The Effects of Physical Activity in Parkinson's Disease: A Review

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Research Report

The Effects of Physical Activity in Parkinson's Disease: A Review

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Abstract.
Background: Physical activity (PA) is increasingly advocated as an adjunct intervention for individuals with Parkinson's disease (PD). However, the specific benefits of PA on the wide variety of impairments observed in patients with PD has yet to be clearly identified.
Objective: Highlight health parameters that are most likely to improve as a result of PA interventions in patients with PD.
Methods: We compiled results obtained from studies examining a PA intervention in patients with PD and who provided statistical analyses of their results. 868 outcome measures were extracted from 106 papers published from 1981 to 2015. The results were classified as having a statistically significant positive effect or no effect. Then, outcome measures were grouped into four main categories and further divided into sub-categories.
Results: Our review shows that PA seems most effective in improving *Physical capacities* and *Physical and cognitive functional capacities*. On the other hand, PA seems less efficient at improving *Clinical symptoms of PD* and *Psychosocial aspects of life*, with only 50% or less of results reporting positive effects. The impact of PA on *Cognitive functions* and *Depression* also appears weaker, but few studies have examined these outcomes.
Discussion: Our results indicate that PA interventions have a positive impact on physical capacities and functional capacities. However, the effect of PA on symptoms of the disease and psychosocial aspects of life are moderate and show more variability. This review also highlights the need for more research on the effects of PA on cognitive functions, depression as well as specific symptoms of PD.

Keywords: Parkinson, exercise, physical activity, rehabilitation, bradykinesia, tremor

INTRODUCTION

Parkinson's Disease (PD) is a neurodegenerative disease affecting approximately 7 to 10 million people around the world, according to the Parkinson's Disease Foundation [1]. Its prevalence is estimated at 2,802 per 100,000 persons in North America, Europe and Australia [2]. PD's main cardinal symptoms are tremor, bradykinesia, rigidity and postural instability [3]. Other typical motor symptoms can be observed such as altered gait pattern, freezing of gait and motor coordination deficits [3, 4]. Thus, PD has a direct impact on motor control, and on mobility in general. Furthermore, most patients will also experience non-motor symptoms that include, but are not limited to, cognitive impairment and dementia [5], insomnia [6], depression and anxiety [7], apathy [8], bladder dysfunction [9], pain [10], and fatigue [11]. It is important to note the high variability in disease progression and symptoms between patients; the con-

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sequence being that the impact of PD on functional capacities, quality of life, activities of daily living and social participation may differ among individuals. Nonetheless, the progressive nature of the disease will unavoidably worsen the patient's quality of life.

Physical activity (PA) can be seen as a complement to pharmaceutical treatment to manage the inherent decline associated with the disease. The notion of integrating PA in the therapeutic treatment of PD was introduced during the 1950's. Back then, PA was already foreseen as a way of minimizing the limitations induced by the disease [12–14]. Even with the introduction of levodopa, which had a tremendous effect on the treatment of PD, some researchers kept advocating for the integration of exercises as an essential component of therapy in order to maximize the benefits of the medication [15, 16]. From the first experimental studies in the 80's [17, 18] until today, positive effects of PA on people living with PD have been demonstrated and consensually recognized within the scientific community [19–22]. According to these reviews, PA seems to improve mobility, gait, balance and muscle strength of people living with PD. Health professionals and PD patients can surely rely on those positive results to justify the importance of PA. Nevertheless, the positive effects of PA on other health parameters such as superior cognitive functions, activities of daily living and psychosocial aspects of life remain unclear. Moreover, the extent of the positive results observed in some areas does not seem to be reflected on clinical symptoms as measured by PD-specific scales. Therefore, there is a need to clarify when PA has a clear positive effect, when PA appears to have less convincing health benefits, and where research is needed. Accordingly, the aim of this article is to present, through an extensive search of the literature covering the last three decades, an overview of the effects of PA on people living with PD.

Our goal is to highlight the aspects of health that, so far, have shown the most improvements as a result of PA interventions. This will also allow us to identify the areas where PA seems to be less effective. Finally, we aim at identifying those areas that have been less studied and that could benefit from further research.

To our knowledge, this is the first paper to present a compilation of the results published in the last thirty-four years. This review will provide a clear and unique picture of the situation with regards to what researchers have brought forward so far in terms of benefits of PA in PD. In the end, we hope that this overview will provide factual basis to promote PA and enhance its practice among people living with PD.

METHODS

Literature search

In order to identify relevant references, we searched PubMed and SCOPUS databases for clinical trials, using mainly a combination of the following keywords: Parkinson's disease, physical activity, exercise and effects. We also searched for reviews with the same keywords. From those reviews, we identified relevant cited articles from lists of references. For the purpose of this review, physical activity is simply defined as a body movement produced by the action of skeletal muscle that increases energy expenditure [23]. This may include, but is not limited to, fitness exercises, sports, dance, martial arts, walking, physical therapeutic movements and occupational therapy. It is the authors' view that physical activity can bring benefits as long as it raises the level of energy expenditure, engages the musculoskeletal system, and causes some level of physical exertion. Modality and intensity of exercise were not taken into consideration, only whether the exercise generated significant benefits on the outcome measures studied.

To be included in this review, a study had to meet the following criteria: *(a)* it targeted subjects diagnosed with idiopathic PD who participated in PA as a mean of intervention; *(b)* the outcome measures included effects of PA on physical, cognitive, psychological or social parameters in terms of performance, function or symptoms; *(c)* evaluations were conducted at baseline and post-intervention; *(d)* the effects of PA were statistically measured; *(e)* the peer-reviewed article was published in English or French. Were excluded from this review studies that met at least one of these criteria: *(a)* it was mainly comprised of passive movements (for example electrostimulation and massage therapy); *(b)* it was founded on the effects of external stimulations such as visual or verbal cueing; *(c)* the experimental group was comprised of less than four subjects. Accordingly, we included controlled studies, as well as case series, cross over studies and studies comparing different types of interventions with baseline and post intervention evaluations. In the end, 106 studies published from 1981 to early 2015 were selected. The methodological approach chosen for this review differs from other analysis as it includes almost the entire literature on the subject. In order to provide an overview of current knowledge, the high number of papers included in this review allows, in our view, for an equal treatment of all studies.

Identifying and combining outcome measures

For each study, primary and secondary outcome measures were extracted. A total of 868 outcome measures were identified throughout the 106 papers. Since one specific outcome measure (e.g., Time-up-and-go) could have been administered in a different manner between studies, we simply dealt with each outcome measure as being a distinct one.

The results were compiled into a database. All 868 outcome measures were then grouped into four main categories, and further divided into sub-categories. This categorization was inspired by the work of Rikli and Jones [24]. Their model is based on a relationship between physical parameters, functional capacities and activities. For instance, a parameter such as muscular strength can directly affect a capacity such as walking, which in turn can affect the performance of a daily activity such as shopping. This classification is presented and further explained in Table 1.

For each outcome measure, the result reported by the authors was then sorted as having a positive effect or no effect. In order to be considered as having a positive effect, the result for an outcome measure had to show a statistically significant improvement from baseline to post intervention assessment ($p < 0.05$) within the intervention group. We did not take into consideration the persistence of effects after a follow-up period, since many studies did not include this assessment, and those that did were rarely conducted within the same time frame. This decision was also based on the fact that PA should be a persistent therapy, and stopping it is known to reverse its benefits [25]. For studies based on the comparison of intervention methods, we took into account the effect of each intervention. For this review, we were interested in the effects of PA, this regardless of the type of exercises, volume or intensity. Furthermore, in order to get an overview of the effects of PA on PD, we categorized the potential for improvement in accordance with the proportion of positive results obtained from outcome measures, using a scale as follows: ≥70% = Excellent, 60 to 69.9% = Very good, 50 to 59.9% = Good, 40 to 49.9% = Fair, 30 to 39.9% = Poor and <30% = Very poor.

Finally, we compared the effect size of outcome measures that were shown to have a positive effect or no effect for the categories with Fair, Poor and Very Poor effectiveness. Here we used Hedge's g as a measure of effect size [26] since it provides a better estimate; especially for smaller sample sizes. It is important to note that the data required to compute the effect size was not available for all studies; nor for all outcome measures in each study. Effect sizes were compared using a *t*-test and a significance threshold at $p < 0.05$.

RESULTS

The results are presented in Table 2. They include, for parameters of each category and its sub-categories, the number of outcome measures that were identified throughout the reviewed papers and the number of research papers in which they were identified. This is followed by the proportion, in percentage, of outcome measures that resulted in positive effects after a PA intervention, i.e. statistically significant improvements. In the case of Fair, Poor and Very Poor effectiveness, we also compared the effect size of the studies that were effective to those that were not effective if the data allowed it.

Physical capacities

Potential for improvement in this category is good with 57.2% of all reported outcome measures resulting in positive effects.

Lower limbs, trunk and upper limbs strength, endurance or speed

Potential for improvement in *Lower limbs strength, endurance or speed* is good; as 59.6% of outcome measures resulted in positive effects. It is very poor for *Trunk strength, endurance or speed*; as 14.3% of outcome measures resulted in positive effects. However, the data available in the literature only enabled us to assess the effect size in the study yielding positive outcomes; which was 0.935. As for the potential improvement in *Upper limbs strength, endurance or speed,* it is very good as 66.7% of outcome measures resulted in positive effects.

Flexibility or range of motion

Potential for improvement in *Flexibility or range of motion* is fair; as 46.7% of outcome measures resulted in positive effects. Analysis of the effect size between the studies exhibiting significant improvements in flexibility (0.73 ± 0.3) and those showing no improvement (0.33 ± 0.1) demonstrated a statistically significant difference between the two groups. Note that the data from two studies did not allow for the calculation of the effect size of interventions with

Table 1
Classification of outcome measures into categories and sub-categories

1) Physical capacities	Physical capacities are comprised of basic physical parameters required to perform functional activities such as walking, sitting down and getting up, etc.
(a) Lower limbs, trunk and upper limbs strength, endurance or speed	This sub-category includes measures of strength, endurance or speed for lower limbs, trunk and upper limbs. Results are presented distinctively.
(b) Flexibility or range of motion	This sub-category includes measures of *Flexibility or range of motion* for the main body articulations; ankle, knee, hip, trunk and shoulder.
(c) Motor control	This sub-category includes measures of fine motor skills, gross motor skills and reaction time.
(d) Metabolic functions	This sub-category includes measures of oxygen consumption, respiratory functions, heart rate, blood pressure and body mass index.
2) Physical and cognitive functional capacities	Functional capacities, whether they are physical or cognitive, are comprised of common activities performed by people and abilities required to function independently. These capacities also include parameters that can alter these abilities (*e.g.* depression).
(a) Gait, mobility, posture and balance	This sub-category includes measures related to gait, mobility, posture and balance. Results are presented distinctively.
	Outcome measures of *Gait efficiency* are comprised of evaluation of stride or step length, stance, swing, gait initiation, gait cycle, arm and leg movements, etc. Outcome measures of *Gait velocity and cadence* are comprised of assessments conducted on short distances (usually between 4 and 20 meters) at preferred or maximal speed and in various conditions such as forward, backward, around obstacle, and multiple tasks walking. Outcome measures of *Mobility* are comprised of the Six and Two Minute Walking tests (2MWT and 6MWT), Time-up-and-go (TUG) tests, step and stair tests as well as walking distances and ambulation performances. Outcome measures of *Balance, posture and risks of fall* are comprised of static and dynamic balance, postural and risks of fall assessments as well as fall records.
(b) Cognitive functions	This sub-category includes measures of executive functions, memory and sensorimotor tasks as well as cognitive abilities questionnaires (Mini Mental Status Examination and Montreal Cognitive Assessment).
(c) Depression	This sub-category includes measures of depression using clinical scales such as the Beck Depression Inventory and the Geriatric Depression Scale.
(d) Activities of daily living (ADL)	This sub-category includes measures based on clinical scales assessing the level of independency such as the Functionnal Independence Measure, the Northwestern University Disability Scale or the Schwab and England ADL scale as well as measures of performance during daily living tasks such as sitting on a chair and getting up, getting dressed, going from supine to sitting position or doing transfers.
(e) Level of activities	This sub-category includes measures assessing level of activity with questionnaires such as Physical Activity Scale for Elderly and Phone-FITT, or devices like a pedometer or an accelerometer.
3) Clinical symptoms of Parkinson's disease	Clinical symptoms of PD are comprised of global and specific symptoms assessed using clinical scales or apparatus. They are based on the patient's own assessment and objective measures.
(a) Overall symptoms and disabilities	This sub-category includes all measures related to clinical scales when the result was reported as a global score. Results reported by section were not included in this sub-category, but rather in the next one. The most used clinical scale was the Unified Parkinson's Disease Rating Scale (UPDRS), in its former and more recent version, the Movement Disorder Society – Unified Parkinson's Disease Rating Scale (MDS-UPDRS). Other clinical scales were also used as an outcome measure, namely the Columbia University Rating Scale (CURS), the Webster Rating Scale for Parkinsonian Disabilities (WRS) and the Self-assessment Parkinson's Disease Disability.
(b) Specific components of UPDRS	This sub-category includes all measures related to clinical scales when the results were reported by section. Only UPDRS results were reported in that fashion. We have merged the results coming from both the former UPDRS and the MDS-UPDRS.
(c) Specific symptoms of PD	This sub-category includes all measures related to specific symptoms of PD using clinical scales or, in few cases, measurement devices. Included symptoms are *Bradykinesia, Freezing, Gait and posture alterations (specific component of the UPDRS Part III), Rigidity and Tremor*. Results are presented distinctively.
4) Psychosocial aspects of life	Psychosocial aspects of life are comprised of clinical scales and questionnaires that assess the participant's perception of health and well-being and the impact of the disease on many life dimensions.
(a) Quality of life (QoL)	This sub-category includes all measures related to *QoL* questionnaires such as the 39-Item Parkinson's Disease Quality of Life Questionnaire (PDQ-39), the 8-Item Parkinson's Disease Quality of Life Questionnaire (PDQ-8), the 5 Dimension European Quality of Life (EQ-5D), the Parkinson's Disease Quality of Life scale, the Quality of Life scale from the Oregon Health and Sciences University, a modified Westheimer questionnaire, the Nottingham Health Profile (Health related QoL) and the De Bore's Parkinson's Disease Quality of Life scale. Results were further subdivided into *QoL – total score* when the result was reported as a total score and *QoL–specific components* when they were reported in such manner (e.g. mobility dimension of the PD-39 or energy level of the Nottingham Health Profile).
(b) Health management	This sub-category includes all measures related to questionnaires like the Global Assessment of Change, the Stanford self-efficacy for managing chronic disease, the Sickness Impact Profile and the Short Form Health Surveys (commonly called SF-12 and SF-36) as well as fatigue and pain scales.

positive ($n = 2$) and null ($n = 5$) outcome measures related to flexibility.

Motor control

Potential for improvement in *Motor Control* is good; as 52.2% of outcome measures resulted in positive effects. In addition to the results presented in Table 2, we looked into specific aspects of *Motor control*; potential for improvement is poor for fine motor skills with 33.3% of positive results out of 12 outcome measures, and very good in gross motor skills with 66.7% of positive results out of 9 outcome measures. Analysis of the effect size between the studies exhibiting significant improvements in fine motor skills (0.87 ± 0.6) and those showing no improvement (0.56 ± 0.5) did not demonstrate a statistically significant difference between the two groups. Note that the data from six studies did not allow for the calculation of the effect size of interventions with positive ($n = 8$) and null ($n = 5$) outcome measures related to fine motor skills.

Metabolic functions

Potential for improvement in *Metabolic functions* is good; as 57.1% of outcome measures resulted in positive effects. In addition to the results presented in Table 2, we found that potential for improvement in oxygen consumption is very good with 63.3% of positive results out of 11 outcome measures.

Physical and cognitive functional capacities

Potential for improvement in this category is good with 55.3% of all reported outcome measures resulting in positive effects.

Gait, mobility, posture and balance

Potential for improvement in *Gait efficiency* is good; as 59.8% of outcome measures resulted in positive effects. It is also good in *Gait velocity and cadence*; as 59.8% of outcome measures resulted in positive effects. Potential for improvement is also good in *Mobility*; as 50% of outcome measures resulted in positive effects. In addition to the results presented in Table 2, we looked into the results for the two most reported *Mobility* measures, the 6 Minute Walking test (6MWT) and the Time-up-and-go (TUG). Potential for improvement is excellent using the 6MWT as an assessment tool with 72% of positive results out of 25 outcome measures, and very poor using the TUG as an assessment tool with 35.3% of positive results out of 34 outcome measures. Analysis of the effect size between the studies exhibiting significant improvements in the TUG (0.71 ± 0.4) and those showing no improvement (0.50 ± 0.4) did not demonstrate a statistically significant difference between the two groups. Note that the data from ten studies did not allow for the calculation of the effect size of interventions with positive ($n = 4$) and null ($n = 6$) TUG outcome. Finally, potential for improvement is very good in *Balance, posture and risks of fall*; as 61.2% of outcome measures resulted in positive effects.

Cognitive functions

Potential for improvement in *Cognitive functions* is very poor; as 29% of outcome measures resulted in positive effects. Analysis of the effect size between the studies exhibiting significant improvements in cognitive functions (0.69 ± 0.3) and those showing no improvement (0.19 ± 0.1) demonstrated a statistically significant difference between the two groups. Note that the data from two studies did not allow for the calculation of the effect size of interventions with positive ($n = 1$) and null ($n = 2$) outcome measures related to cognitive functions.

Depression

Potential for improvement in *Depression* is poor; as 38.9% of outcome measures resulted in positive effects. Analysis of the effect size between the studies exhibiting significant improvements in depression (0.42 ± 0.1) and those showing no improvement (0.18 ± 0.2) demonstrated a statistically significant difference between the two groups. Note that the data from eight studies did not allow for the calculation of the effect size of interventions with positive ($n = 2$) and null ($n = 6$) outcome measures related to depression.

Activities of daily living

Potential for improvement in *Activities of daily living* is good; as 59.5% of outcome measures resulted in positive effects.

Level of activity

Potential for improvement in *Level of activity* is fair; as 41.2% of outcome measures resulted in positive effects. Analysis of the effect size between the studies exhibiting significant improvements in the level of activity (0.90 ± 0.4) and those showing no improvement (0.70 ± 0.9) did not demonstrate a statistically significant difference between the two groups. Note that the data from four studies did not

Table 2
Proportion of outcome measures resulting in positive effects

	Number of outcomes measures	Positive effect of PA intervention	Number of papers	References
1) Physical capacities	*136*	*57.2%*		
(a) Lower limbs, trunk and upper limbs strength, endurance or speed				
Lower limbs	47	59.6%	17	[28–44]
Trunk	7	14.3%	2	[38, 45]
Upper	9	66.7%	7	[18, 29, 30, 37, 46–48]
(b) Flexibility or range of motion	15	46.7%	6	[29, 30, 36, 43, 45, 49]
(c) Motor control	23	52.2%	13	[17, 18, 41, 47, 50–58]
(d) Metabolic functions	35	57.1%	13	[40, 49, 58–68]
2) Physical and cognitive functional capacities	*485*	*55.3%*		
(a) Gait, mobility, posture and balance				
Gait efficiency	92	59.8%	39	[17, 18, 28, 33, 35, 38, 41, 43, 44, 50, 51, 53, 55, 57, 61, 65, 67, 69–90]
Gait velocity and cadence	92	59.8%	56	[28, 29, 32, 35–38, 40, 41, 43, 44, 48, 50, 51, 53–55, 61–65, 67, 69–86, 88–102]
Mobility	72	50.0%	54	[17, 28–32, 35–37, 39, 40, 46, 48, 49, 54, 56, 58, 60, 62–64, 67, 70, 75, 78–80, 82–85, 87–89, 91, 95, 96, 98–114]
Balance, posture and risks of fall	121	61.2%	62	[17, 28, 29, 34–39, 41–44, 47, 49–51, 53–58, 62, 65, 66, 68, 72, 73, 75, 78–80, 82–85, 87–90, 95–99, 101, 103–105, 107–110, 112–119]
(b) Cognitive functions	31	29.0%	9	[52, 58, 85, 89, 90, 112, 119–121]
(c) Depression	18	38.9%	18	[30, 41, 49, 52, 58–60, 68, 75, 89, 92, 97, 118, 120–124]
(d) Activities of daily living	42	59.5%	23	[18, 36, 45, 49–51, 58–60, 62, 63, 66, 69, 77, 91, 101, 103, 105, 118, 125–128]
(e) Level of activity	17	41.2%	10	[29, 36, 41, 45, 59, 63, 65, 90, 109, 111]
3) Clinical symptoms of PD	*152*	*50.0%*		
(a) Overall symptoms and disabilities (rating scales–total score)	27	51.9%	25	[30, 36, 45, 50–52, 59, 63, 65, 66, 68, 70, 71, 77, 88, 89, 93, 103, 104, 106, 113, 118, 122, 124, 129]
(b) Specific components of UPDRS				
Part I – Non-Motor Aspects of experiences of Daily Living (formerly Mentation, behavior and mood)	13	38.5%	13	[29, 43, 54, 56, 58, 70, 71, 77, 89, 93, 94, 122, 124]
Part II – Motor Aspects of experiences of Daily Living (formerly Activities of Daily Living)	20	50.0%	20	[28, 29, 43, 52, 54, 56, 58, 60, 66, 70, 71, 77, 84, 87, 89, 90, 93, 113, 122, 124]
Part III – Motor examination	45	71.1%	45	[29, 32, 35, 43, 46, 47, 49, 52, 54–56, 58, 60, 61, 66, 67, 70, 71, 75, 77–81, 83–87, 89, 93, 96, 98, 104, 110, 112–115, 117, 122–124, 128, 130]
Part IV – Motor complications (formerly Complication of therapy)	9	22.2%	6	[29, 43, 52, 70, 71, 89]
Part V – Clinical fluctuations or Modified Hoehn and Yahr Staging	2	0.0%	2	[43, 52]

(*Continued*)

Table 2
(*Continued*)

	Number of outcomes measures	Positive effect of PA intervention	Number of papers	References
Part VI – Other complications or Independence in daily living	2	50.0%	2	[43, 52]
(c) Specific symptoms of PD				
Bradykinesia	9	22.2%	7	[17, 18, 32, 41, 50, 54, 58]
Freezing	7	14.3%	7	[37, 54, 73, 79, 96, 101, 112]
Gait and posture alterations (specific component of UPDRS Part III)	4	75.0%	3	[54, 58, 98]
Rigidity	9	55.6%	6	[17, 18, 50, 54, 58, 130]
Tremor	5	20.0%	5	[17, 18, 50, 54, 58]
3) Psychosocial aspects of life	*95*	*45.3%*		
(a) Quality of life (QoL)				
QoL–total score	36	50.0%	34	[30, 32, 46, 49, 58, 60, 64–67, 72, 75, 84, 85, 87, 89, 100, 101, 103, 105, 106, 109–112, 119, 120, 123, 124, 126, 127, 129, 131, 132]
QoL–specific components	42	38.1%	7	[58, 72, 87, 89, 124, 131, 132]
(b) Health management	17	52.9%	12	[49, 52, 58, 65, 67, 68, 88, 93, 105, 111, 112, 115]

allow for the calculation of the effect size of interventions with positive ($n = 2$) and null ($n = 4$) outcome measures related to the level of activity.

Clinical symptoms of Parkinson's disease

Potential for improvement in this category is good with 50% of all reported outcome measures resulting in positive effects.

Overall symptoms and disabilities

Potential for improvement in *Overall symptoms and disabilities* is good; as 51.9% of outcome measures resulted in positive effects.

Specific components of UPDRS

Potential for improvement in *Part I – Non-Motor Aspects of experiences of Daily Living (formerly Mentation, behavior and mood)* is poor; as 38.5% of outcome measures resulted in positive effects. Analysis of the effect size between the studies exhibiting significant improvements in Part I (0.38 ± 0.1) and those showing no improvement (0.32 ± 0.4) did not demonstrate a statistically significant difference between the two groups. Note that the data from four studies did not allow for the calculation of the effect size of interventions with positive ($n = 2$) and null ($n = 2$) UPDRS Part I outcome. It is good in *Part II – Motor Aspects of experiences of Daily Living (formerly Activities of Daily Living)*; as 50% of outcome measures resulted in positive effects. It is excellent in *Part III – Motor examination*; as 71.1% of outcome measures resulted in positive effects. As for the potential for improvement in *Part IV – Motor complications (formerly Complication of therapy)*, it is very poor as 22.2% of outcome measures resulted in positive effects. However, the data available in the literature did not enable us to assess the effect size of any study yielding positive outcomes in the UPDRS Part IV. As for the potential improvement in *Part V – Clinical fluctuations or Modified Hoehn and Yahr Staging*, it is also very poor as none of the outcome measures resulted in positive effects. Additionally, no data was available for the calculation of the effect size. Finally, it is good in *Part VI – Other complications or Independence in daily living*; as 50% of outcome measures resulted in positive effects.

Specific symptoms of PD

Potential for improvement in *Bradykinesia* is very poor; as 22.2% of outcome measures resulted in positive effects. However, the data available in the literature did not enable us to compare the effect size of the studies yielding positive and null outcomes related to bradykinesia. As for the potential improvement in *Freezing of gait*, it is poor as 33.3% of outcome measures resulted in positive effects. Analysis of the effect size between the studies exhibiting significant improvements in freezing (0.96 ± 0.9) and those showing no improvement (0.08 ± 0.1) did not demonstrate a statistically significant difference between the two groups however, this is likely due to the very limited number of available studies. Note that the data from two studies did not allow for the calculation of the effect size of interventions with null outcome measures related to freezing of gait. As for *Gait and posture alterations (specific component of UPDRS Part III)*, the potential for improvement is excellent in as 75% of outcome measures resulted in positive effects. It is good in *Rigidity*; as 55.6% of outcome measures resulted in positive effects. Finally, it is very poor in *Tremor*; as 20% of outcome measures resulted in positive effects. The data available in the literature did not enable us to compare the effect size of the studies yielding positive and null outcome measures related to tremor.

Psychosocial aspects of life

Potential for improvement in this category is fair with 45.3% of all reported outcome measures resulting in positive effects.

Quality of Life (QoL)

Potential for improvement in *QoL – total score* is good; as 50% of outcome measures resulted in positive effects. It is poor in *QoL - specific components*; as 38.1% of outcome measures resulted in positive effects. Analysis of the effect size between the studies exhibiting significant improvements in QoL (0.65 ± 0.7) and those showing no improvement (0.23 ± 0.1) demonstrated a statistically significant difference between the two groups. Note that data to compute effect size was available for all studies reporting outcome measures related to QoL.

Health Management

Potential for improvement in *Health management* is good; as 52.9% of outcome measures resulted in positive effects.

DISCUSSION

In this review, we were able to extract 868 outcome measures from 106 papers published from 1981 to 2015, providing an overview of the effects of PA on people living with PD. After regrouping those outcome measures into four main categories (*Physical capacities, Physical and cognitive functional capacities, Clinical symptoms of PD* and *Psychosocial aspects of life*), we were able to look at specific parameters and identify the proportion of positive results for each of them.

Throughout this review, we were able to determine that PA seems the most effective for improving *Physical capacities* as well as *Physical and cognitive functional capacities,* with good overall results. Specifically, for *Physical capacities*, positive results were greater for *Lower and upper limbs strength, endurance or speed* as well as for *Metabolic functions*. For *Physical and cognitive functional capacities*, the sub-categories *Activities of daily living* as well as *Gait, mobility, posture and balance* presented greater positive results. We further divided this latter sub-category into specific parameters, showing that effects of PA seemed more effective on *Balance, posture and risks of fall*, but less on general *Mobility*. The lower score obtained for the *Mobility* parameter could be explained by the considerable gap between the results of two tests widely used to assess mobility, the 6MWT that ended with excellent results, being positive in 72% of cases, and the TUG test that ended with poor results, being positive in only 35.3% of cases. The reasons leading to low effects of a PA intervention on TUG performance compared to this other test are unclear and should be further investigated. Nevertheless, we propose that the continuous pattern of movement associated with the 6MWT may help patients perform better, while the discontinuous pattern of the TUG (standing, walking, turning, sitting) is more challenging for the basal ganglia related disease that is PD.

Overall, the parameters classified in the *Physical and cognitive functional capacities* category were the most widely measured in the reviewed articles. Yet, the number of outcome measures differed greatly between sub-categories. *Gait, mobility, posture and balance* outcomes were measured 377 times within the reviewed papers while *Cognitive functions* and *Depression* outcomes were measured respectively 31 and 18 times. We must mention that the very poor results for *Cognitive functions* were based on only 31 outcome measures originating from 9 papers. Moreover, these were all published in 2009 or later, except for one that was published in 1999. In our view, this indicates that research on the effects of PA on cognitive functions of PD patients is fairly recent and emerging. Our analysis of the observed effects of PA intervention highlights the fact that some outcome measures related to cognition seem to have a greater sensitivity to PA; whether it be in the test used or in the specific cognitive process being assessed (e.g. cognitive dual task performance). Further studies are certainly required to draw stronger conclusions on potential for improvements in this field. As for *Depression*, even though the results show poor potential for improvement, the low number of outcome measures, 18, makes it difficult to bring out a trend; it only highlights the need for further investigation.

This review also shows that the effects of PA on *Clinical symptoms of PD* and *Psychosocial aspects of life* were not as positive, with respectively good and fair results. It is important to note that the *Clinical symptoms of PD* category exhibited the highest and lowest effectiveness results in the current study. Indeed, the *UDRS Part III – Motor Examination* as well as the *Gait and posture alterations (specific component of UPDRS Part III)* showed excellent potential for improvement after a PA intervention. On the other hand, outcome measures related to symptoms of *Bradykinesia*, *Freezing of gait* and *Tremor* revealed very poor potential for improvement. Nonetheless, we must be cautious in the interpretation of these results. First, some *Specific components of UPDRS* and some *Specific symptoms of PD* have not been the object of many post PA intervention assessments. Therefore, results based on a very small pool of outcome measures may be drawn upward or downward and not reflect the reality. Second, some clinical scales may not be sensitive to the changes in symptoms following PA interventions. Clinical ratings of symptoms are performed during a short specific time-window before and after the PA intervention. Symptoms of PD have been shown to be variable over time; from day-to-day and even within one day. It is possible that PA interventions have a positive effect on *Clinical symptoms of PD* that cannot be captured in those small measurement time-windows but would require other assessment methods such as wearable sensors for long-term monitoring. Third, as we previously mentioned, there is high variability in symptoms between patients. It is reasonable that patients not exhibiting *Freezing of gait* or having only very mild *Tremor* not show improvements in those outcome measures after PA interventions. In our view, not only do further studies seem required to draw stronger conclusions on potential for improvements in clinical symptoms of PD, but there is also a need to use sensitive assessment tools to detect subtle changes, especially in specific motor symptoms.

According to our review, *Psychosocial aspects of life* show, overall, the least potential for improvement as a results of a PA intervention. However, it is interesting to note that *Health management* was more positively influenced by PA than *QoL*. Our explanation is that, in the short term, general health might benefit more rapidly and more importantly from a PA intervention, showing better results immediately after its completion. We also hypothesize that *QoL* would be more positively influenced by a persistent PA program, which would be demonstrated on a long term scale. This is in part supported by our analysis of the observed effects of intervention as those exhibiting the largest effects of PA seem to be in areas where short-term variations can readily be observed by patients (e.g. mobility, ADL, symptoms) whereas those exhibiting the smallest effects may require longer periods of time to change (e.g. social support, communication). Further research would be needed to confirm this hypothesis.

Lastly, this review aspects of PA intervention in PD patients that would benefit from further research. In this review, we have not examined in details the modality of PA delivery since our goal was to bring out aspects of health that, so far, have shown the most potential for improvements regardless of the activity undertaken. We must emphasize that there was a high variety of modalities used across the studies. Also, the duration of the interventions spanned from 2 to 96 weeks, and frequency from once every two weeks to 7 days a week. However, we were able to observe that walking exercises, closely followed by multimodal interventions, seemed to provide the best results, regardless of volume and intensity. However, this observation does not allow us to determine the best-suited activity for PD patients. Moreover, the long term effects of PA on the outcome of PD remain to be determined. Even though it is agreed that type and dosage of PA may influence the results in terms of benefits, it is also agreed that similar results may be obtained through interventions that vary in mode, duration, volume and intensity. In the perspective of improving health and well-being of people living with PD, it would be, in the authors view, relevant to measure the impact of a PA interventions on participants' lifestyle habits with regards to exercise. Even though the American College of Sports Medecine (ACMS) considers regular exercise as an adjunctive to PD treatment and provides general guidelines for the prescription of PA [27], specific guidelines for exercises remain to be determined, particularly in terms of identifying the optimal type, frequency and intensity of PA. It is our view however, that any PA program that engages the musculo-skeletal and cardiovascular systems, as well as cognitive functions, has the potential to have a positive effect on the lives of patients with

PD. Clinicians should therefore set realistic goals with their patients, based on scientific observations that improvement might be possible in all aspects of health, but that some present a greater potential.

LIMITATIONS

One limitation of the present review is the heterogeneity of the studies included. Indeed, there were various types of studies, including controlled and uncontrolled, as well as randomized and non-randomized trials. Furthermore, as mentioned above, there was a very high variability in PA modalities. Taken together, this may have skewed our interpretation of the potential effectiveness of PA on different aspects of PD; in one way or another. Finally, we have to acknowledge that the classification of parameters and outcome measures was based on *a priori*, informed and deliberate choice by the authors of this review. A different classification may have changed somewhat the results.

CONCLUSION

This overview of the literature highlights the positive effects of PA on *Physical capacities* and *Physical and cognitive functional capacities*, more specifically on *Gait, mobility, posture and balance*. The parameters that were classified in this sub-category have been studied thoroughly in the last 34 years and our findings are in line with recent meta-analyses assessing the effects of PA on PD [20, 21]. This review also brings out the mitigated effects of PA on *Clinical symptoms of PD*. PA appears to have highly positive effects on gait-related motor symptoms as measured by the *UPDRS Part III – Motor examination*, but much lower effects on other symptoms. It also highlights the less effective results reported on *Psychosocial aspects of life*, especially on *QoL*. Finally, this paper brings out the need for further research on the effects of PA on some health parameters that have not been looked at as extensively in the literature. Effects of PA on *Cognitive functions*, *Depression* as well as *Specific symptoms of PD* could benefit from additional assessments.

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