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Research paper

Effects of shiatsu on the health-related quality of life of a person with secondary progressive multiple sclerosis: A mixed methods N-of-1 trial within a whole systems research case study

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ABSTRACT

Introduction: Multiple Sclerosis (MS) is a chronic neurological disorder with high prevalence in Finland. Most people with MS will develop Secondary-Progressive MS (SPMS) over time. People with MS report lower than the average Health-Related Quality of Life (HRQoL) and use Complementary and Alternative Medicine (CAM) for their symptoms. Personalised interventions such as shiatsu have an insufficient evidence base. The n-of-1 trial is a promising study design for personalised interventions in chronic conditions but has not little used in CAM research. The aim was to investigate if shiatsu affects the HRQoL of a person with SPMS.

Methods: Six-periods counterbalanced mixed-methods n-of-1 trial within a Whole Systems Research (WSR) case study was used. The short version of the MSQLI, data collected from a semi-structured interview and case notes were used to assess the effect of the treatment. The collected data analysed quantitatively and qualitatively and synthesised as a descriptive case study.

Results: The study was able to document improvements in spasticity, bowel function, fatigue, pain, sleep and relaxation. No adverse events occurred. Preliminary estimations of the onset and wash-out of shiatsu effects were inferred. Advantages and drawbacks of the design are discussed to improve future applicability.

Conclusions: Shiatsu was able to improve some domains of the HRQoL of the specific person with SPMS. It was a safe treatment with no adverse events. Mixed methods n-of-1 trial within a WSR case study was an appropriate design for the study.

1. Introduction

1.1. Background

Multiple Sclerosis (MS) is a complex neurological disorder affecting physically, psychologically, and socially [1] more than 2.2 million people worldwide, with average sex ratio 2/1 female/male and significant association between latitude and prevalence [2], putting Finland in the high-risk region. Most Persons with MS (PwMS) initially diagnosed with Relapsing-Remitting MS. After an average period of 20 years, the majority develop Secondary Progressive MS (SPMS) [3], which is characterised by irreversible disease progression [4].

PwMS experience a lower level of Health-Related Quality of Life (HRQoL) compared to the general population or other chronic disease populations [5–7]. HRQoL in MS correlates with the function of the nervous system, mental and social complications [8], fatigue, pain, sleep disturbances, emotional issues, physical disability, disease progression [9], and comorbidities [10]. There is conflicting evidence for the effect that the commonly used Disease-Modifying Treatments have on the HRQoL for PwMS [11,12], while medicines used by PwMS may also lower their HRQoL, as have been found for drug-related sleep disorders [13].

HRQoL might be the most relevant care outcome for PwMS [14]. Its improvement is an unmet need for many [15]. A multidisciplinary approach combining medical treatment with rehabilitation [16] following individualised, patient-centred principles [17] could be an efficient HRQoL enhancing approach, minimising the impact of the disease [18]. Such programs are offered in specialised rehabilitation centres across Europe [19] with a small part of interventions being of Oriental Medicine (OM) origin [20]. PwMS use Complementary and Alternative Medicine (CAM) [21,22] not only to help themselves with symptom management but as part of a keen interest in wellness [23,24]. The situation is similar in the Nordic countries despite the well-established public healthcare systems [25], with over half of

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PwMS using CAM during a year [26].

Shiatsu is an east-Asian bodywork form of CAM which took unique characteristics while developing by integrating the culture and contemporary realities of 20th century Japan [27]. In Japanese it translates to “finger pressure”. European practitioners use various approaches in their treatment [28,29], but they share at least the following characteristics with the original Japanese style: a) diagnosis and therapy are combined, b) the body is the only tool used, c) treat the whole body [30].

A recent definition of shiatsu reads as:

“Shiatsu is a manual therapy applied by leaning forward in a relaxed manner with the weight of one’s body to an optimum point, and the correct use of fingers, palms, etc., in order to apply sustained, stationary pressure on different parts of the body for the purpose of correcting the imbalances of the body, and for maintaining and promoting health. It is a holistic therapy that aims to treat most of the body in each session.” [31]

The receiver lies fully clothed on a futon, bed, massage couch or wheelchair and the practitioner applies pressure to the body, while other techniques (e.g., stretches, joint mobilisations, gentle touch) could be included. A typical session lasts about an hour, and the practitioner might suggest exercise or dietary and lifestyle changes [32]. There has been some evidence for its effects on various health conditions [28] and physiological effects in humans [33]. The mechanisms of its action are not yet scientifically accessible, but it has been hypothesized that shiatsu may act, or at least influence, the hypothalamus-pituitary-adrenocortical axis functioning [34]. One of the conclusions of the biggest shiatsu study ever conducted [35] is that shiatsu, when performed by qualified practitioners, is a safe therapy with no lasting adverse effects [36], while a systematic safety review is ongoing [37].

As a personalised, whole system of healthcare, shiatsu approaches the receiver as an organic whole with interconnected physical, emotional, and psychosocial aspects [38]. Following a Whole Systems Research (WSR) [39] approach with mixed-methods and single-subject design could be an appropriate methodology for its investigation [40]. Single-subject research designs are carefully designed studies where the sole unit of observation is an individual patient who acts as his/her own control [41]. They are undertaken using a protocol involving multiple measurements of the desired outcome across time [42]. They are used in medical and rehabilitation research [43,44] and they are methodologically well established in those fields [45]. While not yet well integrated in CAM research, they have the potential to contribute to the evaluation of CAM [46]. They are considered a feasible research approach for the practitioners and a useful tool both for clinical research and for pilot studies while developing bigger and more expensive trials [47].

N-of-1 trials belong to the family of single-subject research designs, and this methodology has been proposed as very appropriate for trials in the contemporary era of personalised medicine [48]. They are considered ideal to evaluate the effectiveness of a treatment of chronic conditions [49].

1.2. Rationale, aims, and objectives

Personalised interventions like shiatsu might be possible to contribute to improving HRQoL for patients with complex diseases such as SPMS. The aim was to investigate if shiatsu affects the HRQoL of a person with SPMS. To achieve it, a mixed-methods n-of-1 trial within a WSR case study designed and implemented.

2. Methods

Ethical approvals were given by The Northern College of Acupuncture (NCA) Research Ethics Committee (11/09/2017) and by the Helsinki and Uusimaa Hospital District Coordinating Ethics Committee (HUS/648/2017, 8/8/2017). No identification data were collected at any stage of the study, and a data processing diary was kept, following all the requirements of the regulation 2016/679 (General Data Protection Regulation) of the European Union. The study was supervised by a Medical Doctor, two PhD students (of which one was a physical therapist with expertise in rehabilitation of PwMS) and a PhD candidate with expertise in shiatsu and multiple sclerosis.

The study was a mixed-methods six periods single-subject crossover experiment (n-of-1 clinical trial), using a minimally optimal [50] counterbalanced design within a WSR case study. Theoretical estimation of the number and length of crossovers, as well as the number of data collection points, that could permit a statistically or visually meaningful quantitative analysis were not performed, since the NCA Research Ethics Committee required the absolute minimal approach that was used. The clinical part took place between 11/2017 and 01/2018.

The practitioner-researcher was fully qualified shiatsu practitioner, having completed three years shiatsu and OM training, one-year postgraduate shiatsu diploma and continuous nursing education for MS care. He had seven years of clinical practice, of which the last five focused on PwMS.

An invitation shared to former practitioner’s patients, to inform possible participants from the PwMS belonging to their social circles. The first responder screened and satisfied the eligibility criteria (Table 1).

An information sheet and consent form were provided electronically, while a face-to-face meeting arranged between the patient and the researcher-practitioner. During this initial meeting all participant’s concerns discussed, the consent form signed and the scheduling of the trial agreed to take place in six periods of paired two-week blocks of standard care (A) followed by intervention plus standard care (B) (AB BA AB) (Fig. 1). The period (A) includes whatever care the patient normally receives (see §3.1. for a detailed description). In the period (B), two weekly shiatsu sessions were added.

Details required to form the natural history of the patient’s MS and to provide a clinically useful initial picture collected with the intake notes. Also, inquiries were made into the patient’s expectations from the trial, and the initial questionnaire (see below) was completed.

The short version of the Multiple Sclerosis Quality of Life Inventory (MSQLI) [51] was the HRQoL questionnaire, chosen due to its coverage of multiple domains in a way that could be possible to complete in a reasonable amount of time. The MSQLI is a validated measure [52] consisted of 10 questionnaires with multiple scales that the patient can complete without help from the researcher. Each of the included scales and the included averages gets a separate score, following a process described in its manual [51]. In order to accommodate the biweekly blocks, it was modified to be completed every two (instead of four) weeks: with the intake notes and at the end of each period, seven times in total.

A semi-structured interview with the patient was made at the end of the trial to explore the experience of the treatment, the influence of the trial in the patient’s life, and possible adverse events. The interview was recorded after obtaining the participant’s consent, with verbatim transcription and thematic analysis to follow. The transcript was checked

Table 1
Eligibility / Exclusion Criteria.

Eligibility Criteria	Exclusion Criteria
SPMS patient	Suffering from chronic or excessive fatigue
Between 35 and 65 years old	Receiving shiatsu, acupuncture or another form of OM during the last six months
Leaving in the central Uusimaa area	Inability to complete short questionnaires without assistance
Speaking good English	
Agrees to the study protocol	

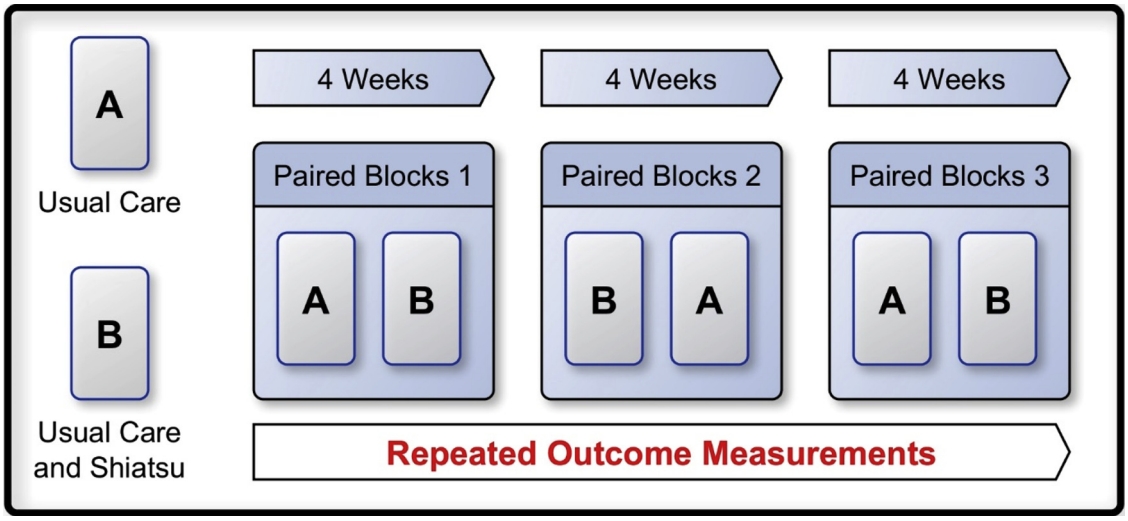

Fig. 1. N-of-1 trial design.

for accuracy by the participant.

The case records were kept by the practitioner and includes reporting of adverse events as inquired into the patient after each session.

2.1. Analysis

A descriptive case study analytic strategy was used to outline the case. It began with a familiarisation phase covering all types of collected data. Then the clinical case was described, followed by a quantitative analysis of the questionnaires, and the interview's thematic analysis.

Due to ethical concerns related to the possible burden to a patient that is considered vulnerable, limited data collection points were included. Having only three pairs of data, the statistical tests used for the analysis of n-of-1 trials [53–55] were not applicable. Even the Wilcoxon Signed-rank test [56,57] that could be considered theoretically appropriate, has no power with less than 5 pairs of data [58,59], since with just simple enumerations is possible to calculate the exact frequencies of the sum of the ranks, that provides a picture of the exact distribution of the Wilcoxon Signed-rank statistic [60]. Thus no statistical test could answer a hypothesis for the study. The scores are presented tabular and visually, as suggested by the CONSORT-CENT extension for reporting N-of-1 trials [61]. For easier processing and interpretation, data values were transformed in a directional scale 0–100 using the POMP formula [62,63]. A table compares the baseline with end scores. All calculations were made using the LibreOffice 6.0.2.

The thematic analysis follows the six-step Braun and Clarke [64] approach flexibly. Due to the single, short interview included in the thematic analysis, steps 3 (themes searching) and 4 (themes reviewing) were compacted in one, while step 6 (writing up) was completed in the synthesis of the findings.

3. Results

3.1. Description of the clinical case and usual care

The participant was a 57 years old woman with SPMS. Her first symptoms appeared when she was 20, but remained undiagnosed until age 32. Six years after diagnosis, she reached a stage where she could walk alone for a kilometre (EDSS 3.5–4) while four years later, at 42, she was already in the SPMS stage. One year later, she had to use a wheelchair for most of her movements, and at age 47, she was essentially restricted to a wheelchair (EDSS 7.5). At that time, her perimenopause began and continued for about four years. At age 49, the MS-related medication (Interferon-beta (IFN-β)) was interrupted, and a year later, she had Chronic Cerebrospinal Venous Insufficiency approach surgery, which helps with her fatigue but no other symptoms.

At the time of recruitment in the trial, she was restricted to a wheelchair, and retains many self-care functions with effective use of arms, needing help to move from bed to wheelchair (EDSS 8). Following an OM-based MS staging approach [65], she was at the last, fourth stage where deficiency dominates with tiredness, urinary issues, and considerably stiff and spastic muscles. Due to her restriction to a wheelchair, she does not move a lot and experiences back and buttocks pain, stiffness and spasticity in her legs and her right hand. There is no nerve pain and does not need painkillers. She uses daily spasticity medication (Baclofen & Phenobarb-Hyoscy-Atropine-Scop). Neurogenic bladder symptoms with chronic repeated inflammation controlled with daily antibiotic medication (Nitrofurantoin-Ascorbic Acid). She suffers from chronic constipation and sleep problems; frequently waking at night. In the early morning, she wakes up with a sense that everything feels bad without knowing why. She has a balance problem, heat makes her worse, and often she finds it difficult to express herself in words. Receiving disability pension since age 46, today she feels her retirement is a gift. In her diet, she avoids meat products.

After the interruption of the MS medication, she had neurologist appointments every three years and 95 physiotherapy sessions per year (25 in a pool and 70 in health care centre physiotherapist). She enjoys most the pool and feels satisfied with the amount of care she receives.

Inquiring about her expectations from the trial, she expresses disbelief in any possible benefit from shiatsu. Questioned about which symptom she would like to be primarily addressed, she chooses spasticity.

3.2. Shiatsu treatments

Treatments offered in the participant's house to a schedule agreed weekly. Due to her mobility difficulties, she suggested having the sessions in a hard bed, which was at the right height for her to move from and to the wheelchair with the practitioner's help. Family members were present in the same big, open room but not focused on the treatments. All 12 treatments included in the trial's plan completed successfully. Sessions varied between 60 – 90 min, according to the practitioner's judgment. In the beginning of each treatment after the first, and at the interview, the participant was asked for her feelings, possible adverse events, or effects from the previous treatment. A therapeutic relationship established without strong rapport. Communication remained mostly focused on health. The treatment was

Table 2
MSQLI scores in 0–100 scale.

	Initial	A 1 st Block	B 2nd Block	B 3rd Block	A 4th Block	A 5th Block	B 6th Block
Health Transition Item* (1-5 scale)	3	3	3	2	3	3	3
Physical Functioning Scale (PF)	5	5	5	10	5	5	5
Role-Physical Scale (RP)	0	0	0	50	50	50	75
Bodily Pain Scale (BP)	84	84	72	74	84	84	84
General Health Scale (GH)	35	35	25	25	30	30	35
Vitality Scale (VT)	30	30	30	30	30	20	30
Social Functioning Scale (SF)	50	50	50	50	50	50	50
Role-Emotional Scale (RE)	100	100	100	100	100	100	100
Mental Health Scale (MH)	84	84	88	92	92	96	92
Physical Components Summary Scale (PCS)	**20.852**	**20.852**	**17.508**	**23.409**	**24.449**	**23.821**	**27.665**
Mental Component Summary Scale (MCS)	**58.28**	**58.28**	**59.933**	**58.603**	**58.653**	**58.604**	**57.702**
Modified Fatigue Impact Scale - 5 Item Version (MFIS-5)	30	30	75	85	75	65	80
MOS Pain Effects Scale (PES)	91.67	91.67	91.67	95.83	87.5	95.83	95.83
Sexual Satisfaction Scale (SSS)	60	60	55	50	55	55	60
Bladder Control Scale (BLCS)	95.45	95.45	100	100	95.45	100	95.45
Bowel Control Scale (BWCS)	65.38	65.38	88.46	100	92.31	84.62	92.31
Impact of Visual Impairment Scale (IVIS)	100	100	100	100	100	100	100
Perceived Deficits Questionnaire - 5 Item Version (PDQ-5)	70	70	75	85	95	95	95
Mental Health Inventory - 5 Item Version (MHI-5)	84	84	88	92	92	96	92
MOS Modified Social Support Survey - 5 Item Version (MSSS-5)	80	80	70	70	70	75	70

focused on the primary complaint (spasticity) and to issues raised before each session. A general OM-based understanding of the participant's condition informed the principles of treatment. The method of treatment specified by incorporating body palpation during each session. Description of the sessions, as documented in the case notes, are available in Appendix A.

3.3. Questionnaire scores

MSQLI scores (transformed when needed in 0–100 scale with 0 = worst, 100 = best possible score) are presented in Table 2, showing that the initial period established a stable baseline of two weeks, while Social Functioning Scale (SF), Role-Emotional Scale (RE) and Impact of Visual Impairment Scale (IVIS) remained stable during the trial. Changing scores during the time are visually presented in Fig. 2. Table 3 summarises scores comparison between baseline and the end of the trial.

3.4. Thematic analysis of the interview

The verbatim transcript of the interview is available in Appendix B. Since the interview aimed to explore the experience of the treatment, the influence of the trial in the patient's life and possible adverse events, a theoretical approach was taken, coding relevant data [66]. Table 4 shows the themes that occurred with corresponding codes and frequency of occurrence.

The definitions of the occurred themes (5th step) follow, omitting direct quotes due to space limitations:

- Treatment effects: The participant focuses a lot and continuously return to the effect of the treatment in her life, including relief from spasticity, constipation, local pains, improvement in sleep and function of her right hand, relaxation.
- Practical aspects of the trial: The participant considered the trial easy to follow, despite its length and intensity, with contributing aspects the lack of need to remove her clothes and the fact that the practitioner visited at her home. Contrarily, she expresses her dislike for the periods without shiatsu.
- Comparison with usual care: The participant thinks that shiatsu complements her usual care nicely by taking care of aspects not addressed during this care. She is satisfied with the amount of the usual care, believing that it is focused on muscle strengthening because she needs it. Inquired about the possibility of covering more aspects during her usual care, she considers it possible and sometimes, if she asks for, she receives massage.
- Adverse events: Inquired about adverse events, she reported none and continued by mentioning positive effects. Considering legs spasticity, she thinks that sometimes it was relieved too much, causing difficulties in standing up.
- Expectations: Confirming her claim at the initial meeting, said she did not expect anything and felt impressed by some effects that occurred. She would recommend shiatsu as a complement to PwMS's usual care.

3.5. Synthesis of results

The results of the study are to be considered based on triangulation of all types of the collected data (raw scores, visual presentation, baseline-end comparison, case notes, interview).

3.5.1. Spasticity

The primary symptom the patient wanted to address at the beginning of the trial was spasticity, besides daily medication usage for it. Spasticity was also the major complain during the first three sessions (period B1) and the three sessions after the four weeks without shiatsu (period B3). MSQLI does not include spasticity domain, an issue identified and commented on by the participant twice during B2 period, after spasticity ceased to be the primary complaint, and the first MSQLI for a period with shiatsu completed. Spasticity relief was a treatment effect the patient mentions as very positive during the interview. She considers it one of the temporary benefits that a PwMS could have from shiatsu, attributing to this the sleep improvement she experienced. However, spasticity relief is also considered to cause difficulties in changing from one place to another, since she had been used to have very spastic legs that could statically support her weight.

3.5.2. Bowel function, bladder control

Relief from constipation was the second important aspect mentioned in the interview regarding treatment effects and as a reason to recommend shiatsu in PwMS. Case notes indicate that after the 2nd session (B1 period) she reported relief from chronic constipation, something confirmed again by her comments during fourth and eighth sessions. Bowel Control Scale indicates improvement during shiatsu periods. Looking at the scores over time we see an improvement of

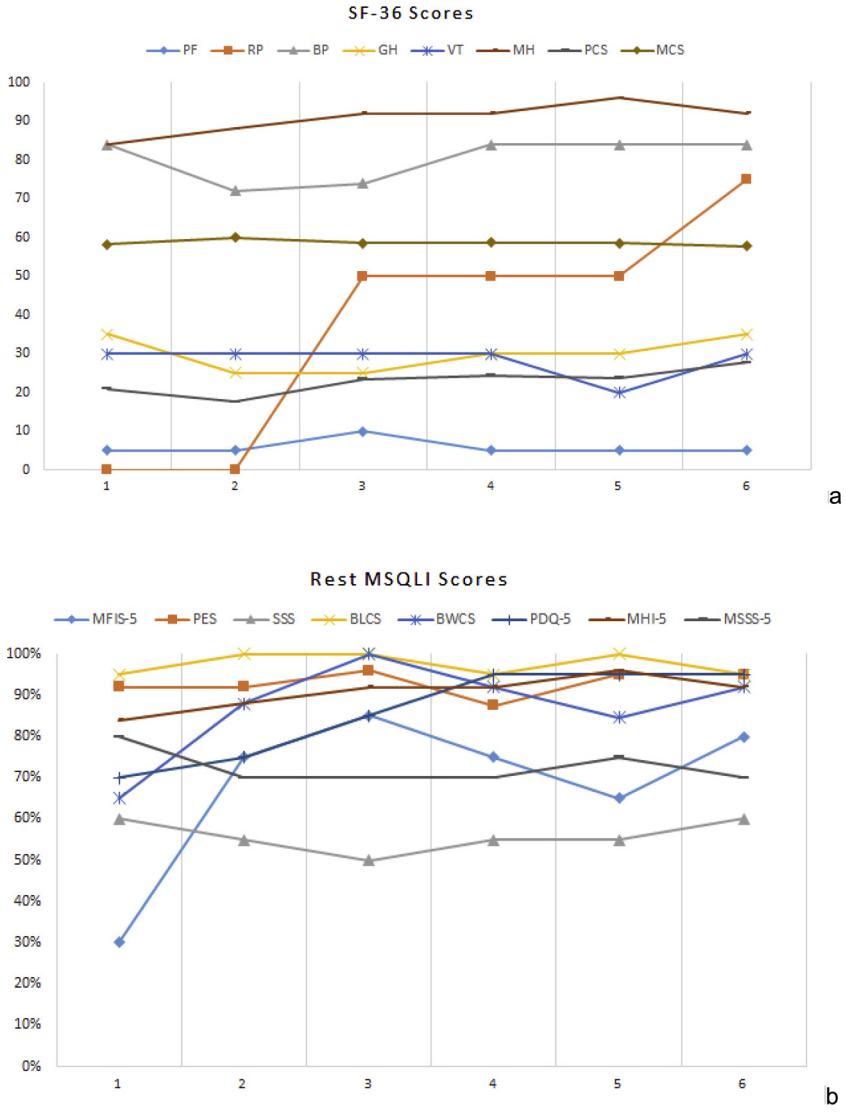

Fig. 2. a) SF-36 scores, b) Rest of MSQLI scores.

more than 23 % during B1 period, which continued improving during B2 period reaching the best possible score. During the A2 and A3 periods, there was a decline with a rhythm of about 8 % for each period. The improvement recovers about 8 % during the last B3 period.

Bladder Control Scale scores suggest slight improvement during the first two shiatsu periods, yet those were always inside the best 5 % of the possible scores. Besides, being on long-term daily medication for bladder issues that seems to work effectively, the chances for real effect of shiatsu in her case could safely be neglected.

3.5.3. *Sleep and relaxation*

During the interview, the participant inquired about essential domains for her life that were addressed by the trial. Improvement of sleep was a major one, attributed by her mostly to spasticity improvement and lower back pain improvements. Case notes indicate that during the treatments, the participant falls asleep at least four times. The

Table 3
Pre-Post Comparison of all domains.

	Worst	Stable	Better
SF-36	Mental Components Summary Scale (MCS)	Health Transition Item Physical Functioning Scale (PF) Bodily Pain Index (BP) General Health Scale (GH) Vitality Scale (VT) Social Functioning Scale (SF) Role-Emotional Scale (RE)	Role-physical Scale (RP) Mental Health Scale (MH) Physical Components Summary Scale (PCS)
Rest	MOS Modified Social Support Survey - 5 Item Version (MSSS-5)	Sexual Satisfaction Scale (SSS) Bladder Control Scale (BLCS) Impact of Visual Impairment Scale (IVIS)	Modified Fatigue Impact Scale - 5 Item Version (MFIS-5) MOS Pain Effects Scale (PES) Bowel Control Scale (BWCS) Perceived Deficits Questionnaire - 5 Item Version (PDQ-5) Mental Health Inventory - 5 Item Version (MHI-5)

Table 4
Themes and Codes.

THEMES				
Effects of the treatment	Practical aspects of trial	Comparison with usual care	Adverse events	Expectations
CODES				
Spasticity (8)	Regularity (3)	Usual care (6)	Spasticity (8)	Temporality (2)
Constipation (5)	Following trial (2)	Physical treatment (2)	Adverse event (2)	Expectations (2)
Sleep (5)	Treatment breaks (2)	Muscular work (2)	More carefully (1)	Recommendation (1)
Relaxing (4)	Cloths (1)	More carefully (1)		
Pains (3)	Home-visit (1)			
Lower-back (2)				
Right-hand (1)				
Legs (1)				

participant connects this with the relaxation she experiences from shiatsu, something differing from her usual care.

3.5.4. Fatigue

Fatigue was not mentioned during the trial or in the interview. However, two of the MSQLI scales showing improvement are fatigue-related. Modified Fatigue Impact Scale assesses the effects of fatigue on physical, cognitive, and psychosocial functioning [51]. By looking at the scores during the time, we see a sharp improvement during B1 period that continues rising during B2 period (from 30 % to 85 %). During the usual care periods A2 and A3 there is some worsening stopping at 65 %, to recover again at 80 % at the end of the last B3 period. Vitality Scale intending to measure energy levels and fatigue [67], suggest a mostly stable situation. Only during the A3 period there was a slight worsening that recovers in the previous value during the last B3 period.

3.5.5. Pain

During the intake, the pain was not indicated as a significant issue, and no pain medication was used. Case records indicate that in the first session, some pain in the sacrum was a major complaint together with spasticity. During the three first treatments (B1 period), some pains occurred during the treatment, on the legs, and in the neck area. During the fourth session (last of the B1 period) those pains had already stopped appearing. Some pain in specific points was indicated again during the seventh and eighth sessions (B2 period). However, the pain was not mentioned in any of the post-treatment adverse effects inquires.

Bodily Pain Scale shows an interesting paradox. From the scores of each period and their visual presentation, we see that the periods with shiatsu did worst. That is due to a decrease in the score during the B1 and B2 periods which return to the original levels afterwards, remaining until the end of the trial. On the contrary, the participant in her interview indicates that the treatment offer relief from local pains, and this was a reason to recommend shiatsu to a PwMS. MOS Pain Effects Scale assess the degree to which pains affect mood, ambulation, sleep, work, recreation, and enjoyment [51]. The scores from the beginning are very close to the best possible. There is a slight improvement during B2 period followed by worsening and improvement during the A2 and A3 period, to remain in the improved level during the last B3 period. It worth to mention that the Bodily Pain Scale follows a different time-trend, implying the idea that the pain caught in it does not correlate with effects assessed by MOS Pain Effects Scale.

3.5.6. Mental and cognitive issues

During the intake, the participant mention waking up with an unexplained bad feeling as well as that she finds it difficult to express herself with words. Role Emotional Scale (mostly relevant to psychiatric conditions [67]) gets the highest possible score during the whole study. Mental Components Summary Scale, offering standardized distribution-based interpretations gained from US population with mean set to 50 and standard deviation 10 [51,68] where scores above 50 indicate better health than the mean of the general population and below 50 indicate worst health [68], seems to have remained almost stable during the trial (57.7–59.9). Mental Health Scale (as well as Mental Health Inventory which is derived from it) which covers four mental health dimensions (anxiety, depression, loss of control, and psychological well-being) [67] suggest complex interactions. During B1 and B2 periods, there is a slight improvement that remains stable for A2 period, increasing slightly during A3 period, to return to the B2 level at the last B3 period. Slight improvement appears comparing before-after trial scores. In Perceived Deficits Questionnaire, covering cognitive aspects (attention, retrospective and prospective memory, planning, and organisation) [51], during B1 and B2 periods, there is an improvement that continues during A2 period and remains stable till trial's end. In the interview, an overall enthusiasm for the treatments was expressed, while at the last 12th session worries regarding the trial's end were expressed. Finally, the Sexual Satisfaction Scale, addressing the degree of satisfaction with aspects of sexual life both for the patient and her partner [51], suggests stability, with no other indications for this domain in other data sources.

3.5.7. Functioning and roles

Initially, the participant said that she felt her retirement was a gift. The Social Functioning Scale, indicates whether the social activities of the patients have been affected by their health problems [67], remained unaffected during the trial. On the contrary, Role-Physical Scale, referring to role limitations (problems with daily activities) due to physical health [67], showed sharp improvement during the 3rd block. From the worst possible score during baseline and period B1, rises to the middle of the scale after period B2 and remains stable for the four weeks without treatment to rise again in the three-quarters of the scale after the new introduction of shiatsu (B3 period).

Physical Functioning Scale assesses levels and kinds of physical limitations (lifting and carrying groceries, climbing stairs, bending, kneeling, and walking moderate distances as well as self-care activities). Considering most physical limitations as chronic, estimates the severity of each limitation without considering its duration [67]. The score remained at a very low level. Minimum fluctuation occurs during the B2 period, that subsides to the original level in the A2 period and does not recover.

3.5.8. Social support

Initially, the participant expressed satisfaction with the amount of care she regularly receives, even if in the interview, she indicates that with shiatsu areas not usually addressed in her usual care were covered. MOS Modified Social Support Survey, relevant to emotional, informational, tangible and affectional support as well as with positive social interaction [51], suggests some worsening during period B1 that tends to remain until the end of the trial.

3.5.9. General health and expectations

Initially, the participant's general health situation was described as very compromised, while she expressed her disbelief that the treatments could help her. The interview indicates that her expectations

changed after the end of the trial. She now expected to get temporary improvements by shiatsu, and she believed that shiatsu complemented her usual care nicely by addressing otherwise ignored aspects. The areas discussed above shows that indeed there were improvements in some domains of HRQoL. Health Transition Item, aiming to get information regarding changes in health status during the year before the administration of the questionnaire [67], remained mostly stable. General Health Scale, evaluating with self-perceived questions the current health situation, resistance to illness and health outlook [67], shows slight worsening during B1 and B2 periods, which take a positive direction during A2 and A3 periods, to recover to its original score after B3 period. Physical Components Summary Scale (similar to the Mental one described earlier) shows slight worsening during B1 period to get slightly better during B2 period. Then remained almost stable for the two usual care periods (A2-A3) and slightly improved during the last B3 period. Impact of Visual Impairment Scale, related to difficulties with simple visual recognition tasks that cannot be corrected by visual aids [51], remained stable during the trial, getting the best possible score.

3.5.10. Summary of the results

Summarising, the results of the study indicate possible improvement in some domains, including spasticity, bowel function, fatigue, pain, sleep, and relaxation. Similarly, there was an improvement in her expectations by the treatment. The domains that are related to mental and cognitive issues, functioning and roles, social support, the impact of visual impairment, bladder control as well as the general health remained unaffected or showed a more complex picture (discussed in §4.1.).

3.6. Adverse events

The participant was asked about possible adverse events in every session. No adverse events were reported. In the interview, she indicated that shiatsu was more careful in addressing some of her issues (local pains). Speaking of spasticity, she indicates the problem that occurred by improving it (difficulty in standing up from chair to bed or toilet). When asked if she identified this as an adverse event, she showed some confusion and declared no further adverse events.

4. Discussion

4.1. On the clinical results

Minimal Clinically Important Difference (MCID) is defined as “the smallest difference in score in the domain of interest which patients perceive as beneficial and which would mandate, in the absence of troublesome side effects and excessive cost, a change in the patient’s management” [69]. Summarising, the findings suggest that the specific PwMS may have experience MCID in some HRQoL domains and symptomatology (spasticity, bowel function, fatigue, pain, sleep, and relaxation).

Spasticity is a prevalent symptom that PwMS need to manage [70]. It influences their HRQoL [71] and daily activities [72] negatively. It can have an impact on many areas, including fatigue, depression, anxiety, pain, bladder function [73], bowel function, and sleep [74]. Spasticity in MS cause substantial costs both regarding HRQoL and economically [75,76] but is usually undertreated, since its pharmacological management is not very efficient [77]. There are non-pharmacological options for its management, with acupuncture and other CAM playing a possibly positive role, besides the lack of adequate evidence [78]. In this case, spasticity could be considered undertreated, despite the use of pharmacological agents and physical therapy.

Additionally, the treatment influence fatigue, sleep problems, bowel function, and possible mental issues suggested by the literature to be impacted by spasticity. The participant herself attribute sleep improvement in the relief from leg spasticity. However, a paradox accompanied the improvement. Even if spasticity was the primary complain, the observed improvement seems to cause ambulation-related difficulties. The participant used to have very spastic legs that could statically support her weight during movement from wheelchair to bed or the toilet seat. The improvement of her leg muscles seems to be the priority during her usual physical therapy so that she has the possibility to stand-up. Leg spasticity is associated with impaired ambulation [79], and the participant is mainly restricted to a wheelchair. Thus possible future treatment for her spasticity should comprehensively consider the sustainability of her basic ambulation.

The participant, during her interview, commented on sleep improvement, attributing it mostly in spasticity and lower back pain improvement. Sleep disturbances in MS remain mostly undiagnosed [80] even if they affect approximately 60 % of the PwMS [81] and can leave their marks in the routine MS neuroimaging [82]. Sleep problems are associated with fatigue in PwMS [83–85] and the general population [85], while diagnosed sleep disorder may be associated with reduced HRQoL in PwMS [86]. Treatment’s effect on sleep supports previous evidence of a possible effect of shiatsu in sleep disturbances [87–89].

Even if the pain was not a major complain and the participant considered shiatsu offering local pains relief so that she would recommend it to PwMS, questionnaires score and case notes show a complex picture. In Bodily Pain Scale, scores show slight worsening during shiatsu periods. Case notes indicate that temporary pains occurred during treatment, but those were not mentioned in post-treatment adverse effects inquires. MOS Pain Effects Scale suggests that pain captured from the Bodily Pain Scale did not lead to effects in the domains it assesses. Considering all sources of data, it is suggested that the temporary pain occurrences during treatment as well as the temporary worsening in Bodily Pain Scale were a form of theory and experientially consistent “transitional effect”, according to the typology of negative responses for shiatsu [36].

After the beginning of shiatsu treatments, participant’s perceptions regarding her health and social support began to show signs of worsening. That is documented with slight worsening in scores of General Health Scale and MOS Modified Social Support Survey. Perceptions of health status and HRQoL of PwMS have been found to differ significantly between the PwMS themselves and those of their neurologists [90,91]. Physical activity correlates with a better health status perception [92] while levels of social support, which includes supportive input received from the social environment and can include almost any type of social interaction [93], are positively associated with perceived health status in PwMS [94]. Considering the interview, where the participant commented that shiatsu complements her usual care nicely by addressing usually ignored aspects, it is possible to speculate that the worsening documented in the relevant scales are related to realisations occurred due to shiatsu effects. That could be attributed to the comparison with usual care together with the expressed worries about not being able to continue the treatment after trial’s end. Those are elements that might have downgraded her perception about her general health condition and the support she usually receives.

4.2. Methodological issues

The present study could take the role of a methodological pilot for the application of n-of-1 trials designs in areas that traditionally are not considered appropriate for them, manual therapies and bodywork. A detailed consideration of the study under that perspective is attempted in a separate paper that is currently in the writing stage, yet crucial issues that are related to the quality of the study and its clinical relevance are discussed below.

4.2.1. Statistical analysis?

Due to ethical concerns, the number of data collection points were minimised, making impossible any meaningful statistical analysis. Most of the published reports of n-of-1 trials use only visual comparisons, and

of those reporting statistical analysis most use simple statistical tests such as *t*-test [95]. When at least three data points per period are included, visual inspection of data for changes of level (the average performance of a period), trend (direction of change during a period), and variability (scale of change during a period) is straightforward for substantial and fast changes [96]. While visual inspections alone can provide evidence of large effects [97], without enough data collection points, a useful visual analysis is not feasible. More complex statistical approaches are required, with more treatment periods necessary to minimise type I and II errors [98]. Overall, the more observations, the better. Usage of daily diaries might help too. It is reminded that any statistical inferences of this study could refer only to what occurred during the specific trial with the specific PwMS. It is not possible to gain any valid inferences for other persons and situations. This is the limit even when the most appropriate statistical analysis for single-subject trials is used. Nevertheless, the purpose of applied research should be to discover inferences with clinical meaning, not just statistical significance [97]. Any generalisation could come only in a clinical context, relying on the common scientific rationale that "similar" outcomes should occur in "similar" situations in the future [99].

4.2.2. Carry-over effects and the "half-life" of shiatsu. How much is enough?

The issue of the carry-over effects is discussed in the single-subject design literature [100]. Carry-over effects could potentially distort the results of the periods following the initial treatment [101], a problem usually solved in pharmacological studies by including a wash-out period [102]. Statistical tests had been proposed to check for pharmacological carry-over effects even if it had been argued that there is no benefit by using them [100,103]. For non-pharmacological treatments, where the concepts of pharmacokinetics and pharmacodynamics are not applicable, the solution of including wash-out periods is not feasible [104]. Carry-over effects are difficult to detect and the results difficult to interpret unless the researcher is confident about their amplitude due to previous knowledge [105]. A way to address possible lack of previous knowledge could be to use ideas proposed in different contexts. In the study of pharmacodynamics, "Physiological Effect Models" are applied when the effect of a drug in the organism is unknown quantitatively, using the physiological results of its effect instead to measure its effect [106]. Additionally, "looking at the data" could be a valuable way to address the issue, as long as this is supported by rich description and transparent, open availability of the data for each period [107], while using the baseline data from the period before the treatment could partially remedy the situation [108].

In this study, a minimal approach was taken with six biweekly periods of twelve treatments in total. While some change in the HRQoL was documented, the potential of the methodology to address the carry-over issue and clarify the "half-life" or "wash-out" period of shiatsu could be further exploited in a more protracted trial. Only some of the MSQLI-assessed domains provides interesting clues towards this aim. The Role-Physical scale suggests that two consecutive treatment periods (four weeks) were necessary to document improvement that persists for two control periods (four weeks) and continue improving during the last treatment period (two weeks). Similar trends show the results of the Bowel Control and the Modified Fatigue Impact scales, with improvement occurring after a treatment period (two weeks) to maximise after the second consecutive treatment period (four weeks). Then a partial reversal of the improvement occurs during the following two control periods (four weeks) to improve again after the re-introduction of the last treatment period (two weeks).

Also, the improvement in spasticity suggests that one period of treatment (two weeks) was enough to bring some improvement that subsides during the two control periods (four weeks) and improve again after a treatment period (two weeks).

Summarising, it can be suggested that four weeks of shiatsu treatment (eight treatments) are enough to provide evidence of effect in some domains. However, four weeks of wash-out period are not enough to show a full reversal of the effect. In addition, when the partial reversal occurs, the re-occurrence of improvement demands shorter treatment periods. Unfortunately, the lack of statistical analysis does not permit more specific suggestions about the "half-life" of shiatsu.

It should also be noted that in this study, for logistic reasons, there was no follow-up period. Informal contact of the author with the participant four months after the conclusion of the trial reveals that the effect had already reversed during that time. The suggestion someone could get from this is in agreement with existing guidelines on the field of Chinese and integrative medicine regarding the usefulness of sufficient follow-up time [109].

Shiatsu in Europe is usually offered in weekly sessions, either for short periods of a few treatments or as a long-term treatment that can continue for months or years. Similar to concerns expressed about physical therapy [110], it is not known what type of treatment and for how long it should be offered to optimise the results. To the knowledge of the practitioner, the amount of physical therapy offered to PwMS in Finland depends on the disability level and the needs of each patient. This can vary during the years and according to the results, with weekly or biweekly physical therapy sessions available. In a recent RCT pilot study for shiatsu as adjuvant therapy for depression in patients with Alzheimer's disease [111], shiatsu was offered once per week for ten consecutive months. In the Chinese context, bodywork modalities such as tuina are often offered daily, similarly to acupuncture [112,113]. While such treatment schedules might seem strange in Europe, the author of the study has positive clinical experience in offering daily shiatsu treatment for periods of two months with PwMS. Such an intensive mode of treatment, even for a shorter period, have been used earlier in the research context of acupuncture n-of-1 trials [114]. Regarding shiatsu and considering the chronic nature of MS, an intensive and long-term treatment perspective seems more appropriate.

4.2.3. What and how to measure

As indicated earlier, the MSQLI even if widely used in HRQoL research for PwMS and covering a broad spectrum of HRQoL areas, it did not cover essential domains for the specific patient. This issue is an integral part of the concept of outcome and HRQoL measures as used in individualised trials of complex treatments, since the underpinnings of outcomes are usually population-based and appropriate for pharmaceutical trials but not so for complex interventions [115,116]. This study strongly supports the need for richer methods to measure the effect of the treatment. Without various data sources, the interpretations of the MSQLI would be challenging, and important aspects could be lost. The mixing of data was able to provide some conclusions, yet it is not known how much stronger these could be if the design were able to accommodate powerful statistical analysis and a more relevant questionnaire. More qualitative and patient-specific measures, such as the interview-based SEIQoL [117] or the MYMOP [118], could be used to offer more relevant and potentially more robust conclusions.

4.2.4. The practitioner as a researcher

Issues related to the role of the practitioner as a researcher has previously concerned researchers. The position of the researcher is unavoidably influencing the research from its conception [119] and can affect the honesty of the participant's interview responses [120]. Including external interviewer would not remedy the situation since the participant would know that the practitioner-researcher will analyse the data; thus, favourable feedback would be more expected [120]. This dual-role probably means that the researcher has a positive attitude for the tested modality, too [120].

Yet it should be noted that this applies to all kind of health practitioners and is not necessarily something negative since this "belief system" of health professions are integral to the clinical practice [121]. Even more, it has been suggested that engaging practitioners in CAM research is essential to improve the validity and ensure that the

therapies are evaluated as they are used in practice [122]. To that aim, the inclusion of Evidence Based Medicine and critical research reading courses in the curriculum of CAM schools is encouraged [123] so that practitioners are better prepared to participate in research projects.

Since the practitioner of the study is also the researcher, the following measures were taken in order to help establish the credibility of the study:

a) Synthesis of data collected from various sources.
b) Supervision (see §2) and peer debriefing.
c) The interview transcript was checked for accuracy by the patient.

Besides, this study highlights a possible drawback of that approach, in terms of the WSR approach. Due to the dual practitioner-researcher role, the methods applied in practice were restricted, even if the study protocol poses no practice restrictions. While the literature indicates that lifestyle consultation and nutritional advice could be parts of shiatsu practice [32,124] the practitioner-researcher still sought to avoid them during the study. Similarly, usage of other OM modalities like cupping was avoided, even if they are often integrated into a shiatsu session [125]. This might be due to the engagement with the designing of the study, that made the practitioner more aware of possible methodological issues, such as that since lifestyle changes are not easy to "switch off", treatments that include lifestyle changes are usually ruled out from candidates of n-of-1 trials evaluation [126].

4.2.5. Shiatsu in the specific context

In the context of the trial, the treatment offered was very close to the real-life practice of the specific practitioner, besides the issues highlighted above. Yet this does not mean that the shiatsu practised by the specific practitioner is representative of shiatsu in general [127].

A general feature of the shiatsu offered in the study that deviates from the norm in Europe is the fact that it was offered in a bed. While originally shiatsu was offered on a futon on the floor, modern Japanese practitioners found more comfortable and safe for the practitioner to work in a massage table or bed [128]. This way of work has also been introduced in the US [129], but it has not flourished in Europe. To work on a bed was proposed by the participant due to her movement difficulties. This is a promising way to work for patients with disabilities, restricted to a bed or wheelchair.

Moreover, working at a table, bed or chair could make shiatsu more easily to offer in a hospital or healthcare-centre setting, as a recent service evaluation of a cancer centre where shiatsu as well a range of CAM were available shows [130]. Even if many practitioners might not have training and experience of working on a table, it should be their responsibility to adjust their practice in a way possible to accommodate the needs of the receiver. Shiatsu schools from their side should offer training to promote safe and effective ways to adjust a shiatsu session for table, bed or chair.

Despite recent efforts by the practitioners association, Shiatsu in Finland is not yet well-developed professionally [37] and is neither recognised as part of healthcare or as a healthcare profession nor covered by health or patient insurance. Even if the study shows possible MCID, currently there is no way shiatsu could be integrated into the care and management plan of the participant. No social structure could support her in receiving shiatsu, and thus there were no practitioners that the researcher could suggest to her. It should be considered that all costs of the trial were covered out-of-pocket by the practitioner-researcher who volunteered the shiatsu treatments and all costs related to the study. This is very concerning since the participant herself expresses her dislike of the periods that she did not receive shiatsu, and she was concerned about how she could continue after the end of the trial. It should be noted that the yearly cost of severe MS in Finland reaches 110.000 euros per PwMS, a cost that is "essentially due to the high requirement of professional services and informal care in the advanced disease stage" [131]. Moreover, most patients would welcome a personalised trial if it can limit their out-of-pocket costs [132].

4.3. Implications for practice, training and policy

The results of this study are not generalizable but refer to the specific participant in the specific setting. Some indicative implications exist both for practice, training and policy. For shiatsu in practice, it can be suggested that a denser treatment schedule, compared to the commonly used once-weekly treatment, might be more effective in chronic and severe conditions. The practitioners should be ready to adjust their treatment in various settings and work in bed, table or chair. Shiatsu schools should prepare future practitioners for work as healthcare providers in various setting and assist current practitioners to this adjustment. Also, EBM and research skills courses should be included in their curriculums. Professional shiatsu associations should ensure that it is possible for patients to reach professionally competent practitioners. The policy-makers should consider how shiatsu as a method that is not currently considered healthcare could be integrated into the healthcare and management plan of severely diseased chronic patients when it has been found to be helpful.

4.4. Limitations of the study

The study has some limitations that are integral to the nature of the examined modality and the research design. The bodywork nature of shiatsu does not allow the application of randomisation and blinding [133]. Yet, the n-of-1 trial crossover design bypasses at least the concerns of selection bias that the lack of randomisation cause, since the same person is at the same time the control of the trial. The design could control better for the therapeutic relationship effect by including meetings without treatment during the usual care periods. This is an issue that needs further investigation, since it would change the nature of the control period from usual care to therapeutic relationship.

Please note, since the study is a single subject trial, the results refer only to what occurred during the specific trial with the specific PwMS and it is not possible to infer relevance for other persons and situations. The study includes very few data collection points, making statistical analysis impossible. The length of the periods was not long enough to permit a full appreciation of the speed of effect and wash-out of shiatsu. No follow-up evaluation was included. The questionnaire was not personalised enough, missing essential domains for the participant. The dual researcher-practitioner role downgraded the WSR approach and inserted potential bias in the interview. The interview and the clinical interaction between the participant and the practitioner-researcher were not optimal since they communicated mostly in English, which is a second language for both of them.

4.5. Suggestions for future studies

A research program consisting of multiple studies following the fundamental design principles and methodological concerns of this study is suggested to evaluate the effect of shiatsu as a personalised treatment for PwMS. More flexible and rich design is needed with the amount of data collection points per period calculated in order to permit a useful visual and robust statistical analysis. A cost-effectiveness aspect would be useful to be included in such a research program.

5. Conclusion

To the knowledge of the author, this is the first study to investigate if shiatsu affects the HRQoL of a person with SPMS, by implementing a mixed methods n-of-1 trial within a WSR case study. The study succeeds to show that in the specific setting with the specific severely diseased patient who already receives physical therapy according to her needs, shiatsu was able to improve the HRQoL of a person with SPMS influencing spasticity, bowel function, sleep and relaxation, fatigue and

pain. Shiatsu was a safe treatment, and no adverse events occurred. In addition, to the knowledge of the author, this is the first study that attempted and partially succeeded to exploit the advantages of the employed design in order to systematically determine the speed of shiatsu's effect onset and wash-out. It is suggested that an improved version of the design that considers the findings and methodological limitations of this study could be promising as part of a research program to investigate the effect of CAM bodywork systems of care (such as shiatsu) on chronic conditions (such as SPMS).

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Declaration of Competing Interest

The author is himself a shiatsu practitioner, working as a personal assistant of PwMS.

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Appendix A. Description of Treatments – Case Records

Period B1

1st session (6/11/17)

Complains: Spasticity, pain in the sacrum

Main Treatment: In the prone position (inquired): Leg Tai Yang Bladder, HuaTuoJiaJi points, Du Mai, sacrum, scapula's, stretching, mobilizations, palming, three fingers, thumb pressure.

In the supine position (turned with practitioners help): neck, head, legs mobilization, GB20 static pressure.

Feeling / Comments: Some pain in the legs, pain in the head/neck.

Inquired Adverse Effects: None, everything fine

Practitioner Observations: Noisy room. Very stiff muscles, extremely spastic legs especially in the back side under the knees, legs under the knees cold, hands under the elbow cold (always), right side more restricted, legs move better towards the center. Legs felt "melting" during treatment. Stiff neck muscles with restricted mobility.

2nd session (9/11/17)

Complains: Spasticity

Main Treatment: In the supine position: Liver Jitsu, Stomach Kyo. Mobilizations, stretching, palming, three fingers, thumbs, Leg Jue Yin Liver, Leg Tai Yin Spleen, Leg Shao Yang Gall Bladder, Leg Yang Ming Stomach, Leg Shao Yin Kidney, ST36, Kid6-BL62, Kid3-BL60, SP4-GB41

In chair: hands, shoulders, neck

Feeling / Comments: Really good generally, some pain, pain in GB20

Inquired Adverse Effects: None, everything fine

Practitioner Observations: Room much quieter. Leg spasticity "melt" during the treatment. While working the Leg Yang Ming Stomach, she fell asleep.

3rd session (16/11/17)

Complains: Spasticity

Main Treatment: In the supine position: right Arm Tai Yin Lung very Jitsu, mobilizations, stretching. Mobilizations, stretching, palming, three fingers, thumbs, Leg Jue Yin Liver, Leg Shao Yang Gall Bladder, Leg Yang Ming Stomach, Leg Shao Yin Kidney. Upper back release with palms. Neck, head.

Feeling / Comments: Very good. Only slight pain in the area of C7. After previous treatment, the digestive system works much better than very long time with constipation relieved.

Inquired Adverse Effects: None, everything fine

Practitioner Observations: Quiet room. Able to deeply connect with points in Leg Yang Ming Stomach, during which she fell asleep.

4th session (19/11/17)

Complains: Stiff back

Main Treatment: In the prone position: Deep work in Leg Tai Yang Bladder in the back and legs, Du Mai, sacral, neck, head.

Feeling / Comments: Very good. No pain. Stools still normal! Mention removal of gallbladder years ago.

Inquired Adverse Effects: None, everything fine

Practitioner Observations: Quiet room. Slow, deep work, she fell asleep.

Period B2

5th session (20/11/17)

Complains: None

Main Treatment: In the supine position: Jitsu Liver, mobilizations, stretching, palming, three fingers, thumbs, Leg Jue Yin Liver, Leg Tai Yin Spleen, Leg Yang Ming Stomach, Leg Shao Yin Kidney, ST36, Kid6, SP4, SP6.

In the chair: Arm Yang Ming Large Intestine, shoulders, neck

Feeling / Comments: Very good. Yesterday's treatment release back problem. No pain. The MSQLI does not cover the spasticity issue that is for her the most important.

Inquired Adverse Effects: None.

Practitioner Observations: The body is much more responsive compared to other times.

6th session (23/11/17)

Complains: Legs

Main Treatment: In the prone position: Leg Tai Yang Bladder, Leg Shao Yin Kidney, Leg Shao Yang Gall Bladder, stretching, mobilizations, palming, three fingers, thumb pressure. Sotai exercises.

Feeling / Comments: Very relaxing. A reminder that the MSQLI does not cover the spasticity issue that is for her the most important.

Inquired Adverse Effects: None.

Practitioner Observations: None

7th session (28/11/17)

Complains: Urination difficulties

Main Treatment: In the prone position (inquired): Leg Tai Yang Bladder, sacrum, buttocks, stretching, mobilizations, palming, thumb pressure. Sp6. Feet bottom.

In the chair: Arm Yang Ming Large Intestine, neck.

Feeling / Comments: Relaxing session. Some pain points. The right hand works much better after the last treatment.

Inquired Adverse Effects: None.

Practitioner Observations: The areas around KID2 in both feet were tender, an area that corresponds to the bladder organ in reflexology.

8th session (01/12/17)

Complains: None

Main Treatment: In the supine position: mobilizations, stretching, palming, three fingers, thumbs, Leg Yang Ming Stomach, Arm Yang Ming Large Intestine, Leg Shao Yang Gall Bladder, neck, head. ST36, GB 34, Kid6-BL62, Kid3-BL60, SP4-GB41, LI7-11

Feeling / Comments: Relaxing session. Pain in some hand points. The leg works a lot better after the last treatment. Stools are still normal.

Inquired Adverse Effects: None.

Practitioner Observations: None

BREAK

Period B3

9th session (02/01/18)

Complains: Spasticity

Main Treatment: In the prone position: Leg Tai Yang Bladder, Leg Shao Yin Kidney, Leg Shao Yang Gall Bladder, stretching, mobilizations, palming, three fingers, thumb pressure.

In the supine position: Leg Yang Ming Stomach, Leg Jue Yin Liver, Leg Tai Yin Spleen, stretching, mobilizations, palming, three fingers, thumb pressure.

Feeling / Comments: Nice session. Legs and hand spasticity get worse during the break (A period).

Inquired Adverse Effects: None.

Practitioner Observations: General body stiffness worst than before the break.

10th session (04/01/18)

Complains: Spasticity

Main Treatment: In the prone position: Leg Tai Yang Bladder, Leg Shao Yin Kidney, stretching, mobilizations, palming, three fingers, thumb pressure.

In the supine position: Leg Yang Ming Stomach, Leg Jue Yin Liver, Leg Tai Yin Spleen, Leg Shao Yang Gall Bladder, stretching, mobilizations, palming, three fingers, thumb pressure. Neck, shoulders, head, Arm Yang Ming Large Intestine points.

Feeling / Comments: Relaxing. Legs spasticity and the right hand difficulties remain.

Inquired Adverse Effects: None.

Practitioner Observations: She fell asleep in the supine position, the body more responsive compared to the previous session.

11th session (08/01/18)

Complains: Leg spasticity

Main Treatment: In the supine position: Leg Yang Ming Stomach, Arm Yang Ming Large Intestine, Arm Tai Yin Lung, stretching, mobilizations, palming, three fingers, thumb pressure. Neck, shoulders, scapula, head.

Feeling / Comments: After last treatment, spasticity improved and the hand somehow better but still not totally ok.

Inquired Adverse Effects: None.

Practitioner Observations: Trying to keep her aware of her body with questions for feeling during the work.

12th session (11/01/18)

Complains: None

Main Treatment: In the supine position: Leg Jue Yin Liver, Leg Tai Yin Spleen, Leg Yang Ming Stomach, stretching, mobilizations, palming, three fingers. Neck, head.

Feeling / Comments: Relaxing, no problem after last treatment. Worries expressed about what is going to happen now that the trail ends.

Inquired Adverse Effects: None.

Practitioner Observations: Easy to “open” the channels worked with multiple palming passing.

Appendix B. Semi-structured interview verbatim transcript

Researcher (R): So, I would like to begin by thanking you for agreeing to take part in this study and for accepting this interview.

Participant (P): You are welcome.

R: I remind again that you can interrupt the interview whenever you want, or you can say that you don’t want to give an answer and that you are free to say whatever you want and this is not going to have any effect to your treatment and your care.

So, I would like to begin by asking you to share your experience of including shiatsu as part of your care during the last period.

P: Ok, well, well, it has been very relaxing in general, and of course it has… with my usual care it has been quit… mmm… so it has complete it, each other. Yeah… my usual care is quit much like physical care, and this one was more relaxing and maybe taking more care of those areas which were a little painful or hearting. Because actually they don’t take care in the usually physical treatment.

R: Do you mean it was physical aspects that are not taking usually in the daily care or was non-physical aspects that was now addressed by shiatsu?

P: More like those hm… local things like local pain in my lower back and my hand and those things. They were more carefully taking care of… like… shiatsu.

R: Was anything that was quite bad about shiatsu?

P: No, everything was great. I liked it, yeah. There were many aspects which were good, firstly the one that I didn’t… I didn’t have to take off my cloths. That was very nice, because it’s so exhausting to take of your cloths and put them back again and such things, yeah…hm…. What was I saying?

R: So, I have asked if there was something very bad about shiatsu but… if see the question from the other side, was something very good about shiatsu? If you have to choose something…

P: And also there were relaxing point, it was very relaxing, well, I feel asleep most of the time so, you can tell from that, and… well yeah, it releases my spasticity, temporarily, so it came back after a while but… maybe if I get shiatsu each week it would be more permanent. Maybe, I don’t know. And especially my right hand has been better after shiatsu, much better. Sometimes my legs have been maybe too, too relaxed so it’s hard to stand up if I don’t have spasticity in them. Because I need it when I change from the chair to the toilet seat or to bed.

R: So, would you say that this was some kind of adverse event?

P: What did you mean?

R: That there was not enough spasticity sometimes in your legs, that makes things to be more difficult afterwards?

P: Yeah, actually yes, yes. But otherwise than standing up and changing from chair to bed or toilet seat it has been very nice feeling when they are not so spastic.

R: Were there any other adverse events after the treatment?

P: No… no, no, and there the other good thing that was also that my stomach was very… working very well when I got this shiatsu often in the middle of this… this treatment time, yeah… it has never work so well.

R: By stomach you mean?

P: Constipation was released.

R: And, in the middle of the treatment period, based on the schedule of the study, you mean during the periods when you receive also shiatsu?

P: Yeah.

R: Ok, was shiatsu experience… first of all you haven’t receive shiatsu before?

P: No

R: Was the experience of shiatsu what you were expecting from?

P: I didn’t expect anything, actually. I didn’t know about shiatsu anything. I haven’t read about it anything. So, I didn’t actually know what to expect. I didn’t expect much, actually, so there wasn’t any placebo effect, but… so, it was actually more than what I expected, yeah… I was actually quite astonished that it releases my spasticity so well and my stomach worked and, yeah…

R: So, if you wanted to speak about or to write about the possible

contribution of shiatsu in the care of people with MS, what would be your opinion?

P: It would be that it helps in some extend, mostly temporally, for the spasticity and also for the constipation and it releases your pain areas, yeah, and, I would recommend it.

R: You will recommend it as a supplement to usual care…

P: Yeah, yeah…

R: Ok, and do you think that those aspects that was addressed are aspects that are not so often addressed from the usual care that people with MS receive?

P: Yes, I believe so, yes, because in the usual care I usually work my muscles, more, so strength for my muscles, like in gym. Yeah, and well, there are also quite a lot of stretching, they stretch my legs and… but mostly it's muscle work what we do there.

R: Could you imagine why?

P: Because I need it. I need muscles in my legs so that I can stand up and so… I think that's… well maybe also that's what I want to do there, because I can't do it at home…

R: So, possibly it would be also available help on those other domains if, for example if you ask from those that are involved in your usual care.

P: Well, yeah, sometimes I tell them that my lower back is aching and they give me massage and sometimes they give me a normal massage for my upper body and… if I ask for that. I have quite a lot of that usual care, I have 95 times a year, so there is much possibilities, much time to do different things. But I usually have to ask. Otherwise we do just the muscle work and stretching of the legs.

R: Ok, then, what if we take a look in the influence that this specific trial might had in your life, do you think that during the trial have been covered important domains for your life, that this trial succeeds to cover important domains for you?

P: What I can say… well, let's say the sleeping, I have slept better because my legs have been not so spastic… so they have not been so… they have been more relaxed during the nights, let's say. That's quite big thing because I always sleep so badly, so little things make the difference. And of course also my lower back has been better… I don't actually suffer of that much because I don't feel it when I'm sitting, but when I have to do something then I feel it, the pain, and it's so stiff and aching… Maybe during night also that has been better. So that I have slept better.

R: So sleep is an important aspect for your life.

P: Yeah, that's true.

R: What else would you said that should be covered?

P: Also the constipation is great thing if it releases that, but otherwise I don't know.

R: So, as a treatment and as a trial, as a research study, was it enough flexible to your needs, according to your needs?

P: You mean the treatment as such?

R: The treatment as such and the trial itself.

P: Yeah, it was ok. There was no complains, it was great, it was great that you were coming to my house and… yeah, no complains.

R: And then, was there, if there was no complains, was there at least some difficulties to follow the study?

P: No…

R: I mean, for example, there was a full month that you have to have twice per week treatment…

P: It was ok, well, I have time, so it was ok. It was nice.

R: So, if see it like a "free-talking" now, is it something that you would like to add to what you have already speak about? Any concern, any idea…

P: Actually, not about the treatment itself but… well, I think that you were very professional, I like your style… but otherwise, I don't know anything else to say… Everything went well and smoothly.

R: In the previous treatment you have mention fear, or worry, I don't remember the exact word, because we try to speak also Finnish during the treatment but… regarding what is happening when the treatment stops.

P: Well, yeah…

R: Is it something that during the study period, when you have to get the breaks of the treatment, is it something that occur that cause the fear, or was it also worry at that time or how it was, how it was this experience for you?

P: The breaks you mean?

R: Yes.

P: Well, I didn't like the breaks… because this was so relaxing and… and pleasant. So I actually… I would like to have the treatments every week it was so nice.

R: Is it something that can contribute in getting worst period, the periods that are like without treatment? So… if I rephrase it… if you were going to take part in a similar study again, would the long break, there was two periods of break so four weeks continuously without treatment, would this be something that would make you think that "hm… maybe I would not take part on this study because this period"?

P: No, if you mean about the break that there was not pleasant, no, no, well, well the breaks were ok, but I would like to have treatment also all the time, yeah, because I liked it.

R: If there is not something else that you would like to add, maybe we can close this short interview here.

P: Yeah.

R: Thank you very much again.

P: Thank you.

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