrow).

In both cases, negative numbers indicated a decrease in RMSSD in response to the trigger condition or in response to the deep breathing condition. Stress Reactivity and Recovery scores were used in subsequent correlational analyses, to explore the association between physiological responses to stress and psychological variables at baseline and in response to CMT.

Spearman correlation analysis was conducted to explore correlations between HRV and clinical variables at baseline and following the treatment. The effect of the experimental condition and of CMT on RMSSD was explored by means of a 3×2 repeated-measures

ANOVA, with "Condition" (Resting, Trigger, Deep Breathing) and "CMT" (T0, T1) as main factors.

RESULTS

Twenty-three PD patients participated and completed the training (12 females, mean age 57.6 ± 8.1 years, mean disease duration 8.9 ± 3.36 years). In a subgroup of 11 patients (8 females, mean age 58.2 ± 6.3 years, mean disease duration 9 ± 3.7 years), HRV data were collected at T0 and T1. Sociodemographic and clinical characteristics of participants are presented in Table 1.

Feasibility

The mean percentage of attendance was 94.3%. There was one dropout where a patient expressed disinterest in continuing with the intervention and the study.

The majority (83%) of patients believed that continuing training for a compassionate mind would be beneficial for them.

Clinical outcome measures

CMT significantly improved quality of life as shown by a decrease of PDQ-39 total score (mean PDQ 39 total score at T0 = 45.3 ± 18.2; mean PDQ 39 total score T1 = 41.3 ± 16.6, $t = 2.5$, $p = 0.02$, Cohen's $d = 0.23$) and Stigma subscore (mean PDQ 39 stigma score at T0 = 3.5 ± 3.1; mean PDQ 39 stigma score at T1 = 2.7 ± 2.8, $t = 2.3$, $p = 0.03$, Cohen's $d = 0.30$) (Figure 2). The improvement in PDQ-39 Stigma subscore was confirmed also in the subgroup that underwent the HRV measurement (mean PDQ-39 Stigma score at T0 = 3.5 ± 2.7, mean stigma score at T1 = 2.2 ± 2.9, $t = 2.6$, $p = 0.02$, Cohen's $d = 0.44$). No significant change was observed on measures of anxiety or depression (all $p > 0.05$; Table 1). No significant change was observed in any of the SCS scores (all $p > 0.05$).

Details on the responses to the self-monitoring questions after the intervention are shown in Material S1.

HRV analysis

Correlational analyses with baseline HRV values

At baseline (pre-CMT intervention), subjects with higher PDQ-39 stigma scores had higher STAI-1 ($\rho = 0.54$, $p = 0.006$), STAI-2 ($\rho = 0.58$, $p = 0.003$) and higher delta RMSSD during the Trigger condition ($\rho = -0.70$; $p = 0.01$). These data suggest that people with PD who have the highest stigma for their disease also exhibit higher levels of trait and state anxiety and the strongest decrease in RMSSD during an emotionally stressful situation (i.e., less functional physiological response to emotional stress). At baseline, we also found a trend for a positive correlation between PDQ-39 stigma scores and severity of depression (BDI, $\rho = 0.37$, $p = 0.07$).

Effect of CMT on HRV

Repeated-measures ANOVA with "Condition" (Resting, Trigger, Deep Breathing) and "CMT" (T0, T1) as main factors showed a significant effect of condition ($F[1, 10] = 5.3$, $p = 0.03$, $\eta_p^2 = 0.54$). Post-hoc analysis showed that RMSSD during the Trigger condition was significantly higher at T1 as compared with T0, indicating a more functional physiological reactivity to stress following CMT (mean RMSSD during Trigger at T0 = 15.65 ± 7.21, mean RMSSD during Trigger at T1 = 24.18 ± 10.18, $t = -3.2$, $p = 0.005$, $\eta_p^2 = 0.31$) (Figure 3).

Correlational analysis with delta RMSSD

Correlational analyses revealed a negative correlation between the delta RMSSD in response to the Trigger interview at baseline, and delta STAI and BDI scores (in response to CMT, $\rho = -0.69$, $p = 0.05$ and

TABLE 1 Demographic and clinical characteristics of the study population with changes in clinical scores between baseline and T1.

Characteristic	T0 (baseline)	T1 (post-intervention)	*P*-value
Age (years)	57.6 ± 8.1		
Gender	13F/11M		
Disease duration (years)	8.2 ± 3.3		
Total LEDD	577.4 ± 201.4		
BDI-II	12 (9,16)	111 (7,17)	0.9
STAI-Y1	41 (27,49)	34 (28,49)	0.8
STAI-Y2	41 (36,49)	37 (34,49)	0.7
SCS total score	3.3 ± 0.6	3.4 ± 0.6	0.4

Note: Values are means ± standard deviations or median (25th, 75th percentiles).

Abbreviations: BDI-II, Beck Depression Inventory; F, female; LEDD, Levodopa equivalent daily dose; M, male; PDQ-39, Parkinson's Disease Questionnaire; SCS, Self-Compassion Scale; STAI, State-Trait Anxiety Inventory; YI, how the individual feels at the moment; Y2, how the individual generally feels.

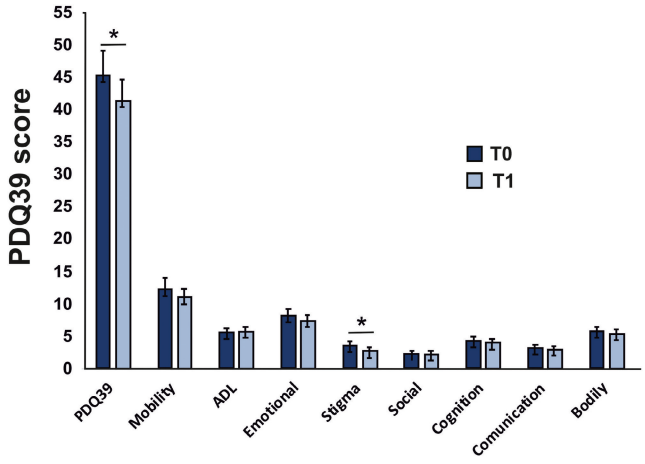

FIGURE 2 Changes in quality of life as per the Parkinson's Disease Questionnaire (PDQ-39) total score and subscores before and after the compassionate mind training (CMT) intervention. There was a significant improvement in total score ($p=0.03$) and Stigma subscore ($p=0.02$) (asterisks indicate $p<0.05$). ADL, activities of daily living. * indicates statistical significance.

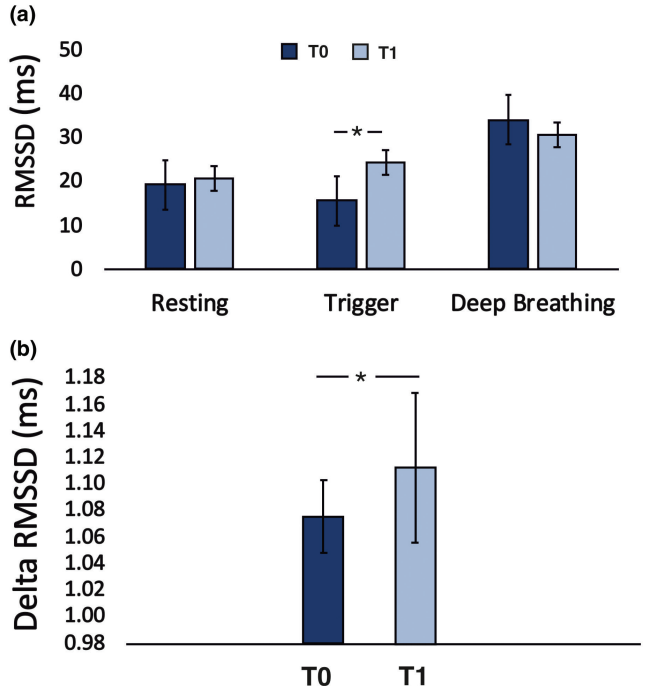

FIGURE 3 (a) Changes in root mean square of successive differences between consecutive heartbeats (RMSSD) of heart rate variability before and after the intervention in the three experimental conditions: resting, after a trigger interview (Reactivity) and after deep breathing (Recovery). A significant difference in RMSSD in the trigger condition is shown ($p=0.005$). (b) Average delta RMSSD at T0 (pre-compassionate mind training [CMT]) and at T1 (post-CMT). RMSSD during stress or in recovery from stress was overall higher following 6 weeks of CMT, indicating a better sympathovagal balance. * indicates statistical significance.

rho = −0.80, $p=0.01$, respectively). These results indicate that people with PD with the lowest decrease in RMSSD in response to stress at baseline (indicating a more functional physiological reaction to stress)

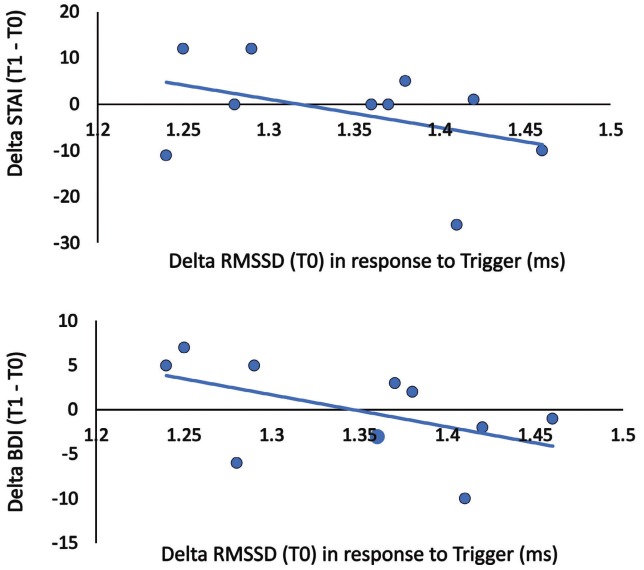

FIGURE 4 Correlation between the delta root mean square of successive differences between consecutive heartbeats (RMSSD) during stress at T0 and the change in anxiety and depression (delta STAI and delta BDI scores) following compassionate mind training (CMT) intervention. BDI, Beck Depression Inventory; STAI, State-Trait Anxiety Inventory.

had the stronger reduction in anxiety and depression (as per STAI and BDI scores) following the CMT intervention (Figure 4).

DISCUSSION

CTM is a well-established psychological approach incorporating both compassion and mindfulness-based practices [10, 11]. A number of studies have shown that CTM is feasible and effective in reducing stress and anxiety in several medical conditions [15, 33].

This is the first study using CMT in people with PD. Our results demonstrate the feasibility of implementing this treatment in people with PD in keeping with previous studies on the potential utility of mindfulness-based therapies in this population [8, 34]. The dropout rate in our sample was minimal, with only one participant discontinuing the training. Almost all (99%) our patients actively participated in the CMT programme until its completion, demonstrating a high level of engagement. Importantly, the feedback received from the participants revealed a positive perception of the training. A significant proportion of participants (88%) expressed their desire to continue practising compassion even after the training had concluded.

Following a course of CMT, we also found an improvement in quality of life scores in people with PD, in particular in the domain of self-perceived stigma. Stigma is defined as the experience of devaluation, discrimination or embarrassment that is self-perceived or other-perceived, and it is often felt by people with PD due to the presence of motor and non-motor symptoms [35]. It is a key

determinant of reduced quality of life in PD, which may cause social isolation [36], and an increase in anxiety, depression and apathy [35, 37]. Previous studies have shown that in people with PD self-compassion is related to stigma, namely that people with higher self-compassion also have a better way of reacting to external stigma and also have fewer neuropsychiatric symptoms [17]. This is supported by our results and explains why enriching self-compassion through CMT can be effective in improving quality of life in general and self-perceived stigma in particular.

In a subset of our patients we used HRV as a physiological marker to (i) evaluate the physiological changes associated with psychological distress at baseline; (ii) measure the physiological changes associated with the outcome of CMT and (iii) predict the response to CMT. Our data showed that self-perceived stigma before the intervention was associated with lower HRV. A recent systematic review has shown scientific evidence on the relationship between stigma/discrimination and cardiovascular health outcomes such as low HRV [38]. A possible mechanism underlying this association could be linked to the way the body reacts to the emotional distress of stigma and discrimination as a stressor. Indeed, cardiovascular changes in response to acute and chronic stress have already been described [39]. The relationship between stigma in PD and stress is complex and might involve social isolation, reluctance in asking for help and loneliness [40].

Compassion-based practices have been shown to increase HRV [41–43]. In our study CMT increased HRV, indicating a functional rebalancing of the autonomic nervous system with an increase in parasympathetic activity. Specifically, post-hoc analyses indicated that CMT increased HRV during the stress induction (trigger condition), where HRV during the trigger interview was higher at T1 as compared with T0. Together with the improvement in clinical scales, these results indicate that CMT can have a beneficial effect on the autonomic nervous systems and could serve as an effective intervention for promoting physiological stress resilience in people with PD. Higher HRV has been linked to both physical and mental well-being, such as higher pain threshold, better metabolic health, including lower levels of inflammation, better glucose regulation, and lower risk of type 2 diabetes [44]. An increase in HRV following biofeedback techniques has been linked to a decrease in pain severity in patients with chronic pain [45]. Future studies will investigate whether CMT, via an increase in HRV, can have a beneficial effect on other PD-related symptoms such as sleep quality or pain.

Whilst we did not observe an overall effect of CMT on depression and anxiety scores, reactivity of HRV to stress predicted the effect of CMT on anxiety and depression, where individuals with a more functional physiological response to stress (less decrease in HRV during the trigger interview) had the highest improvement in scores of anxiety and depression at following CMT. Our data are in accordance with other studies showing a predictive role of HRV in psychological therapy outcomes [46]. Additionally, studies have indicated that elevated HRV values at baseline predict positive changes in quality of life through psychotherapy [47]. An impact of physiological reactions to stress on psycho-therapeutic outcomes has been reported previously. Schechter et al. [48] described an association between negative multisystemic therapy outcomes and either low or high cortisol levels in adolescents. Moreover, children and adolescents undergoing treatment for behavioural issues exhibited poorer treatment outcomes when experiencing more stress [49]. Conversely, Roque et al. [50] showed that higher levels of stress-induced cortisol response predicted greater decreases in symptoms following a psychological treatment targeting negative affectivity. If our preliminary data are confirmed, HRV could be used to guide therapy decisions and offer individually tailored psychotherapy. For example, individuals with reduced HRV might need an additional number of sessions, or an integrated approach where psychotherapy is combined with interventions aimed at increasing HRV, such as biofeedback or slow breathing techniques.

Despite the promising results, the present study has limitations. The study was a feasibility study with a small sample size and lack of a control group, and included a heterogeneous patient group in terms of disease duration and symptoms severity. Also, we cannot exclude the possibility of selection bias due to the fact that participants were recruited from a PD organisation. In the future, fully powered, blinded, randomised control trials will be required to fully elucidate the effectiveness of CMT in PD, and potentially the impact of HRV-enhancing methods potentiating the outcome of CMT therapy.

AUTHOR CONTRIBUTIONS

Lucia Ricciardi: Conceptualization; writing – original draft; methodology; writing – review and editing; formal analysis; project administration; supervision. **Silvia Della Morte:** Conceptualization; data curation; investigation. **Elena Berti:** Investigation; data curation. **Carolina Lalli:** Data curation; investigation. **Nicola Modugno:** Supervision. **Francesca Morgante:** Writing – review and editing. **Anette Schrag:** Writing – review and editing. **Elena Makovac:** Conceptualization; writing – original draft; methodology; writing – review and editing; formal analysis; supervision; project administration.

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CONFLICT OF INTEREST STATEMENT

No conflict of interest in relation to this study has been reported.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Hermanowicz N, Jones SA, Hauser RA. Impact of non-motor symptoms in Parkinson's disease: a PMDAlliance survey. *Neuropsychiatr Dis Treat*. 2019;15:2205-2212.
2. Weintraub D, Mamikonyan E. The neuropsychiatry of Parkinson disease: a perfect storm. *Am J Geriatr Psychiatry*. 2019;27(9):998-1018.
3. Weintraub D, Aarsland D, Chaudhuri KR, et al. The neuropsychiatry of Parkinson's disease: advances and challenges. *Lancet Neurol*. 2022;21(1):89-102.
4. Schrag A, Taddei RN. Depression and anxiety in Parkinson's disease. *Int Rev Neurobiol*. 2017;133:623-655.
5. Dobkin RD, Menza M, Allen LA, et al. Cognitive-behavioral therapy for depression in Parkinson's disease: a randomized, controlled trial. *Am J Psychiatry*. 2011;168(10):1066-1074.
6. Khoury B, Lecomte T, Fortin G, et al. Mindfulness-based therapy: a comprehensive meta-analysis. *Clin Psychol Rev*. 2013;33(6):763-771.
7. Brown KW, Ryan RM. The benefits of being present: mindfulness and its role in psychological well-being. *J Pers Soc Psychol*. 2003;84(4):822-848.
8. van der Heide A, Meinders MJ, Speckens AEM, Peerbolte TF, Bloem BR, Helmich RC. Stress and mindfulness in Parkinson's disease: clinical effects and potential underlying mechanisms. *Mov Disord*. 2021;36(1):64-70.
9. Zarotti N, Eccles FJR, Foley JA, et al. Psychological interventions for people with Parkinson's disease in the early 2020s: where do we stand? *Psychol Psychother*. 2021;94(3):760-797.
10. Gilbert P. Compassion: from its evolution to a psychotherapy. *Front Psychol*. 2020;11:586161.
11. Gilbert P. The origins and nature of compassion focused therapy. *Br J Clin Psychol*. 2014;53(1):6-41.
12. Neff KD. Self-compassion: theory, method, research, and intervention. *Annu Rev Psychol*. 2023;74:193-218.
13. Gilbert P. *Compassion focused therapy: distinctive features*. Abingdon, UK: Routledge; 2010. doi:10.4324/9780203851197
14. Jazaieri H, McGonigal K, Jinpa T, Doty JR, Gross JJ, Goldin PR. A randomized controlled trial of compassion cultivation training: effects on mindfulness, affect, and emotion regulation. *Motiv Emot*. 2014;38(1):23-35.
15. Kirby JN. Compassion interventions: the programmes, the evidence, and implications for research and practice. *Psychol Psychother*. 2017;90(3):432-455.
16. Leaviss J, Uttley L. Psychotherapeutic benefits of compassion-focused therapy: an early systematic review. *Psychol Med*. 2015;45(5):927-945.
17. Eccles FJR, Sowter N, Spokes T, Zarotti N, Simpson J. Stigma, self-compassion, and psychological distress among people with Parkinson's. *Disabil Rehabil*. 2023;45(3):425-433.
18. Kirby JN, Doty JR, Petrocchi N, Gilbert P. The current and future role of heart rate variability for assessing and training compassion. *Front Public Health*. 2017;5:40.
19. Malik M, Bigger JT, Camm AJ, et al. Heart rate variability: standards of measurement, physiological interpretation, and clinical use. *Eur Heart J*. 1996;17(3):354-381.
20. Dishman RK, Nakamura Y, Garcia ME, Thompson RW, Dunn AL, Blair SN. Heart rate variability, trait anxiety, and perceived stress among physically fit men and women. *Int J Psychophysiol*. 2000;37(2):121-133.
21. Ottaviani C, Medea B, Lonigro A, Tarvainen M, Couyoumdjian A. Cognitive rigidity is mirrored by autonomic inflexibility in daily life perseverative cognition. *Biol Psychol*. 2015;107:24-30.
22. Levine JC, Fleming R, Piedmont JI, Cain SM, Chen WJ. Heart rate variability and generalized anxiety disorder during laboratory-induced worry and aversive imagery. *J Affect Disord*. 2016;205:207-215.
23. Taelman J, Vandeput S, Spaepen A, Van Huffel S. Influence of mental stress on heart rate and heart rate variability. *IFMBE Proceedings*, Springer Berlin Heidelberg. 2009:1366-1369.
24. Wang Z, Luo Y, Zhang Y, et al. Heart rate variability in generalized anxiety disorder, major depressive disorder and panic disorder: a network meta-analysis and systematic review. *J Affect Disord*. 2023;330:259-266.
25. Bowen DJ, Kreuter M, Spring B, et al. How we design feasibility studies. *Am J Prev Med*. 2009;36(5):452-457.
26. Peto V, Jenkinson C, Fitzpatrick R, Greenhall R. The development and validation of a short measure of functioning and well being for individuals with Parkinson's disease. *Qual Life Res*. 1995;4(3):241-248.
27. Spielberger CD. State-Trait Anxiety Inventory for Adults. Washington DC, USA: American Psychological Association; 1983. doi:10.1037/t06496-000
28. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961;4:561-571.
29. Neff KD. The development and validation of a scale to measure self-compassion. *Self Identity*. 2003;2(3):223-250.
30. Shaffer F, McCraty R, Zerr CL. A healthy heart is not a metronome: an integrative review of the heart's anatomy and heart rate variability. *Front Psychol*. 2014;5:1040.
31. Hill LK, Siebenbrock A. Are all measures created equal? Heart rate variability and respiration – biomed 2009. *Biomed Sci Instrum*. 2009;45:71-76.
32. Shaffer F, Ginsberg JP. An overview of heart rate variability metrics and norms. *Front Public Health*. 2017;5:258.
33. Craig C, Hiskey S, Spector A. Compassion focused therapy: a systematic review of its effectiveness and acceptability in clinical populations. *Expert Rev Neurother*. 2020;20(4):385-400.
34. McLean G, Lawrence M, Simpson R, Mercer SW. Mindfulness-based stress reduction in Parkinson's disease: a systematic review. *BMC Neurol*. 2017;17(1):92.
35. Salazar RD, Weizenbaum E, Ellis TD, et al. Predictors of self-perceived stigma in Parkinson's disease. *Parkinsonism Relat Disord*. 2019;60:76-80.
36. Ma HI, Saint-Hilaire M, Thomas CA, Tickle-Degnen L. Stigma as a key determinant of health-related quality of life in Parkinson's disease. *Qual Life Res*. 2016;25(12):3037-3045.
37. Schrag A, Jahanshahi M, Quinn NP. What contributes to depression in Parkinson's disease? *Psychol Med*. 2001;31(1):65-73.
38. Panza GA, Puhl RM, Taylor BA, Zaleski AL, Livingston J, Pescatello LS. Links between discrimination and cardiovascular health among socially stigmatized groups: a systematic review. *PLoS One*. 2019;14(6):e0217623.
39. Rozanski A, Blumenthal JA, Kaplan J. Impact of psychological factors on the pathogenesis of cardiovascular disease and implications for therapy. *Circulation*. 1999;99(16):2192-2217.
40. McDaniels B, Pontone GM, Mathur S, Subramanian I. Staying hidden: the burden of stigma in PD. *Parkinsonism Relat Disord*. 2023;116:105838.
41. Arch JJ, Brown KW, Dean DJ, Landy LN, Brown KD, Laudenslager ML. Self-compassion training modulates alpha-amylase, heart rate variability, and subjective responses to social evaluative threat in women. *Psychoneuroendocrinology*. 2014;42:49-58.
42. Petrocchi N, Ottaviani C, Couyoumdjian A. Compassion at the mirror: exposure to a mirror increases the efficacy of a self-compassion manipulation in enhancing soothing positive affect and heart rate variability. *J Posit Psychol*. 2017;12(6):525-536.

43. Kok BE, Coffey KA, Cohn MA, et al. How positive emotions build physical health: perceived positive social connections account for the upward spiral between positive emotions and vagal tone. *Psychol Sci*. 2013;24(7):1123-1132.
44. Lampert R, Bremner JD, Su S, et al. Decreased heart rate variability is associated with higher levels of inflammation in middle-aged men. *Am Heart J*. 2008;156(4):759.e1-e7.
45. Reneau M. Heart rate variability biofeedback to treat fibromyalgia: an integrative literature review. *Pain Manag Nurs*. 2020;21(3):225-232.
46. Balint EM, Daniele V, Langgartner D, et al. Heart rate variability predicts outcome of short-term psychotherapy at the workplace. *Psychophysiology*. 2023;60(1):e14150.
47. Angelovski A, Sattel H, Henningsen P, Sack M. Heart rate variability predicts therapy outcome in pain-predominant multisomatoform disorder. *J Psychosom Res*. 2016;83:16-21.
48. Schechter JC, Brennan PA, Cunningham PB, Foster SL, Whitmore E. Stress, cortisol, and externalizing behavior in adolescent males: an examination in the context of multisystemic therapy. *J Abnorm Child Psychol*. 2012;40(6):913-922.
49. Mathijssen JJ, Koot HM, Verhulst FC. Predicting change in problem behavior from child and family characteristics and stress in referred children and adolescents. *Dev Psychopathol*. 1999;11(2):305-320.
50. Roque AD, Craske MG, Treanor M, Rosenfield D, Ritz T, Meuret AE. Stress-induced cortisol reactivity as a predictor of success in treatment for affective dimensions. *Psychoneuroendocrinology*. 2020;116:104646.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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