The role of lifestyle interventions in symptom management and disease modification in Parkinson's disease

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Emerging evidence indicates that sustainable lifestyle changes—such as increasing physical activity, adopting healthy dietary patterns, and managing stress—can provide symptomatic benefits and potentially slow neurodegeneration in Parkinson's disease. Combining these interventions could produce synergistic effects, addressing multiple aspects of the pathophysiology. Despite the challenges of long-term adherence, innovative approaches such as digital tools and personalised strategies can support sustained lifestyle modifications. Tailoring interventions to individual needs and cultural contexts is crucial, especially in diverse socioeconomic settings. Future research should focus on large-scale, long-term studies to better understand the disease-modifying potential of lifestyle interventions and explore the biological mechanisms underlying their benefits. Overall, integrating lifestyle modifications into routine care offers a promising, accessible avenue to improve quality of life and potentially alter the progression of Parkinson's disease.

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See **Online** for appendix

Introduction

The complexity and heterogeneity of Parkinson's disease is enormous, with marked variations in age at onset, presentation, progression rate, treatment response, and underlying pathophysiology. This multifaceted nature highlights the importance of considering an holistic approach in addition to conventional management (ie, pharmacotherapy and surgical therapies), to optimally support people with Parkinson's disease.[1] Emerging evidence indicates that lifestyle interventions (panel 1) can reduce disability and improve quality of life. Such lifestyle approaches offer opportunities for self-management, which will become increasingly important given the growing prevalence of Parkinson's disease worldwide. Lifestyle interventions can potentially break the vicious cycle of unhealthy behaviours and symptomatic worsening, and perhaps slow disease progression (figure 1).

Several reviews have discussed specific lifestyle interventions separately, including updates on restorative sleep[6] and avoidance of risky substances[7] (eg, alcohol, nicotine, or drugs; appendix p 2–8). In this Review, we discuss evidence published over the past 5 years on three specific domains—physical activity, nutrition, and stress—and address the added, and possibly synergistic, effects of combining different lifestyle interventions. We do not explicitly review the lifestyle domain of social interactions, but address this as an embedded part of many integrated lifestyle approaches. We start with physical activity, for which the evidence is strongest, followed by the two other domains that have been studied less widely. We pay specific attention to the pleiotropic mechanisms of action of lifestyle interventions, and how these might contribute to symptomatic and perhaps disease-modifying effects. We also highlight how the need to address multiple lifestyle domains comes with challenges (eg, long-term compliance) and how new technologies can offer possible solutions. We conclude by presenting several immediate implications for clinical practice and by recommending priorities for future research.

Physical activity

Many types of physical activity have been studied for the management of Parkinson's disease, with tremendous heterogeneity in types of interventions and outcomes. Studied most often were aerobic exercise (n=7),[8–13] resistance training (n=5),[14–18] combined exercises (n=6),[19–24] and interventions supported by innovative technology, such as exergaming (ie, the use of gamification elements to promote adherence to an exercise intervention; n=9).[25–33] The study outcomes were mostly clinical (eg, assessments of motor symptoms and non-motor symptoms). Only three studies included blood-based biomarkers[34–36] and two used imaging as outcomes.[11–27]

Symptomatic effects

Large-scale randomised clinical trials (RCTs; published >5 years ago) had shown that moderate to high intensity aerobic exercise stabilises motor symptoms over a 6-month period, compared with active control groups in whom motor symptoms progressed (appendix p 2–6). This finding has now been extended by additional, smaller-scale RCTs that found high-intensity aerobic exercise improves gait speed, gait kinematics, and quality of life.[10,12]

Evidence from RCTs in patients with Parkinson's disease suggests that light to moderate physical activity might also be beneficial. One RCT compared 26 weeks of brisk walking (at 40–60% of heart rate reserve) with upper limb training (the active control) in 70 people with mild-to-moderate Parkinson's disease.[37] Both interventions were partly supervised and partly done as self-training at home (for a total of 3 times per week). The results showed that brisk walking improved the primary outcome (motor symptoms, measured using the Movement Disorders Society Unified Parkinson's Disease Rating Scale [MDS-UPDRS] part III). Similar improvements were found for some of the secondary outcomes (functional mobility and balance). This insight is relevant for daily practice, because not everyone enjoys or is able to engage in a vigorous workout. It is also relevant for cultures in which brisk walking is an intrinsic

Panel 1: Glossary of terms

Lifestyle interventions

Therapies focusing on lifestyle factors to prevent, manage, or reverse chronic conditions. Lifestyle medicine encompass six pillars: increasing physical activity, nutritional interventions, stress management, restorative sleep, avoidance of risky substances (eg, alcohol, nicotine, or drugs), and fostering positive social connections.[2]

Physical activity

Any body movement produced by skeletal muscles that requires energy.[3] This broad concept includes, but is not limited to, exercise: a type of physical activity that encompasses planned, structured, and repetitive bodily movements to improve or maintain one or more components of physical fitness.[3] Exercise is mostly categorised into aerobic exercise (eg, rhythmic and repetitive physical activity that increases heart rate, such as cycling, rowing, and running), resistance training (eg, repetitively contracting the muscles against resistance), flexibility exercise, and neuromotor exercise (eg, posture, gait, balance, and agility training). Physical activity also includes unplanned, unstructured activities such as walking, household tasks, or leisure activities.

Nutritional interventions

Structured efforts to modify food intake. These interventions can include changes to macronutrient intake (eg, protein, carbohydrate, or fat), calorie intake, specific dietary patterns, or the use of supplements. Supplements are discussed briefly in the appendix (pp 9–10).

Stress

A process by which environmental demands (ie, stressors) exceed an individual's adaptive capacity, resulting in psychological and biological responses. The biological stress response intends to restore homoeostatic balance by initiating fast, sympathetic changes, and by activating the hypothalamic–pituitary–adrenal axis resulting in cortisol release. Chronic exposure to stressors can lead to dysregulation of the stress response and result in psychological symptoms such as anxiety and depression. Whether or not an individual develops these symptoms depends on several resilience factors, including, for example, cognitive appraisal of the stressor, coping styles, cognitive abilities, and social support.[4,5]

Gene–environment interactions

The effect of external factors on disease risk or disease progression, for which a different genotype can modify this role. In other words, the same environment or lifestyle factor can lead to different phenotypes depending on an individual's genetic make-up.

part of daily routines, such as a need to cover long distances by foot.

A recent network meta-analysis revealed a U-shaped dose–response relationship between exercise and overall motor symptom improvement.[38] Specifically, exercise alleviated motor symptoms in a dose-dependent manner, with effects already at a low dose of 60 metabolic equivalent of a task per minute per week (MET-min per week; quantifying the duration, frequency, and intensity of an activity), and with an optimal dose at 1300 MET-min per week; beyond this point, the effect diminished. The optimal dose was different for different types of exercise. Dance was most effective, with an optimal motor improvement at 850 MET-min per week.[38]

Resistance training is gaining popularity. Several small-scale RCTs (n=22–40) found positive effects on muscle strength,[17,18] functional mobility,[14,16,18] balance,[14] freezing of gait,[15] and motor symptoms.[16] A large RCT (n=236 people with early stage Parkinson's disease) suggested that combining aerobic exercise with resistance training might provide synergistic benefits.[23] Specifically, this study compared 12 months of combined training (3 times per week) with aerobic exercise alone. The combined group showed greater improvements in motor functioning, sleep, and aerobic capacity. Adverse events were comparable between both groups, but adherence or drop-outs were not reported, making it difficult to interpret the feasibility of the interventions. Quality of life improved more for the aerobic exercise group than for the combined exercise group; perhaps because these were standardised exercise programmes, and randomisation does not consider personal exercise preferences. Previous studies showed that quality of life improvements differ with different types of exercise interventions,[39] which highlights the need to develop tailored physical activity interventions.

High intensity interval training (HIIT) is receiving increasing attention in both research and clinical practice. HIIT involves short exercise bouts of approximately 1 min at a very high intensity (eg, 90% of maximum heart rate), followed by recovery exercise bouts at a low intensity. A main advantage is that a workout takes a relatively short time (around 20 min per session), making it more appealing for some people. Recent small RCTs (n=29–33) suggest that HIIT is feasible for people with Parkinson's disease, conveying greater improvements in muscle strength and peak maximum aerobic capacity than continuous training at moderate intensity.[40–42] There were no consistent effects in these studies on functional outcomes; this finding deserves further investigation.

Recognition is growing among clinicians and people with Parkinson's disease that, to promote adherence, physical activity is ideally organised in the community. Study findings in the past 5 years suggest benefits from several community-based interventions, including climbing,[43] boxing,[44–46] Tai Chi,[35,47–49] dance,[50,51] karate,[52] and pilates.[21,53] The social element, the generally good accessibility (not requiring travels to specialised facilities), and low costs of group-based interventions makes this type of activity attractive to many people with Parkinson's disease.[54] Innovative ways are emerging to

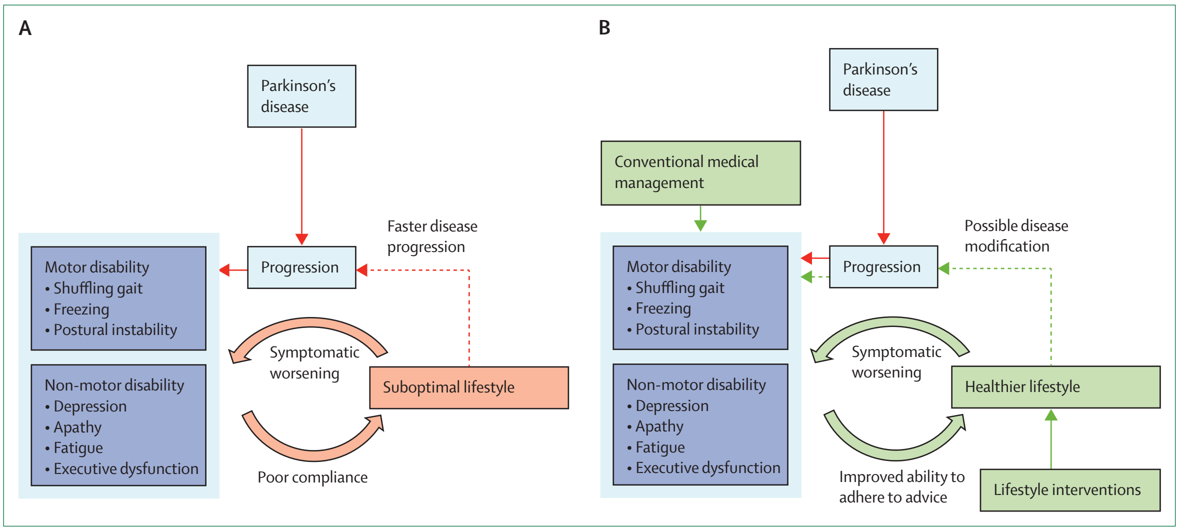

Figure 1: **The role of lifestyle interventions in the management of Parkinson's disease**
(A) Parkinson's disease is characterised by a complex constellation of motor and nonmotor symptoms. Both interfere with a person's ability to engage in a healthy lifestyle. For example, the combination of gait disability and postural instability can create a fear of falling, which in turn makes people more reluctant to remain physically active. This inactivity is compounded by an inability to exercise, caused by fatigue, or by difficulties to engage with exercise in the first place, due to depression or apathy. Swallowing difficulties, hyposmia, and a fear of bloating or flatulence are reasons why many people with Parkinson's disease have a suboptimal diet. These symptoms can result in an unhealthy lifestyle, which will lead to further symptomatic worsening, thus completing a vicious cycle. An unhealthy lifestyle might also lead to hastening of the underlying disease progression, which will only further accelerate the vicious cycle. (B) There are many opportunities to break this vicious cycle, and to turn this into a so-called virtuous cycle. A first step is to optimise conventional medical management, aiming to reduce the level of disability and thereby making people eligible for a lifestyle intervention. A second step would be to start cautiously, with one lifestyle intervention that is easiest to attain, and for which the patient is most motivated. Once this is implemented, symptoms will improve, thereby creating further opportunities to enhance the intensity of the first intervention, or to take on additional lifestyle interventions. Red arrows indicate worsening, green indicate improvement, and dashed lines indicate a speculative link.

increase physical activity in the home by using telehealth, gaming, virtual reality, or different types of apps (eg, to motivate physical activity, offering exercises, or gaming).[55,56] Overall, these remote approaches seem feasible, adherence is good, and participants find them enjoyable.[28,30,51,57,58] However, one study found that the intensity of a home-based e-health programme was inadequate;[57] this dosing aspect deserves further study. Virtual reality and augmented reality seem to facilitate motor learning[33] and improve balance, gait, and sensory-motor functioning.[32,59] A large RCT in 192 people with Parkinson's disease evaluated the effects of 12 weeks of balance training by performing exergaming (a video game that required physical activity to interact with the game) on a home gaming platform, compared with traditional balance training.[31] The exergaming group had fewer people who had falls and, in those who fell, a lower number of falls. There was no between-group difference in quality of life. Of note, the cohort included people with a history of falling, and almost half of participants were in Hoehn and Yahr stage 4, as opposed to many other studies on physical activity, which typically included less vulnerable participants (ie, people with lower stage scores). This result is promising, and suggests that people in advanced disease stages (ie, Hoehn and Yahr stages 4 and 5) might benefit from exergaming.

Many studies have also examined the effect of physical activity on non-motor symptoms. Different types of physical activity (eg, Tai Chi, Qigong, functional training, HIIT, and boxing) improved fatigue,[40] mood,[44] anxiety, and non-motor symptoms in general.[41,60] A combined intervention (ie, strength, endurance, and balance training) improved sleep more than sleep hygiene instructions.[19] Mind–body activities, such as Tai Chi and Qigong, also improved sleep.[49,60]

Adverse effects

We found no new studies in the past 5 years that described serious adverse effects of physical activity. Overall, physical activity is considered a safe intervention. Home-based interventions delivered remotely using digital technology[26,30,57] and community-based interventions (eg, boxing)[61] were found to be safe. One potential serious adverse event relates to cardiovascular events, mediated by autonomic dysfunction (eg, orthostatic hypotension and chronotropic incompetence) or underlying cardiovascular disease, both of which are common in Parkinson's disease.[1] However, during our search we encountered no studies that reported adverse cardiovascular events during or after participating in physical activity. Another concern is falls, which might paradoxically increase when people are encouraged to become more active (many types of physical activity require a good balance and ability to engage in double tasking, but these are often impaired in people with Parkinson's disease). Falls can have serious consequences, such as fractures, and are associated with a poor prognosis, including increased mortality.

However, several studies showed a reduced risk of falls following exercise, with the caveat that the intervention itself was delivered under supervised conditions.[31,46] Concerns persist for individuals who are less likely to participate in an exercise intervention than the typical trial candidates, such as those with greater disease severity and impairments of gait, balance, or cognition. We recommend addressing the risk of adverse events before advising people with Parkinson's disease to start exercising, especially when recommending activities that require balancing or dual tasks.[62] Supervised activities should be considered for individuals considered susceptible to adverse events.

Nutrition

Diet is generating a lot of interest in the Parkinson's disease community, with multiple ongoing studies.[63] Many people with Parkinson's disease struggle with questions related to what constitutes an ideal diet. Most questions are difficult to answer because the evidence related to nutritional interventions in Parkinson's disease is limited by a scarcity of high quality clinical trials.[63] Many RCTs were done within the past 5 years (n=21, including 17 studies on supplements), but most involved small sample sizes and brief interventions. Moreover, the types of interventions and outcomes were heterogeneous, making it impossible to draw overall conclusions on the effectiveness of nutritional interventions in Parkinson's disease. Meta-analyses are unfeasible for the same reason. Here we discuss only studies on a dietary pattern such as the Mediterranean diet (n=4). Studies on supplements are briefly discussed in the appendix (pp 9–10).

Certain dietary interventions (especially diets with a high fibre intake) can reduce constipation and improve gastric emptying, which in turn enhances the efficacy of dopaminergic medication. There is considerable interest in the Mediterranean diet, which consists mostly of plant-based food, and is high in vegetables, whole grains, nuts and seeds, but with low consumption of meat (especially red meat) and processed food. We identified three studies that examined this diet in people with Parkinson's disease.[64–66] Together, the results suggest that a Mediterranean diet is feasible, and that it might positively affect cognition[67] and constipation.[64] Effects on motor symptoms were inconsistent.[67] All studies lasted less than 10 weeks, so long-term effects remain unknown.

The ketogenic diet (ie, consuming low amounts of carbohydrates and replacing these with high amounts of fat) leads to formation of ketone bodies, which might positively affect brain metabolism, neurodegeneration, and clinical outcomes. Studies in rodents with experimental parkinsonism showed promising effects on dopamine activity, inflammatory markers, and motor functioning, but clinical trials in humans found no consistent improvement in motor or non-motor symptoms.[68] Importantly, this dietary pattern is difficult to adhere to.[69] A 2024 study did show feasibility, but in only 16 people with mild to moderate Parkinson's disease, and for a period of just 2 weeks.[69]

Adverse effects

There are concerns about possible adverse effects when people with Parkinson's disease initiate specific dietary patterns without expert guidance. One specific concern relates to malnutrition, which can lead to weight loss. Underweight is associated with low muscle mass, poor health outcomes, and even mortality, urging the need for targeted dietary interventions to prevent malnutrition and weight loss. A specific example of a diet that can lead to malnutrition, when not guided by an expert, is the ketogenic diet, in which low amounts of carbohydrates are consumed. There are also concerns around inappropriate restriction of protein intake. Many people with Parkinson's disease refrain from adequate protein intake, because proteins can interfere with gastrointestinal uptake of levodopa and thus reduce its efficacy. However, proteins are necessary to maintain many body functions; lack of proteins can lead to malnutrition and osteosarcopenia. The advice to people with Parkinson's disease should therefore be to redistribute their protein intake around their medication intake, and to not take them simultaneously. A 2024 study found that supplementation of whey proteins two times per day (during breakfast and lunch), in addition to a well-balanced distribution of nutritional protein, did not interfere with levodopa efficacy, as compared with protein redistribution plus magnesium supplementation.[70] Why these whey proteins did not interfere with levodopa absorption was not clarified. If confirmed, this supplement could be recommended to people with Parkinson's disease who need protein supplementation.

Stress

Stress-related symptoms are common in Parkinson's disease. About 35% of patients have depression and 26% have an anxiety disorder. Furthermore, it is well established that stress increases motor symptoms, such as tremor, dyskinesia, and freezing of gait, and that relaxation exercises can reduce tremor. People with Parkinson's disease have elevated glucocorticoid levels, indicating disrupted feedback loops of the hypothalamic–pituitary–adrenal axis.[71] Stress can also affect the core pathophysiology of Parkinson's disease. In parkinsonian rat models, chronic stress increased the degree of nigrostriatal cell loss induced by neurotoxins,[72] and injection of corticosterone aggravated cerebral α-synuclein pathology.[73] These findings suggest that stress-reducing interventions might have beneficial symptomatic effects in Parkinson's disease, and potentially also exert disease-modifying effects.[74]

It is important to also recognise the role of factors that promote resilience, which is the ability to maintain mental health despite the presence of stressors. This resilience

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concept was addressed in a prospective longitudinal study (n=350) that used the COVID-19 pandemic as a naturally occurring stressor in people with Parkinson's disease.[4] In this study, resilience was quantified as the deviation of each individual from the group regression line between stressor exposure and perceived stress.[4] The results showed that social support, better cognitive abilities, and a positive appraisal style were associated with better resilience during the pandemic. Conversely, Parkinson's disease-specific factors, such as disease duration or motor severity, were not associated with resilience. Other studies have suggested that social isolation might be a risk factor for developing Parkinson's disease. Among 192 340 participants of the UK Biobank Study, 2048 individuals developed Parkinson's disease after a median follow-up of 12·5 years; social isolation was associated with a higher risk of Parkinson's disease.[75] However, these findings do not prove causality, because stress from social isolation might have triggered the earlier appearance of symptoms in individuals who already had underlying, undiagnosed Parkinson's disease.[76]

Non-pharmacological lifestyle interventions designed to reduce stress include mind-body exercises, such as mindfulness, yoga, Tai Chi, and Qigong. Psychotherapy and pharmacotherapy can also treat depression and anxiety in Parkinson's disease, but these fall outside the scope of this Review.

Mindfulness, originally a Buddhist tradition, describes the capacity to purposely experience the present moment, without judging current emotions or thoughts.[74] Mindfulness-based interventions focus on developing this capacity, complemented by approaches of modern psychology, and have resulted in well documented and standardised programmes such as mindfulness-based stress reduction and mindfulness-based cognitive therapy. In people without Parkinson's disease, a meta-analysis of RCTs showed that mindfulness-based interventions had consistent beneficial effects on stress (pooled effect size of 0·40 [95% CI 0·14–0·45, I^2=46·1]) across 2346 individuals from 20 studies of mindfulness-based intervention versus passive control.[77] A large RCT (n=137) in people aged 67–72 years (median [IQR] 68 years) showed that an 18-month meditation training improved a global composite score reflecting attention regulation, socioemotional, and self-knowledge capacities, compared with no-intervention and active controls (learning a new language).[78] In Parkinson's disease, a large RCT (n=138) showed beneficial effects of a combined mindfulness–yoga intervention, versus an active control condition (stretching and resistance training), on anxiety and depressive symptoms (Hospital Anxiety and Depression Scale [HADS], the primary outcome measure).[79] Beneficial effects on secondary outcomes, such as quality of life and motor symptom severity (MDS-UPDRS III), were also observed for up to 3 months post intervention. A follow-up RCT (n=68) showed that mindfulness meditation (ie, without yoga) was more effective than stretching and resistance training in improving depressive symptoms,[80] albeit with a smaller effect size than in the previous trial. The most recent RCT[81] (n=159) that we identified directly compared yoga, meditation, and treatment as usual (waitlist control) on anxiety and depression (with the HADS score as a primary outcome). Both meditation and yoga improved anxiety compared with treatment as usual, whereas only meditation improved depression compared with treatment as usual; a comparison of meditation versus yoga showed no differential effect on either anxiety or depression.[81] Other smaller RCTs confirmed the benefits of mindfulness-based interventions on quality of life in Parkinson's disease,[82] one even using a video call-based approach,[83] but without effects on depression or anxiety. A recent meta-analysis analysed 12 RCTs that tested the effect of mindfulness-based interventions (total n=288) versus controls (total n=283, treatment-as-usual) on depression and anxiety in Parkinson's disease.[84] Mindfulness-based interventions significantly reduced depression and anxiety, but did not improve motor symptoms (MDS-UPDRS). There were no regional differences (between Europe, Asia, America, and Australia) for the effects on depression and anxiety, but mindfulness-based interventions had a larger effect on mindfulness skills in Asian participants.[84]

The evidence for other stress-reducing strategies is scarce. A meta-analysis of five RCTs showed that yoga improved motor symptoms, but the effects on anxiety were not significant.[85] A recent RCT (n=95) compared Tai Chi with brisk walking and no intervention, showing that Tai Chi improved cognition and sleep, but not anxiety or depression.[47] Positive effects of Tai Chi on cognition and sleep were also observed in a smaller RCT.[49]

Adverse effects

Adverse effects associated with stress-reducing interventions are rare, and are related mostly to the body exercise component of these interventions.[79]

Potential disease-modifying effects

Pharmacotherapeutic approaches aimed at the underlying neurodegenerative processes can thus far not convincingly reduce Parkinson's disease progression. One possible explanation is that drugs typically tackle one specific component of the complex pathophysiology. However, given the multifaceted nature of this pathophysiology, multiple additive or synergistic strategies to effectively mitigate disease progression might be needed.[86] The generally more pleiotropic biological mechanisms of action of lifestyle interventions make them attractive as a putative disease-modifying strategy.[86] Lifestyle interventions could influence the course of Parkinson's disease by influencing neurodegeneration (ie, slowing the

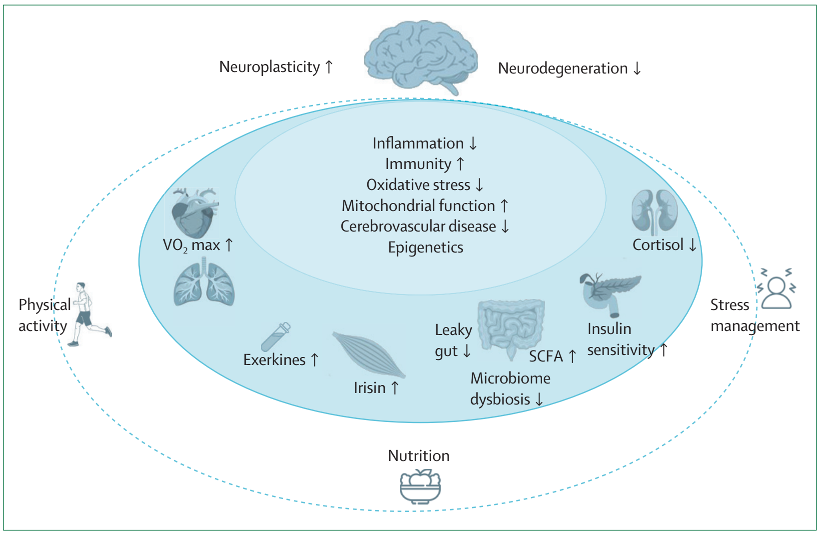

Figure 2: **Shared biological mechanisms of action across lifestyle interventions**
Disease modification might be mediated by several mechanisms. This figure does not offer a complete overview of all putative disease-modifying mechanisms, but rather summarises several elements that have generated interest in the past 5 years. The various lifestyle interventions all have their own principal mode of action, but also have generically shared elements: reduced inflammation, diminished oxidative stress, and improved mitochondrial function, on both a systemic level and in the CNS. Epigenetics are also a potential regulator of mechanisms in Parkinson's disease. Age-related DNA methylation (so-called epigenetic clock) correlates with the age at onset of Parkinson's disease.[87] Physical activity, nutrition, and stress can directly cause epigenetic changes. These physiological effects might act as mediators that help to slow neurodegeneration and improve neuroplasticity. SCFA=short-chain fatty acids. VO_2 max=the maximum amount of oxygen that an individual can use during intense or maximal exercise.

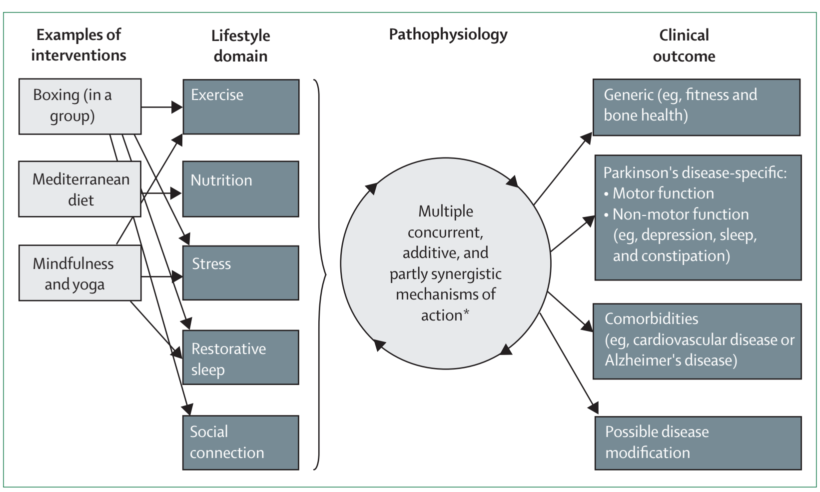

Figure 3: **Possible additive and synergistic effects of different lifestyle interventions**
Specific interventions can have a beneficial effect on different lifestyle domains, which in turn might affect a range of underlying biological mechanisms of action involved in the development and progression of Parkinson's disease. Through this pleotropic effect, improvements in multiple different clinical domains can be expected, including a possible benefit on comorbidities, and even a disease-modifying effect.*There are multiple biological mechanisms of action, summarised in figure 2.

primary disease processes), promoting neural plasticity (ie, boosting compensatory mechanisms), or both (figure 2). We discuss several studies that investigated the biological effects of lifestyle interventions in Parkinson's disease. These findings must not be overinterpreted. In the absence of well-validated biomarkers for disease progression, it is difficult to disentangle symptomatic effects from disease-modifying effects.

Most insights are available for physical activity whose possible neuroprotective effects might be mediated by different mechanisms: reduced inflammation; increased secretion of exerkines (molecules that are released in response to exercise such as hormones, metabolites, and proteins); greater variety in gut microbiota composition; improved metabolic homoeostasis; enhanced cerebral blood flow; better mitochondrial function; and neuroplasticity.[88] Neuroimaging studies (functional and structural MRI) showed that moderate-intensity aerobic exercise led to increased functional connectivity between the basal ganglia and cortex, suggesting enhanced functional neuroplasticity.[11] Brain atrophy was also less, suggesting an effect on brain structure.[11] Similar results were found following an exergaming intervention[27] and resistance training.[15] Physical activity increases the concentration of BDNF, which could be a mediator of the observed neuroplasticity.[89] Physical activity is also associated with changes in inflammatory markers such as C-reactive protein.[90] This association is interesting, as inflammatory tone is increased in Parkinson's disease, and neuroinflammation might contribute to neurodegeneration.[91] An area of particular interest relates to irisin, the levels of which increase with physical activity.[92] Irisin, which is produced in exercising muscles, might be neuroprotective by restoring mitochondrial functioning and by reducing oxidative stress and neuroinflammation.[93,94] These combined biological mechanisms could translate into disease-modification, as was suggested by the aforementioned stabilisation of symptoms following aerobic exercise.[11,62] Some indirect epidemiological work supports this hypothesis. The prevalence of Parkinson's disease is fast growing, and various factors might account for this growth. Of relevance is the notion that the risk for Parkinson's disease is lower for individuals who adhered to an active lifestyle than for those with a sedentary lifestyle.[95] This association falls shy from proving causality, but cautiously suggests that an active lifestyle might help to protect against Parkinson's disease.

Future studies will test the disease-modifying potential of physical activity in the prediagnostic phase of Parkinson's disease (NCT06600438, NCT06193252). This approach of tackling the earliest disease phase is conceptually promising as more healthy neurons could be preserved. However, it is also challenging because people with minimal symptoms might be less motivated to adhere to a lifestyle intervention. If proven to be effective, physical activity could serve as a secondary prevention strategy, aiming to postpone or perhaps even prevent the clinical diagnosis.

Much less is known about the mechanisms of action of dietary interventions. Nutritional interventions might influence the gut microbiome, which in turn could affect the gut–brain axis. For example, the microbiome changes gut permeability,[96] which in turn might affect the degree of systemic inflammation in Parkinson's disease.[97] Whether such biological effects could culminate into disease modification remains to be tested; the only preliminary hint is that people who followed a Mediterranean diet have a reduced risk of developing Parkinson's disease.[98] Nutrition is also potentially linked to Parkinson's disease risk via exposure to food products contaminated with pesticides. Certain pesticides are associated with an increased Parkinson's disease risk, and perhaps also with faster disease progression if exposure continues after the diagnosis.[99] Many people with Parkinson's disease therefore ask about the possible benefits of organic diets, because these should contain fewer or lower concentrations of pesticides. A possible protective or disease-modifying effect is conceivable, but this hypothesis remains to be tested.

The biological effects of stress are beginning to be understood. Chronic stress leads to impaired regulation of inflammatory responses, and stress-reduction through mindfulness effectively reduces inflammatory tone in non-parkinsonian populations[100] and in people with Parkinson's disease.[81] Whether inflammation contributes to nigrostriatal degeneration in Parkinson's disease is unclear,[91] but if it were the case, then this would be a potential target for disease-modifying effects of stress-reducing interventions. Another mechanism that might play a role is cerebral compensation. Increased cortical activity can compensate for nigrostriatal dysfunction in Parkinson's disease, thereby minimising clinical deficits.[101] Chronic stress is associated with cortical atrophy,[74] which can interfere with these cortical compensatory mechanisms. Mindfulness has the potential to counteract some of these effects, but there is no direct evidence in people with Parkinson's disease. This hypothesis is currently being investigated in a large RCT of the effects of a mindfulness-based intervention on clinical symptoms, MRI measures, and blood-based biomarkers, such as inflammatory tone (MIND-PD; NCT05779137).

Combining multiple lifestyle interventions

People with Parkinson's disease often need to make multiple behavioural changes simultaneously to manage their disease. Although challenging, combining these interventions offers opportunities for synergistic benefits, with the potential for greater symptom relief and disease modification (figure 3). Also, combining medication with lifestyle approaches could be complementary, improving the effectiveness of the treatments. Combining multiple lifestyle changes comes with considerable challenges, but several helpful solutions exist (panel 2). Long-term adherence to lifestyle changes is also affected by issues related to diversity (panel 3).

Gene–environment interactions

A further area of research involves gene–environment interactions. For example, individuals with the same

Panel 2: Barriers and facilitators for combining multiple lifestyle interventions

Changing lifestyle behaviour is difficult, especially for some people with Parkinson's disease who have executive problems (due to frontal lobe dysfunction), depression, apathy, or physical impairments that hamper adherence to physical activity. When offered multiple recommendations at the same time, it can be difficult for patients to take the initiative and incorporate the various changes into daily routines, which can negatively affect long-term compliance. A complicating factor is that health-care professionals report insufficient expertise and time to provide integrated lifestyle guidance. Moreover, many contradictory recommendations are present online, and patients often do not know where to find reliable information and how to implement this information in their daily life.

Several practical solutions could be helpful. First, it is important to offer reliable information about lifestyle, to set personalised goals, and to make a personalised implementation strategy (using small steps to reach a goal). This approach can be done using shared decision making. In the Netherlands, a lifestyle decision aid support tool[102] was developed for this purpose. This online tool gives reliable information about all lifestyle domains, considers personal circumstances and preferences, and helps the user to decide on personal goals and strategies to improve lifestyle. The tool can be used in isolation by an individual, but also together with a family member or health-care professional. However, very few people with Parkinson's disease will have access to such personal supervision. It is, therefore, important to search for innovative technological solutions, such as smartphone apps that act as digital coaches. Other apps include elements of gamification, which can help to promote compliance. Digital opportunities are beginning to emerge in the domain of physical activity; for nutritional interventions and stress management, these developments are still in their infancy.

Panel 3: Diversity issues

In low-income countries, lifestyle interventions are often the most accessible treatments for Parkinsons' disease due to low availability of medications and surgical interventions.[103–105] Lifestyle advice must be tailored to cultural differences, considering socioeconomic factors that affect adherence, such as lack of time (for those who work even more than 40 h per week to provide for their family), safe environments, or resources. For example, physical activity might be limited by work demands or unsafe conditions, but in rural areas with physically demanding lifestyles or regular walking for religious practices, activity levels can be higher. Gender differences also influence participation, with women often more interested in stress-reduction strategies than men.[80]

Research limitations include the focus on specific populations. For example, studies on Tai Chi or Qigong mostly involved east Asian populations, while aerobic exercise research often involves European and American cohorts, with few studies in under-represented populations. Examples such as the Walking Football clinics in Africa are promising.[106] Dietary interventions face economic barriers; healthy diets are costly, and low-income groups often consume high-fat, high-sugar foods, increasing obesity risk. Conversely, rural African populations might have access to fresh products but lack animal proteins, risking malnutrition. The Mediterranean diet's cultural roots limit its global applicability because of differences in culturally related preferences in different parts of the world.[107] Higher stress levels in low socioeconomic regions further complicate intervention implementation (chronic stress reduces individuals' coping resources, impairs mental wellbeing, and exacerbates barriers to participation and effectiveness of interventions). Future efforts must address these diversity issues to ensure equitable access to lifestyle strategies for people with Parkinson's disease across all backgrounds.

Panel 4: Recommendations for clinical practice

Advice is based on the latest scientific evidence and on the authors' practical experience*. Level of evidence is provided according to the Oxford Centre for Evidence-Based Medicine and the GRADE systematics.

Physical activity

- Do aerobic exercise, at least 3 times per week, for at least 30 min. If possible, strive for a high intensity (70–80% of maximum heart rate), although a moderate intensity (60–65% of maximum heart rate) is better than no exercise. (Level of evidence: 1a; grade: high)
- Do resistance training of large muscle groups, 2–3 times per week, at 60–80% of the one repetition maximum.† (Level: 1a; grade: high)
- Consider flexibility and neuromotor physical activities (eg, balance and agility training) 2–3 times per week. (Level: 1a; grade: high)
- Increase the volume (frequency and duration) of daily activities, even at low intensities; this is ideally used in addition to (but if needed as alternative to) aerobic exercise. (Level: 5; grade: low [authors' opinion])
- Consider adverse effects: cardiopulmonary risk, and falls in those with deficits in gait, balance, or cognition, or those with orthostatic hypotension. A specialised physiotherapist or sports trainer can offer guidance. (Level: 1a; grade: high)

Nutrition

- There is no conclusive evidence to recommend any specific dietary pattern. Some evidence suggests the benefit of a Mediterranean diet.[117] (Level: 1a; grade: moderate)
- Although vitamin C, vitamin K, and antioxidants are promising, no specific supplements can be recommended at this point.[117] (Level: 1a; grade: moderate)
- Dietary patterns should follow the general advice for healthy food for a given region or country, and consist of adequate amounts of the different macronutrients, fruit and vegetables, whole grains, unsaturated fats and nuts, with small amounts of highly processed food.[118] (Level: 2b; grade: low)
- A dietary pattern using probiotics, or a diet high in fibre or both, seems beneficial for constipation. (Level: 1a; grade: moderate)
- Weight should be monitored to prevent malnutrition and underweight. (Level: 5; grade: low [authors' opinion])
- Adequate fluid intake, to prevent or reduce constipation, and as part of the management of orthostatic hypotension; possible adverse effects include increased urinary frequency and nocturia. (Level: 5; grade: low [authors' opinion])

Stress management

- Mindfulness-based interventions (weekly group sessions during an eight-week period) are effective in reducing stress-related symptoms (depression and anxiety).[79,84] (Level: 1a; grade: high)
- Mindfulness-based interventions might improve motor symptoms,[79] but pooled evidence across seven randomised controlled trials in a systematic review did not find a significant effect.[84] (Conflicting evidence; grade: moderate)
- The long-term effects of mindfulness-based interventions on stress-related symptoms (eg, depression and anxiety) and motor symptoms are unclear.[79,81] (Level: 5; grade: low)
- Interpersonal relations and social support are likely effective in promoting stress-resilience.[4] (Level: 2a; grade: moderate)
- Yoga could be effective in reducing stress-related symptoms (ie, anxiety),[81] but not all evidence points in the same direction.[47,85] (Level: 1b; grade: moderate)

Integrated lifestyle management

- An optimal lifestyle might require adjustments in all different domains, but it is difficult to change all of them simultaneously. A personalised approach with priority setting is needed. (Level: 5; grade: low [authors' opinion])
- A multidisciplinary team with Parkinson's disease expertise to guide and to counsel behavioural change strategies to support long-term adherence for each individual person. (Level: 5; grade: low [authors' opinion])
- Consider the effect of comorbid conditions. (Level: 5; grade: low [authors' opinion])

*Note with respect to the clinical expertise of the authors: most authors are neurologists with expertise in multidisciplinary care, while NMdV is a physiotherapist and an integrated lifestyle coach in training. Our recommendations do not apply to all countries, but rather to those that have access to the respective interventions, including the presence of, for example, specialist nurses or lifestyle coaches that can support patients in making the proper treatment decisions, and to oversee long-term adherence to lifestyle recommendations. †Large muscle groups include the biceps, triceps, chest, upper and lower back, abdominal muscles, quadriceps, hamstrings, and calf muscles. A one-repetition maximum is the weight that an individual can lift with a specific muscle only once. It is advised to train with a weight of 60–80% of this maximum. The weight therefore differs for each muscle group.

pathogenic variant (eg, *LRRK2* p.G2019S) can have varying ages at onset, with some remaining unaffected into old age. This variability might be influenced by lifestyle and cultural factors.[108] Studies in carriers of these mutations in the past 5 years found that black tea intake was linked to a later onset of disease, whereas caffeinated sodas were associated with earlier onset.[109,110] Some lifestyle effects might involve mitochondrial function, as higher mitochondrial polygenic risk scores are associated with an earlier age at onset, especially among people who drink caffeinated soda.[111] However, this finding could also reflect that regular caffeinated

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soda consumption acted as a proxy for an overall less healthy lifestyle.

Machine learning models can integrate genetics and lifestyle measures to predict outcomes for disease progression and prognosis in a personalised manner, helping to establish a basis for precision medicine research. Artificial intelligence (AI) integrated into sustainable lifestyle solutions can help foster long-term behavioural outcomes. For example, personalised machine learning predictions successfully identified individuals most likely to have weight loss with a lifestyle intervention.[112] Data were used from Action for Health in Diabetes (Look AHEAD), a multiscale clinical trial that ran for more than 10 years.[113,114] The treatment included an individually tailored diet and physical activity programme. An algorithm was then generated for making predictions on individual treatment outcomes based on 23 baseline covariates selected a priori (eg, sex, age, and education). The study found a new target group of 864 participants (19·1% of 4526) in whom they could expect more than 10% weight loss within the first year with treatment.[112] There are also opportunities to further strengthen the quality of gamification elements to enhance motivation and engagement. For eating habits, there are already AI-driven lifestyle interventions. One AI tool with tailored guidance, support, gamification, and progress tracking was tested in a multinational field trial by 391 participants with a broad range of BMI (range of 20–78 kg/m²), aiming to lose weight over 24 weeks.[115] The investigators used a mobile app with an internet-connected scale and a form of AI to provide individualised guidance and weight-loss management. Almost all (98·7%) participants lost at least 5% of body weight, 75% lost at least 10%, 43% at least 15%, and 9% at least 20%. A major limitation of that trial is that no control group was tested.[115] 20 participants with Parkinson's disease were recruited for an AI-based chatbot study with a trial phase and a randomised phase.[116] In the trial phase, in which participants used an AI-based chatbot app daily for 1–4 months, the content of the AI chatbot was revised based on feedback from participants and neurologists. In the 5-month randomised phase, participants were randomly assigned to either an intervention group that received both daily chatbot and weekly video-conferencing sessions or a control group that received weekly video-conferencing sessions only. This study showed that an AI-based chatbot had significant positive effects on smile parameters and speech features.[116]

Conclusions and future directions

Over the past few years, lifestyle has progressed from an interesting but understudied concept into an increasingly evidence-based component of an holistic approach to the management of Parkinson's disease. More evidence is needed to better understand the full potential of lifestyle interventions, but the time has come to use a tailor-made personalised approach to support people with Parkinson's disease worldwide to sustainably adopt a healthier lifestyle. There is a lack of original studies evaluating multimodal lifestyle interventions with objective outcomes, acknowledging the challenges that come with conducting such studies. This type of trial remains an aspirational goal for future research. Pending the arrival of novel evidence, current recommendations are based largely on expert opinion (panel 4).

Future research should involve large-scale, long-term clinical trials focused on sustainable behavioural changes and addressing adherence. These studies should include participants in different stages of Parkinson's disease, especially those with severe symptoms (who are often excluded) and those in the prodromal phase (in which disease modification is thought to be more effective). These studies should explore how behavioural strategies, such as gamification and behavioural change techniques, can enhance engagement with lifestyle interventions, ideally developed using theoretical frameworks and co-created with patients and stakeholders (eg, physiotherapists and dieticians). Additionally, future work should investigate the mechanisms of action underlying lifestyle interventions to understand and optimise their symptomatic and possible disease-modifying effects. Such studies should assess the effect on disease progression markers, including metabolic changes, digital biomarkers, microbiome, and imaging biomarkers, to evaluate biological effects. Advances in single-cell and multiomics approaches, such as transcriptomics, applied to the brains of people with

Search strategy and selection criteria

We searched PubMed for articles published between Jan 1, 2020, and March 26, 2025. We used the search terms: ((("Parkinson's disease") AND (("Exercise" OR "Physical activity" OR "nutrition" OR "diet" OR "food" OR "dietary intervention" OR "ketogenic" OR "Mediterranean" OR "vitamin" OR "supplement" OR "stress" OR "stress management" OR "mental health" OR "anxiety" OR "depression" OR "mindfulness" OR "lifestyle" OR "lifestyle intervention") OR ("gene AND environment" AND "lifestyle interaction") OR "non-pharmacological intervention"))). We did an additional search on ((("Parkinson's disease") AND (("relationships") OR ("social interaction"))). The most recent search was done on March 26, 2025. We included: (1) randomised controlled trials studying an intervention related to exercise, diet, or stress management, published in the years 2020–25; (2) studies evaluating the mechanisms of action of these lifestyle interventions; and (3) studies addressing diversity issues in these domains. There were no language restrictions.
The selection was done by two authors (JT and NMdV) based on consensus. The PubMed search yielded 14 151 articles; after screening on inclusion and exclusion criteria, we retained 58 articles on physical activity, four on nutritional interventions, three on stress management and one on social interactions. Of these, we selected studies that we perceived to be most innovative in terms of methodology, type of intervention or outcomes, or that offered a good illustration of important developments in the field (as reflected by trends noted in recent meta-analyses; studies are listed in the appendix pp 2–8). Of note, many mind–body interventions included both a physical activity and a stress management component; depending on the relative weight of each component, we discuss these interventions in either the section on physical activity or the section on stress management.

Parkinson's disease, could help link molecular data to individual phenotypes, paving the way for precision dietary and lifestyle interventions to treat or prevent neurodegeneration.[126]

Contributors

JT and NMdV did the literature search, wrote the first draft of the manuscript, and all authors participated in editing and revising the manuscript. NMdV reviewed the literature on physical activity and nutrition. RCH reviewed literature on stress and combined mechanisms, edited and revised manuscript. BRB supervised all writing and literature searches, reviewed and revised all drafts. MCJD and PC revised drafts with a focus on diversity and cultural aspects. All authors provided final approval of the manuscript content, and had responsibility for the decision to submit the manuscript for publication. The funders of the study had no role in writing of the report.

Declaration of interests

JT serves as associate editor for *Frontiers of Neurology*; has received research funding from the German Research Foundation, Michael J Fox Foundation, and the Netherlands Organisation for Health, Research and Development (ZonMw); and serves as a genetic consultant to company Acurex. NMdV serves as associate editor for the *Journal of Parkinson's disease*; received research funding from Netherlands Organisation for Health, Research and Development (ZonMw), Michael J Fox Foundation, and the Dutch Brain Foundation. RCH serves as editor for *Tremor and Other Hyperkinetic Movement Disorders*; is on the scientific advisory board of ParkinsonNL; received fees for consulting work for UCB Pharma and Roche Pharma; has received research funding from Neurocrine Biosciences, the Netherlands Organisation for Health, Research and Development (ZonMw; VIDI grant #9150172010044), Michael J Fox Foundation, Dutch Brain Foundation, and ParkinsonNL. PC received honoraria from serving on the scientific advisory board for Lundbeck, Purapharm, and Green Valley; has received fees for speaking at conferences from Roche, Lundbeck, Eisai, Green Valley, Luye, Medtronic, and Boehringer Ingelheim; and has received research grant support from the Chinese Ministry of Science and Technology and the Michael J Fox Foundation. BRB serves as the co-Editor in Chief for the *Journal of Parkinson's disease*; serves on the editorial board of *Practical Neurology and Digital Biomarkers*; has received fees (paid to institution) from serving on the scientific advisory board for the Critical Path Institute, Gyenno Science, UCB, and Zambon; has received fees (paid to institution) for speaking at conferences from AbbVie, Bial, Biogen, GE Healthcare, Oruen, Roche, UCB, and Zambon; and has received research funding from Cure Parkinson's, Davis Phinney Foundation, Edmond J Safra Foundation, Fred Foundation, Gatsby Foundation, Dutch Brain Foundation, Horizon 2020, IRLAB Therapeutics, Maag Lever Darm Stichting, Michael J Fox Foundation, the Netherlands Ministry of Agriculture, Ministry of Economic Affairs & Climate Policy, and Ministry of Health, Welfare and Sport, Netherlands Organization for Health, Research and Development (ZonMw), Not Impossible, Parkinson Vereniging, Parkinson's Foundation, Parkinson's UK, Roche, Stichting Alkemade-Keuls, Stichting Parkinson NL, Stichting Woelse Waard, Topsector Life Sciences and Health, UCB, Verily Life Sciences, and Zambon. MCJD reports no competing interests.

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