How to Assess the Benefit of Acupuncture?

Abstract: The introduction to this paper describes how in the year 2008 I was first diagnosed with Parkinson's disease (PD). Seven years later in 2015 it was suggested to me that I should try acupuncture as a therapy that might slow down the progression of the illness. Whether this is true or a product of my imagination is difficult to judge. I began to feel a need for a way of measuring the strength of the progression with and without acupuncture and later that year I was introduced to the 'Unified Parkinson's Disease Rating Scale' (UPDRS) and with that as my measuring tool I have assessed the strength of my symptoms since August 2015. Most strikingly this is shown in diagram 1, page 5.

For the purpose of this paper I have divided the period into three sub-periods during which I did NOT receive acupuncture and four sub-periods during which I did receive acupuncture as described under 'Method and Results'. The two sets of sub-periods were then compared graphically and numerically of which the numerical comparison may imply some slowing down of the progression while undergoing acupuncture therapy.

The paper finishes with a discussion that concludes in a plea for more, better resourced and better designed research into the effect of acupuncture on a mal functioning nervous system especially Parkinson's disease.

INTRODUCTION

The autumn of the year 2006 – approximately 1 year before my retirement - was the point in time when I first became aware of unusual tremors, primarily in my left arm. At first I did not pay much attention, but as the tremors grew stronger, I eventually, in the summer of 2008, sought the advice of my local GP. He subsequently referred me to a neuro-specialist who without hesitation diagnosed me as having Parkinson's disease (PD), a diagnosis which has since been confirmed when I sought a second opinion.

I was born in 1942 and it is now 2021 which means that I am 79 years of age and have had to cope with PD for the past 15 years. I am not particularly interested in medical matters generally, but I am interested in how PD affects me, particularly how it may progress, how it may affect me in the future, and how I might adjust my style of living to make it easier to cope with PD.

The PD affects my whole body, but the symptoms are particular pronounced in the left arm and leg. I have had regular acupuncture therapy since August of 2015 with the addition of electro-acupuncture to the limbs on my left. The frequency of therapy sessions has varied, but at present I have settled for fortnightly sessions every two weeks.

In the summer of 2015 I also learnt about the Unified Parkinson's Disease Rating Scale (UPDRS) and began to rate myself regularly. And an idea gradually took shape in my mind, the idea that I could use the UPDRS as an instrument by which to measure the progression of the disease and possibly how symptoms might react to treatments one way or another.

The regular acupuncture therapy have continued until March 2020 and beyond until the present day. The regular therapy sessions were of course brought to a close by

the Covid-19 outbreak from March to July of 2020. I cannot be 100% sure, but after a couple of months I began to feel that tremors have got stronger than I would expect given the 'natural' progression, and I cannot think of any other reason for this than the absence of acupuncture.

At £30 per hour or more, therapy by acupuncture is not cheap so for economic reasons alone, I felt a need for a kind of fool-proof, objective method of measuring the effect of acupuncture on the standard symptoms of PD. This might also help me assess whether the improvements, I have felt, were real or products of my imagination.

Individual 'readings' of UPDRS fluctuate too much for these on their own to be a practicable, useful yardstick. I need some yardstick or benchmark against which to assess the progression with or without acupuncture.

What is described in the following is in part the outcome of a search for such a yardstick and in part an attempt at an objective assessment of the effect of acupuncture treatment. I have sought to summarise the outcome of these activities which span a 6 year period. It does not constitute formal research, but are my own creation except for reference to scientific literature which has been downloaded or copied from the internet.

THE THREE ELEMENTS

Parkinson's disease

There are three – what I will describe as 'elements' in this investigation. The first of which is the disease itself known as Parkinson's disease (PD), simply Parkinson's, sometimes also referred to as Parkinsonism.

It is a long-term degenerative disorder of the central nervous system that mainly affects the motor system. The symptoms usually emerge slowly, and as the disease worsens, non-motor symptoms become more common. The most obvious early symptoms are tremor, rigidity, slowness of movement, and difficulty with walking. Cognitive and behavioural problems may also occur with depression, anxiety, and apathy occurring in many people with PD and they can also have problems with their sleep and sensory systems. The motor symptoms of the disease result from the death of cells in the substantia nigra, a region of the midbrain, leading to a dopamine deficit. The cause of this cell death is poorly understood, but involves the build-up of misfolded proteins into Lewy bodies in the neurons.¹)

So far my problems have been what is referred to as 'early' symptoms. I am not aware of any significant or behavioural problems.

UPDRS

The second element is the unified Parkinson's disease rating scale (UPDRS) used to follow the longitudinal course of Parkinson's disease. The UPD rating scale is the most commonly used scale in the clinical study of Parkinson's disease.

The UPDRS is made up of four sections which are evaluated by interview and clinical observation. Some sections require multiple grades.

Clinicians and researchers alike use the UPDRS and the motor section in particular to follow the progression of a person's PD. Scientific research use it to measure benefits from a given therapy in a more unified and accepted rating system. Neurologists also use it in clinical practice to follow the progression of their patients' symptoms in a more objective manner.

Following the UPDRS scores over time provides insight into the patient's disease progression. For instance Michael J. Fox's symptoms started with a slight tremor, so his motor score would have been less than 10 (and with full use of the scale it could theoretically reach 199!). For most patients, the "mentation, behaviour and mood" scores increase later in the disease.²) ³)

The four sections referred to above are:

- 1. Mentation, behaviour and mood.
- 2. Activities of daily living (for both "on" and "off").
- 3. Motor examination.
- 4. Complications of therapy (in the past week). 2) 3)

However, for the purpose of this paper, I have mainly used section 2, 3 and 4.

Acupuncture

The third element is acupuncture, a form of alternative medicine and a key component of traditional Chinese medicine (TCM) in which thin needles are inserted into the body. There is a range of acupuncture variants with two main foundational philosophical applications and approaches, the first being the modern standardized form called eight principal TCM and the second an older system that is based on the ancient Taoist Wuxing. Acupuncture is most often used to attempt pain relief though acupuncturists say that it can also be used for a wide range of other conditions. Acupuncture is generally used only in combination with other forms of treatment.

It is generally safe when done by appropriately trained practitioners using clean needle technique and single-use needles. When properly delivered, it has a low rate of mostly minor adverse effects. Accidents and infections do occur, though, and are associated with neglect on the part of the practitioner.⁴)

The dominant view of acupuncture seems to be that trials and reviews are inconsistent and acupuncture therefore probably not effective; they found "little evidence" of effectiveness in treating pain and "seemed to lack clinical relevance and could not be distinguished from bias".

In fairness it would seem relevant to mention that most 'honest' reviewers of research into acupuncture recognize that much of this research appears to be

underfunded and conducted with a number of participants too small to render any possible conclusions meaningful or trustworthy.

"In conclusion, the evidence for the effectiveness of acupuncture for treating PD is not convincing. The number and quality of trials as well as their total sample size are too low to draw any firm conclusion. Further rigorous trials are warranted." ⁵)

"The results were limited by the methodological flaws, unknowns in concealment of allocation, number of dropouts, and blinding methods in the studies. Large, well-designed, placebo-controlled RCTs with rigorous methods of randomization and adequately concealed allocation, as well as intention-to-treat data analysis are needed." ⁶)

My own experience of acupuncture is that it is a kind of life-saving, recovery therapy in which slumbering or dying nerve cells such as the dopamine producing cells are reawakened and brought back and stimulated into full activity at least for a period. However it is a very slow process and benefits are slow to emerge.

As acupuncture therapy is only working slowly it is difficult for an individual patient, such as myself, to know with certainty whether or not it is having any effect, but people around me commenting on my physical state of health tells me that this is better than they would have expected given the length of time since I was first diagnosed. For me therefore, the research by Bai-Yun Zeng et al seems especially relevant:

".... acupuncture treatment is in fact a neuroprotective therapy that increase the release of various neuroprotective agents such as brain-derived neurotrophic factor, glial cell line-derived neurotrophic factor, and cyclophilin A. In addition, acupuncture therapy slows cell death process and attenuates oxidative stress to dopaminergic neurons in the substantia nigra. These results suggest that early application of acupuncture therapy to Parkinson's patients may be helpful for the best efficacy of acupuncture treatment." ⁷)

LONGITUDINAL OBSERVATIONS

In diagram 1, overleaf, page 5 is set out nearly all (except for holiday periods) the daily average UPDRS "observations" since August 2015 when this monitoring exercise first began, covering in total 2278 days. Each daily observation is the average of 1, 2 or more observations made that day, so the diagram is the visual expression of approximately 7,700 observations.

It will come as no surprise to a person familiar with the progression of PD that the graph shows a positive slope from left to right starting with average observations of around 10 in August 2015 and ending with observations of an average score in the upper 50s in October 2021.

Diagram 1

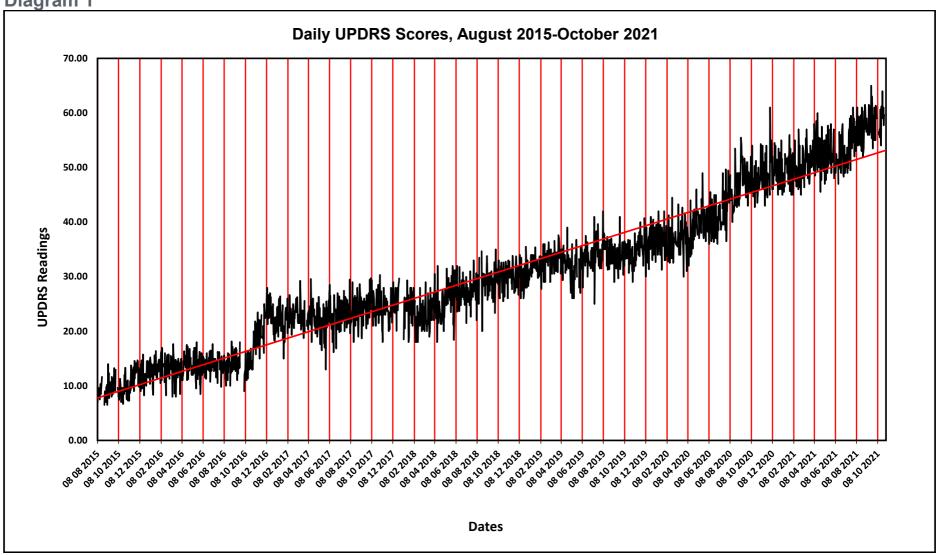


Table 1

Year					
	No of Months	1	2	Difference	Monthly Increase
2015	5*)	8.79	12.02	3.23	0.65
2016	12	13.00	23.37	10.37	0.86
2017	12	21.56	25.96	4.40	0.37
2018	12	24.46	30.40	5.94	0.50
2019	12	31.63	36.28	4.65	0.39
2020	12	36.89	50.25	13.36	1.11
2021	10**)	49.51	59.67	10.16	1.02
	75	8.79	59.67	50.88	0.68

^{*)} August to December. **) January to October.

The average annual and monthly scores are set out in table 1 above, and it is noted that the annual rise in each year falls within the range referred to by Holden et al ⁸): "Several studies have examined – the ability of UPDRS to track symptom progression over time, reporting rather wide ranges for annual score increases (total score, 3.0-14.0 points per year;)" – and it would seem that these studies as the relevant yardstick have used changes in the UPDRS per unit of time ie one year, but surely one could also use another unit say changes in UPDRS per week or per month as shown in the last column of table 1.

However, the progression is not uniformly straight and linear. There are periods when the PD apparently has progressed faster than at other times, the graph showing a steeper slope eg in November-December 2015, in December 2016, in April-May 2018 and July-August 2020. Likewise there are periods when progression is virtually stagnant like during most of the year 2015 before November, during most of the year 2016 before December of that year and again during most of the year 2017. The challenge now is how these observations can be related to ongoing sessions of acupuncture therapy.

METHOD AND RESULTS

The sequence of therapy and UPDRS observations has been divided into a number of sub-periods according to when therapy was received or not received as follows:

Without acupuncture: 1) 18. Aug '16-10. Oct '16 (55 days); 2) 2. Aug '17- 12. Mar '18 (224 days); 3) 1. Apr '20- 15. Jun '20 (77days).

<u>With Acupuncture:</u> 1) 8. Aug '15 – 17. Aug '16 (377 days); 2) 11. Oct '16 – 1. Aug '17 (296 days); 3) 13. Mar '18 – 31. Mar '20 (751 days); 4) 16. Jun '20 – 30. Apr '21 (320 days).

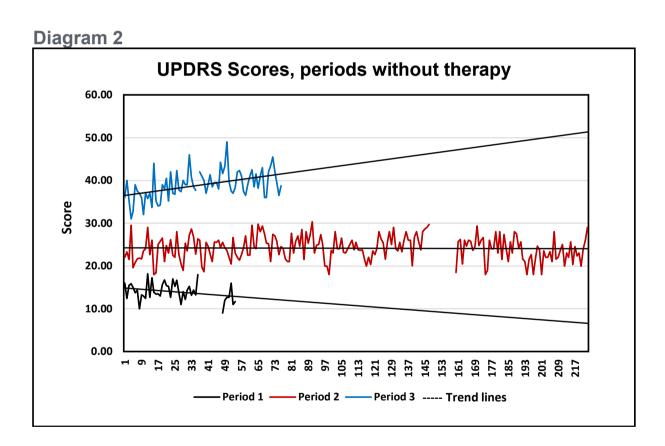
It is noted that there were three relatively short periods during which acupuncture therapy was not received. By contrast there were four relatively longer periods when such therapy was received.

The decision to terminate receiving acupuncture in the beginning of the first two periods when acupuncture were not received was based on financial considerations; the third period was forced upon me by the covid-19 lockdown from March to July 2020. The pattern of sub-division is therefore totally random rather than the result of a rigorous research design.

Graphic representations - without therapy

The results of monitoring the symptoms during the three periods, when the patient (myself!) has not undergone acupuncture therapy, are plotted in diagram 2 below.

The condition is progressive and therefore the first period is shown as the graph nearest the horizontal axis while the two subsequent periods are shown above that.



Graphic representations - with therapy

Diagram 3, page 8, below, concerns the four periods during which the therapy of acupuncture was received. There are four graphs, one for each period, and each graph showing the expected features that the earliest with the lowest UPDRS scores

is closest to the horizontal axis and the latest graph with the highest scores is higher up in the frame.

The second expected feature is the sloping from left to right as is also shown diagram 1.

A third - unexpected - feature is that all four graphs seem to have two parts: one depicting the earliest part of the period with a relatively steep slope covering the first approximately 60 days of the period. After these 60 days the second part of the graphs seems to show a less steep, but steady progression.

Having noticed these features an average of all four graphs was calculated and set out as one graph in one diagram, diagram 4.



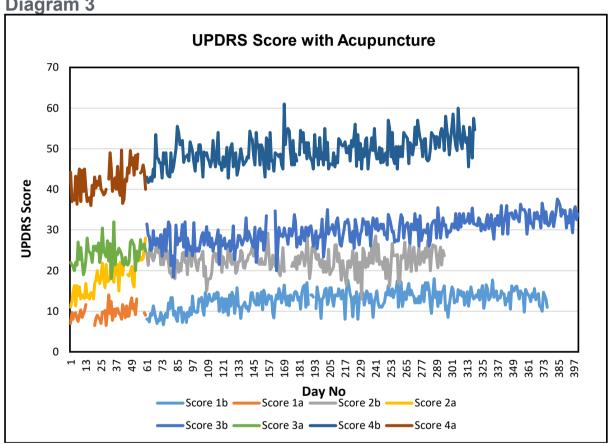
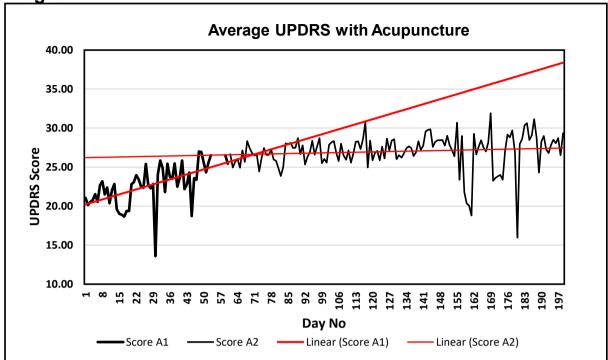


Diagram 4



Note: Score A1 ~ the average score of the first 61 days of each of the four periods <u>with</u> acupuncture. Score A2 ~ the average score of the following138 days of each of the four periods <u>with</u> acupuncture.

If there is a reality behind these features it may be that when a period of therapy commences after a long period without receiving any, the nervous system responds as if being shocked into action and later settles into slow and steady progress.

Numerical representation

Table 2

	No days	End	Start	Change	
				Total	Daily Mean
	(1)	(2)	(3)	(4)	(5)
Without 1	36	12.28	14.28	-2.00	-0.056
Without 2	194	22.67	23.18	-0.51	-0.003
Without 3	51	39.86	36.64	3.22	0.063
With 1	345	13.63	8.80	4.83	0.014
With 2	265	23.72	15.65	8.07	0.030
With 3a	348	33.21	23.85	9.36	0.027
With 3b	343	38.38	33.27	5.11	0.015
With 4	289	53.03	40.17	12.86	0.044

Notes:

- (1) ~ No of days between start and end of period with/without acupuncture
- (2) ~ Average UPDRS observations at the end of period
- (3) ~ Average UPDRS observations at the start of period
- (4) ~ Difference between (3) and (2)
- $(5) \sim (4)/(1)$

An alternative to the analysis of the graphical representation of the progression of PD would be an analysis of the numerical observations of the UPDRS.

In table 2 above is set out average observations at the start and end of the periods outlined on page 6, column (2) and (3), and the difference is calculated, column (4). Also included in the table is the number of days of each period, column (1), and this is related to column (4) to arrive at the daily mean set out in column (5).

The table is further split into two halves of which the upper half depicts the findings for the three periods 'without' acupuncture when therapy was not received. The lower half depicts the findings for the four periods (period 3 has been split into two numbered 3a and 3b) 'with' acupuncture when therapy was received.

It is worth noting that the daily progression for each of the four periods 'with' therapy is lower than the 0.063, which in turn signify that the progression during each of these periods was slower than during the last periods 'without' therapy.

DISCUSSION

Acupuncture

It seems that there is a growing consensus among scientist with neurological expertise that the insertion of needles into the nervous system under the skin as in acupuncture stimulate the system to release certain chemicals and possibly a nerve growth factor into the muscles, spinal cord and brain. This in turn may stimulate the body's natural healing abilities, promote physical and emotional well-being, and help the nerves to regenerate.

While it may promote physical and emotional well-being we still need to see this changed and hopefully improved well-being expressed in a way that can be reasonably accurately assessed against the UPDRS scale or similar, both at selected points in time and as changes over a period.

Johns Hopkins Medicine in their website note: "Some people report acupuncture makes them feel energized. Others say they feel relaxed." However, it should be possible to include both cases under a common label of 'improved well-being'.")

UPDRS

The symptoms of PD are numerous and can be difficult to communicate and quantify. The variability in symptoms week-by-week, day-by-day and hour-by-hour can make this even more difficult. It poses a challenge to the patient when he/she need to explain to the PD specialist or family how they have been. The purpose of the above investigation has been to find a reliable way of monitoring symptoms and especially tracking day-by-day variation and the long-term progression.

In order to do this I have used the UPDRS system, but in so doing there is a danger, as in all research and investigations, that the researcher, consciously, subconsciously, deliberately or not will give the record of his/her observations a bias that may twist the final result and obscure a final conclusion.

Each of the four sections referred to above (page 2) is divided into a number of subsections, one for each sign or symptom. Each sub-section is rated on a 5-point scale (ranging from 0 to 4), with higher scores indicating more severe impairment with descriptions such as "Normal, Slight, Mild, Moderate or Marked" or similar. The task for the researcher is to classify each symptom within this framework. However, to classify the manifestation of each symptom as say "mild" or "moderate" in a consistent and reliable manner over time would seem difficult if not impossible even for a trained observer. And it will be even more so if we seek a consistent description of progression over time and have to decide when the manifestation of a symptom moves from "mild" to "moderate".

Using the UPDRS in constructing the diagrams and tables that are shown above I have used the whole of the Rating Scale and every-one of the said sections in arriving at every 'observation'. This may not be the correct way of using the scale. Some symptoms vary more than others and the timing and frequency of use should probably be adjusted to take account of that fact.

Having used the Rating Scale extensively for a number of years one also feels that in its present form it has some strikingly obvious omissions. It might for example be useful to record when the assessment was done vis a vis the consumption of medication, receipt of therapy such as acupuncture i.e. was the assessment done before or after the intake of medication and if so how long before or after. Timing in terms of the point in time of assessment during the course of a normal day i.e. immediately after rise in the morning, before or after any meals or before going to bed may also be a useful pointer.

Similarly, there is only one question relating to the presence or otherwise of *dystonia* with the answer being 'Yes' or 'No'. It has been my experience that a rating on a scale as described above would be very useful.

Section 2, *Activities of Daily Living*, seems to have more to do with ageing rather than PD as such.

More directly one may ask why some symptoms or tell-tell signs of PD are not included in the Rating Scale like for example constipation, changes to the patient's eye-sight, loss of smell and taste, dryness of the patient's scalp and may be more.

Factors other than acupuncture therapy

Whether or not we accept the influence of acupuncture on the symptoms of PD, it is increasingly realised that other factors are also active. In the assessment of the visual manifestation of symptoms it therefore becomes difficult and ultimately possibly impossible to determine whether an observation of slight tremors is due to

acupuncture therapy or the effect of some other factor such as diet or even the weather.

One factor that has received increasing attention is that of nutrition and diet. Seidl et al write: "A growing body of evidence suggests that nutrition may play an important role in PD. (S)tudies have recently identified promising components in certain food groups that may elicit neuroprotection in PD. However, inclusion or exclusion of other food groups may trigger or exacerbate neurodegeneration." ¹⁰)

They conclude:"A poor diet may lead to increased oxidative stress, which could impede the antioxidant defense system. In contrast, a well-balanced diet rich in a variety of foods, including numerous servings of vegetables and fruits (especially those containing nicotine) and moderate amounts of omega-3 fatty acids, tea, caffeine, and wine may provide neuroprotection." ¹⁰)

In other words a poor diet may reduce the effect of acupuncture and give the impression of negligible effect of the therapy. By contrast a "well-balanced diet" may enlarge the effect of acupuncture and give the impression of an enhanced effect.

The effects of changing weather are acknowledged, but mostly ignored. However, Parkinson's UK (2020) offered the following advice for the winter 2020/21:"Cold weather, ice and seasonal illnesses can cause more complications for people with Parkinson's. Keep yourself and your house warm: Parkinson's affects the nervous system, which controls body temperature, so people with Parkinson's can be more sensitive to heat and cold."11)

Rowell et al (2017) analyse the use of prescriptions "to test what effect the weather may have on medications prescribed to treat Parkinson's disease." Their results suggest seasonality exists in Parkinson's disease symptoms and this may be related to temperature. They recommend further research "as a better understanding of the causes of any seasonal variation in Parkinson's disease may help clinicians and patients manage the disease more effectively."¹²)

The possible effects of weather conditions must be taken into account when individual observations are assessed using the UPDRS. If they are not assessment and subsequent interpretation is likely to be erroneous.

Research Design

The investigation suffers from the fact that it is just a one man project in which the results of measurements or observations as well as reporting and analysis has all been done by one and the same person. Some may therefore question whether the investigation has been appropriately un-biased and objective.

As described on page 3 above much research into the efficacy or otherwise of acupuncture therapy generally suffers from a lack of involvement of human resources which may lead to doubting the significance of the research.

It would be desirable if the design of a research project could include the specification of a number of PwP, some to undergo acupuncture therapy, and a control group, who should not receive therapy. Both groups should be monitored simultaneously over a specified time period of significant length, probably a few - say five! - years.

It is described above how there are several different factors that influence the observations we make of symptoms. It may well be that the research design will need to include a methodology to separate the effects of different individual factors.

If the UPDRS is the measuring system of choice it will have to be decided whether symptoms should be assessed with reference to either one of the four sections separately or with reference to all four sections.

It may be that in this task recently developed sensors worn by the patient as wrist bands will facilitate remote monitoring of a patient's symptoms. In any case it would probably remove any doubt that may exist in respect of the quality of the data and objectivity of the observations.

References:

- 1) en.wikipedia.org/wiki/Parkison%27s_disease
- 2) en.wikipedia.org/wiki/Unified_Parkinson%27s_disease_rating_scale.
- 3) https://neurotoolkit.com/updrs/
- 4) https://en.wikipedia.org/Wiki/Acupuncture
- ⁵) Lee MS et al, *Effectiveness of acupuncture for Parkinson's disease: a systematic review,* Movement Disorder Society, University of Exeter, Aug. 2008
- ⁶) Lam YC et al, *Efficacy and safety of acupuncture for idiopathic Parkinson's disease: a systematic review*, Complementary Medicine, Hong Kong Baptist University, July 2008.
- 7) Bai-Yun Zeng et al, *Current development of acupuncture research in**Parkinson's disease, International Review of Cell and Molecular Biology.2013;111:141-58.doi: 10.1016/B978-0-12-411545-3.00007-9.
- ⁸) Holden, Samantha K, et al, *Progression of MDS-UPDRS Scores Over Five Years in De Novo Parkinson Disease from the Parkinson's Progression Markers Initiative Cohort*, Movement Disorders Clinical Practice, Jan.-Feb., 2018.
- 9) https://www.hopkinsmedicine.org/health/wellness-and-prevention/acupuncture
- 10) Seidl, S E et al, The emerging role of nutrition in Parkinson's disease, Frontiers in Aging Neuroscience, March 2014.
- ¹¹) Parkinson's UK, *Managing Parkinson's this winter.* November 2020. Copied from: www.parkinsons.org.uk/news/managing-parkinsons-winter
- ¹²) Rowell, David et al, **Seasonal temperature is associated with Parkinson's disease prescriptions: an ecological study,** International Journal of Biometeorology, 30. August 2017