Reset your Immune System: Acceptability and Preliminary Effects of a CMT-Based Intervention in Patients with Hashimoto Thyroiditis

Citation for published version (APA):

Portokalidou, Z., Huysse-Gaytandjieva, A., & Peters, M. L. (2022). Reset your Immune System: Acceptability and Preliminary Effects of a CMT-Based Intervention in Patients with Hashimoto Thyroiditis. *Mindfulness*, *13*(7), 1769-1781. https://doi.org/10.1007/s12671-022-01914-7

Document status and date:
Published: 01/07/2022

DOI:
10.1007/s12671-022-01914-7

Document Version:
Publisher's PDF, also known as Version of record

Mindfulness (2022) 13:1769–1781
https://doi.org/10.1007/s12671-022-01914-7

ORIGINAL PAPER

Reset your Immune System: Acceptability and Preliminary Effects of a CMT-Based Intervention in Patients with Hashimoto Thyroiditis

Zoi Portokalidou[1] · Anna Huysse-Gaytandjieva[2] · Madelon L. Peters[3]

Accepted: 19 May 2022 / Published online: 6 June 2022

Abstract

Objectives Patients with Hashimoto thyroiditis (HT) experience mental health complaints due to the immune system dysregulation. Preliminary evidence suggests that psychological interventions could improve patients' quality of life. Compassionate mind training (CMT) is part of compassion-focused therapy (CFT) and can be used to help individuals address physical and mental health difficulties. The present study sought to assess the acceptability and preliminary efficacy of Reset Your Immune System, a 6-week CMT-based online intervention, in patients with HT.

Methods Nine women were randomly selected from a wider sample that undertook the online intervention. Upon completion, they were interviewed with nine standard open-ended questions. Additionally, pre- and post-intervention questionnaires were filled out.

Results Qualitative analysis indicated that participants observed improvements in symptoms, sleep quality, self-awareness, stress-management, and self-regulation skills. Participants did experience some difficulties in undertaking compassion-related exercises. Quantitative analyses showed that negative affect, social/role limitations, and HT symptoms indicated a reliable change from pre- to post intervention.

Conclusions Overall, Reset Your Immune System showed beneficial effects on patients with HT, suggesting that including psychological care as part of the standard treatment of HT might have added value. It is important to assess long-term effects in a larger sample through a randomized control trial.

Keywords Hashimoto thyroiditis · Compassion-focused therapy · Compassionate-mind training · Autoimmune diseases · Mindfulness-based interventions

Hashimoto thyroiditis (HT) is one of the most common autoimmune diseases and the most frequent cause of hypothyroidism. HT is portrayed by the manifestation of antibodies that attack the thyroid cells and it is affecting mostly women. Patients with HT experience persistent complaints such as impairments in cognitive functioning and physical and psychological symptoms, have a higher chance to develop other autoimmune diseases, and as consequence experience a decreased quality of life (Boelaert et al., 2010; Gulseren et al., 2006; Uysal & Ayhan, 2016). Because HT can provoke changes in body appearance and anatomy such as skin dryness, hair loss, weight gain, and hoarseness, feelings of shame may occur. Patients' quality of life is inversely related to the level of circulating antibodies against thyroid cells (Uysal & Ayhan, 2016) while psychological symptoms such as fatigue, irritability, nervousness, and depression increase with higher antibody levels (Müssig et al., 2012; Ott et al., 2011). In some instances, the psychological symptoms experienced by patients with HT lead to a mental health disorder as diagnosed with DSM-5 (Bauer et al., 2008; Müssig et al., 2012).

Recent evidence suggests that early adversity and trauma are associated with an increased prevalence of inflammatory and autoimmune diseases in adulthood (Schubert, 2013) and higher chances of hospitalization for these diseases (Dube et al., 2009). Additionally, negative emotions increase inflammatory responses and thereby aggravate the condition

✉ Anna Huysse-Gaytandjieva
info@hashimoto.help

1 Leiden, The Netherlands

2 Hashimoto Help, Brightlands Health Campus, Gaetano Martinolaan 85, 6229 GS Maastricht, The Netherlands

3 Department of Clinical Psychological Science, Faculty of Psychology and Neuroscience, Maastricht University, Maastricht, The Netherlands

(Moons et al., 2010). Shame and threats to the social-self have been found to be associated with increased cortisol and pro-inflammatory cytokine activity (Dickerson et al., 2004). This cascade of events in turn can affect the course of autoimmune diseases in general, including HT.

The relationship between psychological symptoms and the immune system dysregulation is not taken into account in the standard therapy for HT, which is usually thyroid hormone replacement treatment. However, patients' sense of self-efficacy and self-esteem have shown to be moderate predictors on healthful behaviors, appropriate eating habits, and positive psychological attitudes (Rode & Rode, 2018). Furthermore, after participating in a stress management intervention, patients' levels of stress, depression, anxiety, and healthy lifestyle were improved (Markomanolaki et al., 2019). Thus, intervening on the psychological aspect of the disease could improve quality of life for patients with HT by downregulating negative and promoting positive emotions.

Inducing compassion is effective in lowering psychological suffering. Self-compassion is negatively correlated with threat emotions such as anxiety and mood states such as depression. These are common in patients with HT and are associated with increased inflammatory responses (Moons et al., 2010). Compassion is also positively correlated with positive mental health outcomes, including quality of life in autoimmune diseases such as multiple sclerosis and celiac disease (Dowd & Jung, 2017; Nery-Hurwit et al., 2018).

One way of cultivating compassion is with compassionate mind training (CMT) which was developed within compassion-focused therapy (CFT) (Gilbert, 2020; Gilbert & Procter, 2006). CMT helps people develop courage and wisdom to engage with various aspects of suffering. Many clients suffering with physical and mental health difficulties tend to experience elevated threat processing associated with the physiological effects of threat. CMT helps clients become mindful of being caught in the threat system and of how to switch attention to a caring and compassion motivational system that re-balances the threat system by stimulating physiological systems associated with caring. These include the vagus nerve oxytocin and the frontal cortex (Brown & Brown, 2015; Carter et al., 2017; Gilbert, 2020; Porges, 2017).

CMT is a skills-based program that has several techniques and strategies aimed to improve compassion, such as breathing, compassion-imagery, remembrance of compassionate other, and acting techniques (Gilbert, 2014, 2020). Through practicing these skills, individuals can empathically engage with their distress, work through different threat-based emotions, and validate compassionate ways that facilitate more acceptance and wise action.

Online interventions based on CMT have been effective in reducing depression and promoting well-being (Sommers-Spijkerman et al., 2018), reducing pain sensitivity, and helping people with chronic pain to avoid analgesic misuse (Dhokia et al., 2020). Additionally, interventions based on compassion help patients with chronic conditions accept their condition and associated limitations, instead of feeling guilty or blaming themselves (Austin et al., 2021). Because there is no permanent cure for HT, patients typically struggle with chronic symptoms and may be prone to develop hopelessness. Through developing compassion and sensitivity to one's suffering, CMT can help them reconcile themselves with their disease.

Taken together, CMT has been shown to promote coping strategies and reduce depression and anxiety (Gilbert & Procter, 2006), while improving immune system functioning, physical well-being (Gilbert et al., 2011; Pace et al., 2009), and health-related quality of life in patients with long-term conditions (Austin et al., 2021). The particular framework of CMT as a foundation was selected as it could help patients with HT manage their symptoms, engage empathically with and accept their disease, come to terms with feelings of shame or fears, while decrease the risk of developing another autoimmune disease.

In HT, when disease itself is viewed as the source of distress, as well as the potential early adversity and stress factors that are implicated in autoimmunity are taken into account, patients can benefit by an integrated approach to become more mindful in relation to these particular aspects of their experience. The purpose of the present study was to explore the effects and acceptability of the Reset Your Immune System, a CMT-based intervention, in patients with HT.

Method

Participants

Participants for this study were recruited from the Thyroid UK Association, a charitable company that provides information and support to patients with thyroid diseases. An internal forum of the Thyroid UK Association and social media channels were utilized for the recruitment process and patients voluntarily decided to participate in the study. Inclusion criteria were as follows: diagnosed with HT, 18 years or older, good command of English, access to the Internet, and able to work with a computer. There were no exclusion criteria.

Seventy-eight participants were recruited and started the intervention, after filling in the pre-intervention questionnaires. Upon completing all intervention modules, twenty-two of these participants filled in the post-intervention questionnaires. Nine participants from the initial sample were randomly selected and participated in the interviews. Due to a technical problem, only for seven participants we could

match the post-intervention data to their pre-intervention. We used this data for supporting quantitative analysis.

All nine participants that were randomly selected for the interviews were women, aged between 28 and 65 with a mean of 48.2 years. Six of them were married and five were mothers. For the quantitative data, all seven participants were women, aged between 33 and 55, with a mean of 44.1 years.

Procedures

Reset Your Immune System is an intervention based on CMT, designed and adapted to meet the needs of HT pathology. In addition to regular CMT exercises, it incorporates elements of Eye Movement Desensitization and Reprocessing (EMDR) and Acceptance and Commitment Therapy (ACT). Both approaches have similarities with CMT in that they lead to new ways of engaging with distresses. Moreover, both interventions can effectively enhance adaptation to, and self-management of, chronic somatic conditions (Kuba & Weissflog, 2017; Mazzola et al., 2009; Royle, 2008). Kennedy (2014) has previously argued for the added value of integrating EMDR and compassion-focused therapies, as both address shame and self-criticism. In a similar vein, others have advocated the integration of ACT and compassion-based therapies, especially in the context of somatic complaints (Skinta et al., 2015; Trindade et al., 2021).

The intervention incorporated several evidence-based CMT components that have been proven effective in previous studies (Gilbert & Procter, 2006). The specific selection and order of components, and their adaptation to HT patients, was done by one of the authors, AHG, a psychotherapist that suffers from HT herself. The intervention was further shaped and adapted by her longstanding experience with guiding patients with HT through her intervention and the feedback received from them. Reset Your Immune System is normally offered as a guided intervention, but for the purpose of this research, it was modified to an online self-learning training without therapist guidance. It consists of 6 modules with themes that are delivered in the course of 6 weeks. Each module starts with theoretical underpinning in the form of psychoeducation, followed by experiential exercises, and concludes with homework practice and reflection. Table 1 describes the focus of each module, number of themes, and examples of experiential exercises. The intervention utilizes materials such as written text, embedded videos, downloadable audio recordings with meditation exercises, and workbooks. The intervention encourages patients to understand how emotions affect the immune response and to cultivate a compassionate self. Through using techniques that increase emotion regulation and self-awareness, participants become aware of their symptoms, their emotions toward the disease and themselves, and how they can cope with these emotions. Experiential exercises such as breathing and meditation help participants engage empathically with their distresses. The EMDR component consists of auditory bilateral stimulation during some of the meditation practices. It is meant to induce relaxation, decrease physiological arousal, and promote access to brain regions that can lead to more adaptive processing (i.e., changing the intensity/direction of the distress). The ACT components mainly addressed contact with the present and acceptance of the disease.

A welcoming email provided detailed instructions on how to access the online platform. After finishing one module, participants could access the next module. They received a weekly schedule that included all activities planned for that week and the time needed to accomplish them. Throughout the intervention, participants received reminder emails that encouraged them to proceed and finalize the intervention. Participants had the autonomy to plan their schedule as they wished and they were

Table 1 The intervention modules along with their themes (including reflection and homework) and example of experiential exercises

Module	Learning goals/description	Themes	Example of experiential exercise
Introduction	Introduction to intervention; creation of plan and schedule	4	–
Emotion and immunity	Understanding emotions; Understanding how the tricky brain works; building internal resources by making use of different experiential exercises	11	Safe island, Facial expression and tone of voice
Emotion regulation	Understanding the three types of emotion regulation systems and how they interact; stimulating vagus nerve and developing compassion	12	Create a Compassionate image, Spiral technique
Threat system	Analysis of different forms of threat-based emotions; making use of compassion to calm down the threat system	10	Compassionate smell
Multiple selves	Understanding the importance of all different emotions; developing abilities to work with blended emotions and multiple feelings; accessing blocked emotions	8	Letter from compassionate self
Next steps	Developing future plan; person-activity fit questionnaire; personal statement and commitment	5	-

encouraged to repeat some of the themes and exercises as homework. The platform also included a discussion section where participants could comment on each module and reply to other participants' posts. Towards the end of the intervention, participants were invited to make a future plan on how they are going to integrate what they have learned into their daily lives. Once all the modules were completed, participants were given access to the post-intervention questionnaire that was completed on the same online platform. Nine participants were interviewed upon completion. All video interviews were conducted by one of the authors, AHG, online.

Measures

Interview Questions The interview followed a structured format with nine standard open-ended questions, followed by additional ones emerging from participants' answers. The questions focused on four key topics: (1) patients' experiences of developing and living with HT, (2) compassion and relationships with others throughout lifespan and before and after the intervention, (3) acceptability and fidelity of the intervention, and (4) feedback and recommendations on the intervention (see Supplementary File 1).

Quantitative Measures The following self-report measures were completed pre- and post-intervention:

1. Demographics. The demographic questionnaire asked participants to report their gender, age, education, marital status, and maternity/paternity status.
2. Health Distress scale (Lorig et al., 1996). The health distress scale consists of 4 items assessing the distress caused by an illness. Respondents have to indicate at what extent the four items represented their thoughts the past month, ranging from 0 (none of the time) to 5 (all of the time). The total score is calculated by the mean of the four items. The scores can range from 0 to 5 with higher scores implying more distress about health. Cronbach's alpha in this study is 0.87.
3. Satisfaction with Life scale (SWLS) (Diener et al, 1985). This scale measures one's cognitive judgments of satisfaction with their life. Participants indicate how much they agree or disagree with each of the 5 items by selecting a score from 7 (strongly agree) to 1 (strongly disagree). The scores on each item are summed up and provide a final score. Higher scores indicate higher satisfaction. Cronbach's alpha in this study for the SWLS is 0.81.
4. Positive and Negative Affect Schedule (PANAS) (Watson et al., 1988). The PANAS is an instrument measuring one's positive and negative affect. It contains 20 items on two subscales (10 each) that assess a person's positive and negative trait affect using a 5-point scale (1 = "very slightly or not at all"; 5 = " extremely"). Higher scores indicate higher levels of positive or negative affect respectively. In this study, Cronbach's alpha for the PA subscale is 0.88, whereas for the NA is 0.87.
5. Social/Role Activities Limitations (Lorig et al., 1996). This scale consists of 4 items that assess how much one's illness has interfered with role activity during the past 4 weeks. For each item, score can range from 0 (not at all) to 4 (almost totally). The score of the scale is the mean of the four items, with higher score indicating greater activities limitations. Cronbach's alpha for this scale in this study is 0.93.
6. Defeat Scale (Gilbert & Allan, 1998). This self-report scale consists of 16 items that assess the sense of failed struggle and losing rank. These are series of statements, which describe how much the respondents had felt defeated in the last 7 days, rated on a 5-point Likert scale (0 = never, 4 = always). Cronbach's alpha in this study is 0.94.
7. Fears of Compassion Scales (Gilbert et al, 2011). The Fears of Compassion Scales were used, measuring compassion as a flow. Three self-report subscales measure fears of compassion for self (15 items), from others (13 items), and for others (10 items). The items are rated on a 5-point Likert scale (0 = don't agree at all, 4 = completely agree). The items for each of the 3 scales are summed up to calculate the scoring. Cronbach's alpha in this study is 0.85 for the Fear of Compassion from others subscale, 0.84 for the Fear of Compassion for others, and 0.92 for the self-compassion subscale.
8. Experienced symptoms. A checklist of 18 hypothyroidism symptoms where patients can indicate which symptoms they experience. Items included symptoms like feeling tired, muscle pain, anxiety, dry skin, and sensitivity to cold. The total number of symptoms listed was calculated. Cronbach's alpha for the checklist in this study is 0.90.

Fidelity, feasibility, and acceptability were assessed qualitatively in the interviews. Participants were asked whether they had finished the intervention, whether they followed the homework exercises, and whether they practiced and implemented what they had learned into their daily lives. Fidelity was also examined by means of two questions in the post-intervention questionnaire (*How many sessions of the training did you complete? For how many hours per day have you practiced?).* Acceptability and feasibility were measured with two categorical variables (yes/no), i.e., *Did you practice what you have learned during the training outside the training sessions?* and *Would you recommend the training to others?*, and two continuous variables *What grade would*

you give to the training in general? (1–10, with 1 = poor and 10 = excellent) and *How did you appreciate the quality of the following aspects of the training program?* (1–5 with 1 = bad, 5 = excellent per aspect, e.g., topics included, number of sessions, experiential exercises, discussion group).

Data Analyses

This study uses primarily a qualitative research design to provide profound understanding of the intervention effects and the experiences of patients with HT. Secondarily, a reliable change index (RCI) for each questionnaire was calculated using the formula of Jacobson and Traux (1991).

Results

Qualitative Analyses

The step-by-step guide from Braun and Clarke (2006) was used to analyze the qualitative data. The person doing the analysis was not involved in the interview design and execution and was blind to the intervention during the analysis time. First, all interviews were transcribed verbatim including all verbal and nonverbal comments and cues, and checked against the recorded files. All interview transcripts were read repeatedly, allowing initial understanding of patterns in the data. Then codes were manually generated and provided some initial ideas around the meanings of data. This happened first on a question-individual level and then across participants on the same question or across questions for more participants, allowing a more inductive approach. Codes and the relationship between them were then examined and grouped together to form themes. An initial theme list was identified and re-examined. Some themes were merged and sub-themes were developed instead, while others were removed and re-named. Upon final theme selection, the data were analyzed and interpreted for each theme with the relevant extracts being put together.

Four key themes were identified: Developing Compassion, Understanding the Self and the Disease, Experiencing Better Quality of Life, and Intervention Acceptability. Figure 1 depicts how the different themes and subthemes are connected.

Theme 1: Developing Compassion

The intervention has helped participants develop self-compassion, face their inner thoughts about being self-critical, and perceive their problems as part of the disease and common humanity instead of over-identifying with them.

From Isolation to Common Humanity After finishing the intervention, participants acquired a sense of belongingness and connection. They reported that they do not feel alone in the disease and that both other people's comments and the content itself have been comforting and reassuring. There, they found relatable situations that they could identify with:

> People were largely reporting what I'd felt when I was doing it.

Importantly, participants stepped back and put their experiences into a larger perspective. Specifically, they learnt to accept and view their emotions and behaviors as a result of their human nature instead of attributing them to their personal situation or blaming themselves:

> And actually, it is okay to be human and I'm okay to have bad days and that's just it really.

Replacing Self-criticism with Self-compassion Participants explained that before the intervention, they had not been aware of being critical towards themselves and lacking self-compassion, or of the effects of styles of self-critical thinking:

> That's because before I didn't realize I was doing so. And that's really good to have the techniques to be able to overcome and not beat myself up if I haven't finished something. Because I realized that's damaging me.

After the intervention, participants reported kinder and more compassionate reactions towards themselves. Instead of being critical, they learned to let things go and treat themselves with sensitivity and compassion:

> Instead of going you stupid cow or whatever I'd say to myself, I'd just say never mind. And actually, I started to adopt that quite a lot and it has made a massive difference.

Importantly, participants realized that they are able to be compassionately sensitive to their needs:

> I never give myself time, I never do anything. And actually, I have been stealing a little bit of time that actually was mine in the first place, so…

Furthermore, the knowledge provided in the intervention helped participants perceive their situation as something they do not necessarily control. This reduced self-criticism and enabled them to develop new wisdom and insights to underpin self-compassion:

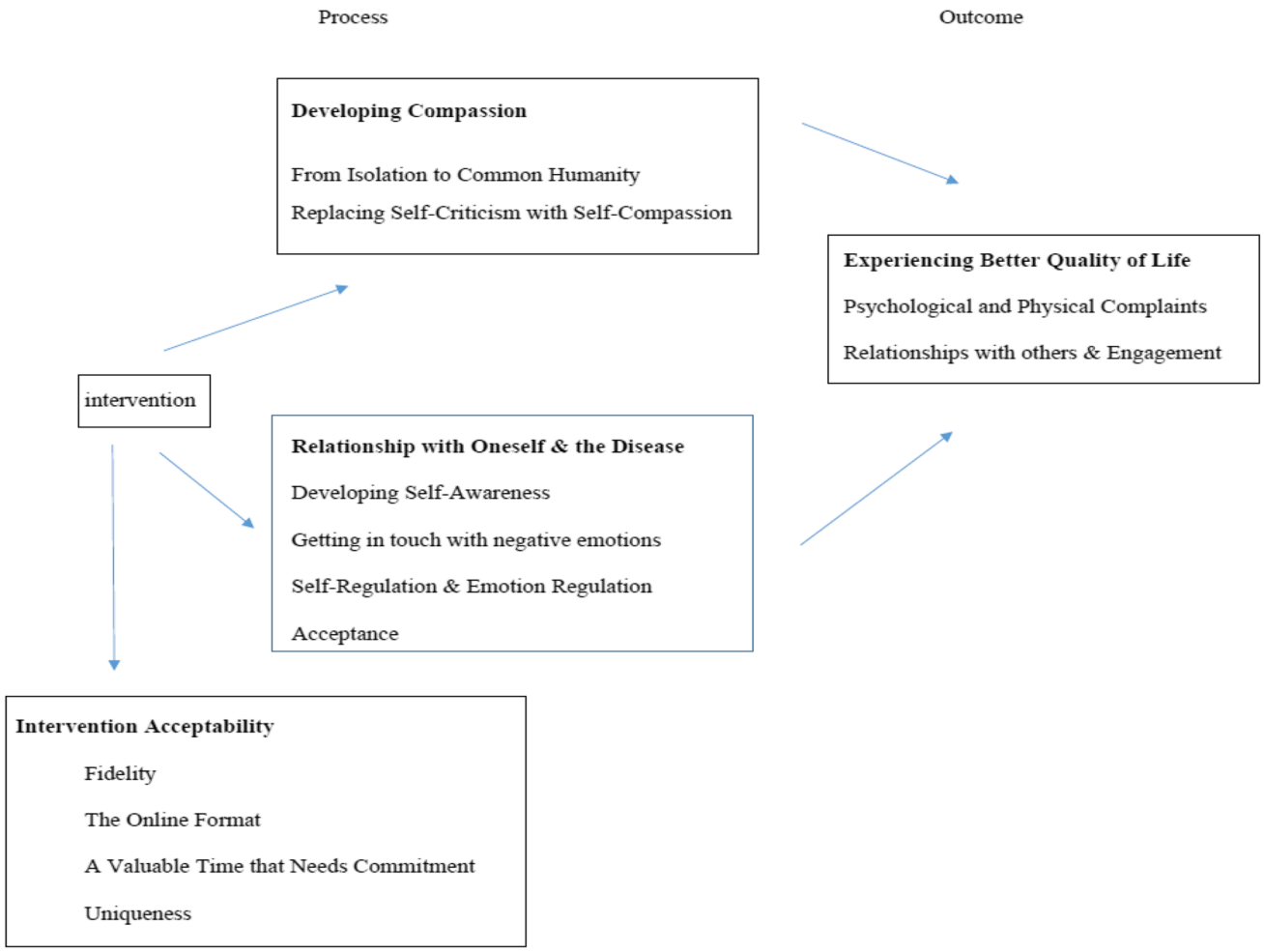

Fig. 1 The interaction between the themes and subthemes of thematic analysis

> I didn't know there was link with your hormones or the cortisol levels so that's something I learned and I think it will make me think before I try and beat myself up for something I should be doing rather than resting or meditating or whatever it is that I need to invest in myself.

Theme 2: Relationship with Oneself and the Disease

Developing Self-awareness Participants reported that the program helped them understand more about themselves and how they function, enabling them to become more thoughtful and reflective about their motives, behaviors, and emotions:

> Yeah, I think it's making me more thoughtful and aware, which is a big step forward for me.
>
> The course is helping me almost to just walk through, you know, walk the way in, understand it, recognize how it's affecting me mentally and physically and actually just spoiling me over the process. So taking it step by step rather than jumping a hundred miles and go what will I do if this happens, oh my god, what if that happens, oh no, I don't like it.

An increase in participants' bodily awareness was also present, including conscious breathing, and noticing emotions' effect on facial expressions, as well as a sense of an energy being transmitted to the body:

> I felt it really helped me focus and concentrate on each area - I could literally feel myself being very aware of those parts of the body - sort of felt like I was pulsing good vibes down each part.

Getting in Touch with Negative Emotions Exercises that related to attachment figures and imagining a compassionate self increased participants' awareness of negative emotions such as anxiety, shame, and grief. When clients become

more aware of the inner sources of suffering such as unprocessed anger or grief, their first reaction can be to pull away or experience what are called "fears, blocks and resistances" which need to be worked through (Gilbert, 2010). This was the case with some participants in the present study, who were unable to finish the exercise at the time or they had to repeat it many times:

> But I found it -it got me very wrought up. So I actually couldn't finish it. I just had to stop because it was making me very emotional and I couldn't control... I don't - I didn't like those feelings.

However, participants explained that the increased awareness of negative emotions with a compassionate focus was an effective way of accepting such emotions rather than just feeling bad about them. They explained that they have learned to process emotions and behaviors differently as in the case of going from suppressed anger to more assertiveness:

> I think maybe the course has made me realize that it's okay to feel angry if I'm angry […] I also found if I didn't state what was on my mind, it would make me more and more angry. So now with some people I'm saying it in a calmer way rather than bottling it up and then coming out in an angry way - which is something I didn't realize I was doing before.

In some cases, working with negative emotions generated some reflection on participants' inner thoughts and the reasons they react in a certain way:

> When I was trying to imagine a person, people who died, came in my mind, which basically made me very upset and I suppose I found that quite hard to deal with it so I think I've got some issues with loss - which made me think that there are emotional things I need to deal with. It brought me some grief. So I got sad a little. But in a way, having to face that it made feel better, you know what I mean?

Self-regulation and Emotion Regulation Participants explained that the intervention helped them combat their psychological difficulties. They talked about experiencing less anxiety and rumination, showing improvements in self-regulation and self-efficacy, and think more clearly.

After the intervention, participants developed the ability to be aware of their thoughts in stressful situations which in turn helped them control their response:

> If something happens that I'm not quite comfortable with or I don't like, I have been more conscious of not reacting immediately and thinking about my response.

Importantly, participants integrated the techniques provided in the intervention to compassionately cope with anticipated stressful situations and improve their emotion regulation. For example, clients could become discerning of when to let go of rumination and shift one's mind to a state that facilitates coping. Here compassionate "distraction" into use of safe place can be in the service of coping rather than avoidance:

> I knew I was going to get really stressed and everything, but I did, and I did, I did use these methods, you know, the methods that I learned about trying to avoid the stress, walk away from it and also to go, you know, go to my little island and think about other things, you know, distract myself. And I got through it.

Participants explained that the intervention has been helpful for controlling the release of their emotions:

> I think you've taught me a few good methods by which I can control some of the outburst of the emotions.

Acceptance Participants mentioned that before undertaking the intervention, they were not able to accept the disease. After the intervention, they developed the ability to accept the fact that they suffer from a chronic disease and can learn to live with it:

> I think probably one of my biggest values to feeling better has been resentment; why would this have to happen to me and all this sort of things you think about… […] I've probably learnt more to accept okay, that's how life is now so I'm going to have to just adjust myself to live like that and that's why I liked this course.

Participants also explained that they developed a healthy relationship with their own feelings in relation to the impact of the disease:

> I resented my disease and what it stopped me doing. And I think life could have been different, I could have worked full time, and I could have more children - various things and that just created resentment. So being able to be more in peace with those feelings and to understand them, I think that's what the program has taught me.
> I think I'm constantly in fight flight against the illness. To try to get away from it and not let it overtake my life […] And I think the program has helped me to see that and to change the relationship a bit with

those feelings and to see them as positive rather than something I have to... it's a part of me, it's not all of me.

Theme 3: Experiencing Better Quality of Life

Psychological and Physical Complaints Participants reported experiencing a better quality of life, in the sense of being calmer, less anxious, and more able to deal with things:

But I just feel different, it's really… I don't know how quite to explain the… I have inner peace and I feel I am a bit more equipped.

Reset Your Immune System involves a lot of focus on physiological processes such as breathing and trying to balance the nervous system. Hence, interestingly participants after the intervention noticed less muscle pain, less headaches, and more relaxation in their bodies:

Again, physically, I've had far less headaches. I was getting almost daily headaches before I started this. But at the moment I have not.

Almost all participants explained that before the intervention, they had severe problems with sleep quality. Because of general anxiety, they used to experience increased heart rate and fast breathing they could not control. Some participants reported ruminating and imagining bad scenarios that in turn impeded sleeping. After the intervention, all participants noticed a better quality of sleep, more energy and less anxiety when going to bed:

So using the meditation techniques and the breathing technique my sleep has definitely improved.

Relationships with Others and Social Engagement After undertaking the intervention, a few participants felt more comfortable to open up and share their problems with others, as well as to ask for help when they need it:

I'd probably be someone that wouldn't seek for help, and I'm trying to ask, if I need help now, I'm trying to ask that sooner.

Participants' relationships were also improved as a result of awareness and self-regulation generated by the intervention:

I'm actually getting now much better with my partner, who probably 3 months ago wanted to leave because everything's been irritating me. But actually it's not him, it's me. And that's been quite a revolution.

Moreover, one participant was able to engage in mentalization and new forms of perspective-taking and show understanding in things that would otherwise bother her:

And I get irritated when my partner's doing things around the house and I don't know why that is! So for example last time he was cutting down a tree in the garden and I hate the thought of cutting trees down and now I understand why he's done it, because it's going to bring light to the garden. And I was trying to not be very angry with him and trying to be positive and kind, and thinking, if you know, it's me, it's my.. I thought I was cutting the tree down.

Finally, participants' close others have been positively affected by the changes in participants' mood:

But I see he's (her son) got quite a lot of learning difficulties and I think sometimes I activate him with my "ugh I'm so tired, I can't cope" so yeah, I think he's much more relaxed and actually his teachers tell me his school-work has improved massively. And I think the two going together.

Furthermore, participants showed interest in sharing knowledge and helping people deal with their health and well-being:

And my new business it's all about publishing a magazine on health and well-being and it's based on my journey if you like, all the things I tried to try make myself go better and I thought of making a magazine that maybe something that didn't help, some sort of stuff that would help other people.

Theme 4: Intervention Acceptability

Fidelity Overall, participants reported completing the intervention and the homework exercises, while also practicing what they have learnt outside the intervention. Specifically, two participants completed all modules except the last one and only one participant stayed halfway through due to personal circumstances and lack of engagement. The rest of the six participants completed all modules, and four of them described in detail the different ways they worked with the intervention: one of them explained that some modules she did twice because she found them helpful, another one went through it but not as thoroughly and carefully as she would like, and two of them expressed they would like to go through it again in order for it to be more beneficial:

I have finished it but I need I think to go through it again, because I found some of it.. I don't think I'm going to kill 30 years of stress in 6 weeks.

Also, one of these participants reported that even though she undertook all modules, she did not manage to finish some exercises due to internal resistance:

> Well I finished the program but there are bits that I didn't complete completely […] So for example, I didn't, I haven't done the letter to the self, the compassionate letter - I haven't managed to do that. I keep going to do it and then I just.. yeah, I pull back. So there are bits that I haven't done.

This demonstrates common struggles that people have with developing compassion but that resistance can be worked through particularly by going one step at a time with gentle encouragement that it needs time to be developed.

The Online Format Participants used the discussion board section and found it helpful to read others' comments, as it made them feel less isolated. In addition, they enjoyed being part of this community as it felt safe:

> I know from the support groups that sometimes people can be lacking in support, which was not the case here—which was nice, so it felt like a safe space, cause nobody was arguing or saying oh your feeling is not quite what I think it should be.

In addition to that, a few participants mentioned that a personal contact with the trainer or with other participants would have been helpful and more engaging. For one participant, real-time interaction with a physical trainer was lacking in the sense that most of the exercises were provided in form of text or recordings, which made it difficult for her to follow the intervention:

> And I just found it really hard, partly because I was engaging with... like not real things?

A Valuable Time that Needs Commitment Participants explained that engaging with the intervention felt like a personal time where one needs to be in the right mood and ready to invest in it rather than doing it superficially:

> It is difficult finding the time to sit down and do it, without thinking about other things. You need to be in a sort of inner zone before you get to begin.

> I think it just feels like a protected time for you where you have to give yourself time.

The intervention was perceived as a way of shifting mental states that help with the daily stressors:

> It makes you going into that… nice space. It stops you for a while in the day. Makes you relaxed.

All participants understand it is a joint effort that needs to be integrated in their daily lives. Some explained that for the optimal results, one should repeat the exercises at least weekly. Indeed something that the intervention emphasizes is that it is not a one-off set of sessions:

> I don't think it's something, a program you're doing and then you're fine. This is just a toolkit and a thing to go back to and yeah, hopefully, this will work as required and equally, it's also realizing that you do weekly time as a minimum, just, just a little reflection, little kind of calmness, and then continue again.

The intervention enabled participants to understand the importance of taking care of themselves by generating a wish for integrating such activities in their daily lives:

> And I think that I'm feeling that I need to do these things. So hopefully I will be able to keep doing them and to take these techniques forward.

Uniqueness Participants found the intervention different from other treatments they have tried. They reported that exploring the connection of emotions with autoimmunity provided valuable insights they had not been aware of before. This helped them to recontextualize their relationship to their disease:

> I found it very interesting, very good, because everything I've tried before or read about before has been from a very physical aspect whereas this I found was much more about the mind, the emotions and the relationship with the illness. […] It's the first time that I've really come across it – I looked out from a psychological point of view as opposed to just a purely physical point of view I think.

Quantitative Analyses

A reliable change index (RCI) for each questionnaire was calculated using the formula of Jacobson and Traux (1991). Calculations of the RCI used the standard deviation and reliability (Cronbach's alpha) from published sources where normative scores from a sufficiently large sample were reported (Crawford & Henry, 2004; Gilbert & Allan, 1998; Gilbert et al., 2011; Glaesmer et al., 2011; Lorig et al., 1996). If separate scores for men and women were given, we used the data from the female sample. For the HT symptom score, we based the calculation on the data of our own sample that had completed this scale pre-interventions ($n = 68$). Table 2 shows the mean pre- and post-intervention scores for each of the questionnaires together with the RCI for that questionnaire. We determined whether the mean difference

Table 2 Pre-and post-intervention means, reliable change index (RCI), and number of participant surpassing the threshold for reliable change

Variable	Pre-intervention mean (SD)	Post-intervention mean (SD)	Mean diff	RCI	No. part
Health distress	3.71 (0.51)	2.68 (0.83)	1.03	1.60	4
Life satisfaction	15.71 (5.50)	20.00 (6.08)	4.29	4.86	6
Positive affect	23.43 (4.04)	28.86 (11.31)	5.43	7.03	3
Negative affect	27.86 (9.32)	18.43 (4.24)	**9.43**	6.42	4
Social/role imitations	3.29 (0.96)	2.21 (0.42)	**1.08**	0.91	3
Defeat	42.86 (10.9)	36.29 (8.40)	6.57	7.33	5
Fear of C to self	16.14 (10.09)	15.86 (10.30)	0.28	8.14	2
Fear of C from others	13.29 (5.65)	15.71 (8.24)	-2.42	8.37	2
Fear of C for others	18.43 (3.64)	16.86 (3.63)	1.57	6.16	3
HT symptoms	5.31 (1.25)	3.40 (1.00)	**1.91**	1.46	3

Bold print means that the mean difference surpasses the threshold for reliable change

indicated a reliable change across participants as well as how many individuals showed a reliable change.

As can be seen from Table 2, the mean change on each of the questionnaires except for fear of compassion from others was in the expected direction. For negative affect, social/role limitations and HT symptoms the mean pre- to post intervention difference indicated a reliable change. Although the mean change in life satisfaction did not reach the reliable change criterion, six out of seven patients did show a reliable change. Five participants showed a significant change on defeat and four on health distress and negative affect. On all other instruments, only 2 or 3 participants showed a reliable change.

Table 3 gives an overview per participant on which questionnaire a reliable change was obtained. As can be seen in the table, participants 1, 2, and 7 showed a reliable change on most of the outcome measures. Participant 3 showed the least reliable changes.

The seven participants provided fidelity and acceptability data as well. Almost all of them tried to practice at home what they had been taught. On average, participants completed 22 out of 50 sessions (ranging from 5 to 50 sessions) and they practiced homework exercises around 1 h per day. Participants reported implementing what they learned during the intervention in their daily lives. The intervention was on average graded with 8 out of 10 with the lowest score being 7 and the highest 10. Moreover, all participants would recommend the intervention to others.

Discussion

The goal of this study was to examine the acceptability and the effects of the Reset Your Immune System CMT-based online intervention in patients with HT. Patients with HT often experience a range of negative emotions and psychological problems that can generate mental health difficulties and are associated with increased inflammatory responses (Moons et al., 2010). These experiences are not addressed through the standard hormone replacement therapy, leaving patients with HT to persistently experience complaints and being at a high risk for developing another autoimmune disease (Boelaert et al., 2010). This CMT-based intervention was selected because compassion is known to downregulate negative emotions, reduce depression and anxiety (Gilbert & Procter, 2006), improve immune system

Table 3 Reliable changes on questionnaires per participant. *X* indicates which measure showed a reliable change for each participant

Variable	P1	P2	P3	P4	P5	P6	P7
Health distress	–	X	X	–	–	X	X
Life satisfaction	X	X	X	X	X	–	X
Positive affect	X	X	–	X	–	–	–
Negative affect	X	X	–	X	–	–	X
Social/role imitations	X	–	–	–	–	X	X
Defeat		X	–	X	X	–	X
Fear of C to self	X	X	–	–	–	–	–
Fear of C from others	X	X	–	–	–	–	–
Fear of C for others	X	X	–	–	X	–	–
HT symptoms	–	X	–	–	–	X	X

functioning and physical well-being (Gilbert et al., 2011; Pace et al., 2009), and lead to a health-related quality of life in chronic conditions (Austin et al., 2021).

The qualitative analysis indicated that the intervention was well received and effective in increasing self-awareness, emotion, and behavior regulation. Participants described feeling more capable of understanding and analyzing their feelings and thoughts, while regulating their behavior. They explained that they moved from resentment to acceptance and that they are more optimistic. They developed more compassionate approaches to themselves and others with improved mentalization. After the intervention, they noticed less muscle pain, less headaches, and more relaxation in their bodies, and they felt calmer, less anxious, and managed to increase their sleep quality.

A supportive RCI analysis also indicated that the mean change on the questionnaires was in the expected direction, in line with the qualitative analysis. The only exception was fear of compassion from others subscale where the score increased after the intervention. This increase is somewhat different from what was reported in the qualitative analysis, as in the interviews some participants referred to tendencies to open up to others. However, they specifically mentioned this is something that it is being worked on and requires effort. Indeed, in the qualitative analysis, self-compassion and compassionate attitude towards others were more omnipresent than the ability to stay open to receive compassion from others. This can potentially be explained by the reactivation of attachment memories.

Compassion is the motivation to engage with suffering and distress which can be difficult. Most of the participants reported difficulties in performing the compassion exercises, especially the ones that increased the awareness of negative emotions, related to attachment figures, or where imagining or practicing self-compassion was omnipresent. CMT exercises can reactivate the attachment and caring system and trigger emotional memories. Previous work has shown that feelings of warmth associated with compassion from others can bring feelings of grief. This can be due to affection needs that were not fulfilled, which can enhance an increased awareness of an inner state of loneliness (Gilbert et al., 2011). Taking steps towards recognizing and addressing these personal sources of suffering can understandably generate resistance and a desire to maintain. Helping clients normalize the process of wanting to resist and avoid while at the same time providing compassionate steps that can be taken overtime can be helpful. The degree to which individuals are able to persist in that practice and see long-term change is an important topic for subsequent studies. Negative reactions, unpleasant emotions, and short-term initial discomfort are common responses to mindfulness interventions, but they constitute a crucial part of the psychotherapeutic process that helps participants rationalize and understand them while learning new coping strategies (Creswell, 2017).

Previous findings suggest that individuals develop "blockages and fears of compassion" due to threat experiences and lack of affiliation in early years (Gilbert, 2009). Compassion is assumed to stem from the affiliate and caring behavior that individuals receive during infancy. The ability to respond with acceptance to being cared for is developed along with the attachment systems. By extension, infants that experienced limited compassion from their caregivers might be resistant to accepting compassion from others as adults (Gilbert, 2009). The possibility of HT development being partially caused by early adversity should be further examined.

Taken together, after the intervention, participants became more mindful and able to mentalize, more able to validate their experiences and hold difficult emotions in a compassionate mind state, started perceiving the disease in a different way, developed a sense of belongingness, worked through difficult emotions associated with the disease, and improved their physical symptoms and sleep quality.

Limitations and Future Research

This study has several limitations, such as the small sample size and the lack of a control group that could provide more solid evidence for a positive effect of the intervention. Also, due to technical problems, there was a large dropout on the quantitative measures. Furthermore, the 6-week timeframe was selected to ensure a balance between acceptability and effectiveness, as well as to spread the content across time to avoid information overload. However, there is no evidence that this duration is the most effective. Participants reported 6 weeks to be a satisfactory duration as a starting point, but only if this is accompanied by repetition in the form of homework or becomes a way of living. Future studies are welcome to try a longer intervention period to investigate the potential of further effectiveness. A shorter intervention time would not be recommended based on participants' views, but also in line with initial resistance that can occur when one is engaging with distress and suffering.

The intervention included several techniques and approaches, including psychoeducational theory, and experiential exercises such as meditation, imagery, and breathing relaxation, based mainly on CMT with elements of ACT and EMDR. It is not clear from the current results which components of the intervention contributed to the beneficial effects. Future studies could in- or exclude specific components in different individuals to shed light on their contribution to overall effectiveness or their specific effect on certain symptoms or processes. Furthermore, considering that in the RCI analysis fear of compassion from others showed an opposite direction than that what would be desired, future studies replicating the

intervention's rationale and methodology could explore how this aspect can be improved. Another limitation of this study is that the intervention's effects in patients are estimated using their own perceptions of their experience, increasing the risk for common method bias.

Moreover, participants were not specifically selected for lack of self-compassion or for high levels of distress. When compared with available norm scores for the various questionnaires, participants showed considerably lower life satisfaction and positive mood and higher negative mood than a community sample (Diener et al, 1985; Watson et al., 1988), and experienced more health distress and social/role limitations than what was previously found in patients with chronic health conditions (Lorig, et al., 2001). Which patients will benefit most from the current intervention remains to be determined. Although our sample appeared quite distressed, one can imagine that patients scoring in the clinical range of depression may experience less benefit from a self-help intervention and would require more intensive or additional treatment.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12671-022-01914-7.

Acknowledgements We would like to sincerely thank Thyroid UK organization for announcing the research among their members, all patients who participated in the study, and Prof. Paul Gilbert for his useful comments on the research paper.

Author Contribution ZP: performed the qualitative analysis and wrote the paper. AHG: designed the study, built the intervention, interviewed the participants. MLP: co-designed the study, performed the quantitative data analyses, and collaborated in the writing and editing of the final manuscript. ZP, AHG, and MLP: approved the final version of the manuscript for submission.

Data Availability Quantitative data are available at the Open Science Framework (https://osf.io/7h2ez). Because no explicit consent was given for sharing the interview transcripts, the qualitative data are not available.

Declarations

Ethics Statement Ethical approval for this study was obtained from the Ethical Review Committee of the Faculty of Psychology and Neuroscience (ERCPN-187_06_01_2018).

Informed Consent Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

Conflict of Interest AHG is the founder and director of Hashimoto. Help. Hashimot.Help is a non-profit organization offering evidence-based services aimed at (1) the early detection and prevention of Hashimoto thyroiditis and (2) the improvement of the quality of life of patients with Hashimoto thyroiditis. MLP is part of the advisory board of Hashimoto.Help. ZP has nothing to disclose.

References

Austin, J., Drossaert, C. H. C., Schroevers, M. J., Sanderman, R., Kirby, J. N., & Bohlmeijer, E. T. (2021). Compassion-based interventions for people with long-term physical conditions: A mixed methods systematic review. *Psychology & Health, 36*(1), 16–42. https://doi.org/10.1080/08870446.2019.1699090

Bauer, M., Goetz, T., Glenn, T., & Whybrow, P. C. (2008). The thyroid-brain interaction in thyroid disorders and mood disorders. *Journal of Neuroendocrinology, 20*(10), 1101–1114. https://doi.org/10.1111/j.1365-2826.2008.01774.x

Boelaert, K., Newby, P. R., Simmonds, M. J., Holder, R. L., Carr-Smith, J. D., Heward, J. M., Manji, N., Allahabadia, A., Armitage, M., Chatterjee, K. V., Lazarus, J. H., Pearce, S. H., Vaidya, B., Gough, S. C., & Franklyn, J. A. (2010). Prevalence and relative risk of other autoimmune diseases in subjects with autoimmune thyroid disease. *The American journal of medicine*, *123*(2). https://doi.org/10.1016/j.amjmed.2009.06.030

Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology*, *3*(2). https://doi.org/10.1191/1478088706qp063oa

Brown, S. L., & Brown, R. M. (2015). Connecting prosocial behavior to improved physical health: Contributions from the neurobiology of parenting. *Neuroscience and Biobehavioral Reviews, 55*, 1–17. https://doi.org/10.1016/j.neubiorev.2015.04.004

Carter, S., Bartal, I.,B. & Porges, E. (2017). The roots of compassion: An evolutionary and neurobiological perspective. In Seppälä, E.M., Simon-Thomas, E., Brown, S.L., Worline, M.C., Cameron, C. D., & Doty, J. R. (Eds). *The Oxford handbook of compassion science* (p. 178–188). Oxford University Press. https://doi.org/10.1093/oxfordhb/9780190464684.013.14

Crawford, J. R., & Henry, J. D. (2004). The positive and negative affect schedule (PANAS): Construct validity, measurement properties and normative data in a large non-clinical sample. *British Journal of Clinical Psychology, 43*(3), 245–265. https://doi.org/10.1348/0144665031752934

Creswell, J. D. (2017). Mindfulness interventions. *Annual Review of Psychology, 68*, 491–516. https://doi.org/10.1146/annurev-psych-042716-051139

Dhokia, M., Elander, J., Clements, K., & Gilbert, P. (2020). A randomized-controlled pilot trial of an online compassionate mind training intervention to help people with chronic pain avoid analgesic misuse. *Psychology of Addictive Behaviors, 34*(7), 726–733. https://doi.org/10.1037/adb0000579

Dickerson, S. S., Gruenewald, T. L., & Kemeny, M. E. (2004). When the social self is threatened: Shame, physiology, and health. *Journal of personality, 72*(6), 1191–1216. https://doi.org/10.1111/j.1467-6494.2004.00295.x

Diener, E., Emmons, R. A., Larsen, R. J., & Griffin, S. (1985). The Satisfaction with Life Scale. *Journal of Personality Assessment*, *49*(1), 71–75.https://psycnet.apa.org/doi/, https://doi.org/10.1207/s15327752jpa4901_13

Dowd, A. J., & Jung, M. E. (2017). Self-compassion directly and indirectly predicts dietary adherence and quality of life among adults with celiac disease. *Appetite, 113*(1), 293–300. https://doi.org/10.1016/j.appet.2017.02.023

Dube, S. R., Fairweather, D., Pearson, W. S., Felitti, V. J., Anda, R. F., & Croft, J. B. (2009). Cumulative childhood stress and autoimmune diseases in adults. *Psychosomatic Medicine, 71*(2), 243–250. https://doi.org/10.1097/PSY.0b013e3181907888

Gilbert, P. (2009). Introducing compassion-focused therapy. *Advances in Psychiatric Treatment, 15*(3), 199–208. https://doi.org/10.1192/apt.bp.107.005264

Gilbert, P. (2010). An introduction to compassion focused therapy in cognitive behavior therapy. *International Journal of Cognitive Therapy, 3*(2), 97–112. https://doi.org/10.1521/ijct.2010.3.2.97

Gilbert, P. (2014). The origins and nature of compassion focused therapy. *British Journal of Clinical Psychology, 53*(1), 6–41. https://doi.org/10.1111/bjc.12043

Gilbert, P. (2020). Compassion: From its evolution to a psychotherapy. *Frontiers in Psychology, 11*, 3123. https://doi.org/10.3389/fpsyg.2020.586161

Gilbert, P., & Allan, S. (1998). The role of defeat and entrapment (arrested flight) in depression: An exploration of an evolutionary view. *Psychological Medicine, 28*(3), 585–598. https://doi.org/10.1017/S0033291798006710

Gilbert, P., & Procter, S. (2006). Compassionate mind training for people with high shame and self-criticism: Overview and pilot study of a group therapy approach. *Clinical Psychology & Psychotherapy: An International Journal of Theory & Practice, 13*(6), 353–379. https://doi.org/10.1002/cpp.507

Gilbert, P., McEwan, K., Matos, M., & Rivis, A. (2011). Fears of compassion: Development of three self-report measures. *Psychology and Psychotherapy: Theory, Research and Practice, 84*(3), 239–255. https://doi.org/10.1348/147608310X526511

Glaesmer, H., Grande, G., Braehler, E., & Roth, M. (2011). The German version of the Satisfaction with Life Scale (SWLS): Psychometric properties, validity, and population-based norms. *European Journal of Psychological Assessment, 27*(2), 127–132. https://psycnet.apa.org/doi/, https://doi.org/10.1027/1015-5759/a000058

Gulseren, S., Gulseren, L., Hekimsoy, Z., Cetinay, P., Ozen, C., & Tokatlioglu, B. (2006). Depression, anxiety, health-related quality of life, and disability in patients with overt and subclinical thyroid dysfunction. *Archives of Medical Research, 37*(1), 133–139. https://doi.org/10.1016/j.arcmed.2005.05.008

Jacobson, N.S., & Traux, P. (1991). Clinical significance: A statistical approach to defining the meaningful change in psychotherapy research. *Journal of Consulting and Clinical Psychology, 59*(1), 12–19. https://psycnet.apa.org/doi/, https://doi.org/10.1037/0022-006X.59.1.12

Kennedy, A. (2014). Compassion-focused EMDR. *Journal of EMDR Practice and Research, 8*(3), 135–146. https://doi.org/10.1891/1933-3196.8.3.135

Kuba, K., & Weissflog, G. (2017). Acceptance and commitment therapy in the treatment of chronic disease. *Psychotherapie, Psychosomatik, Medizinische Psychologie, 67*(12), 525–536. https://doi.org/10.1055/s-0043-118742

Lorig, K. R., Sobel, D. S., Ritter, P. L., Laurent, D., & Hobbs, M. (2001). Effect of a self-management program on patients with chronic disease. *Effective Clinical Practice, 4*(6), 256–262.

Lorig K., Stewart, A., Ritter, P., González, V., Laurent, D., & Lynch J. (1996). *Outcome measures for health education and other health care interventions*. Sage.

Markomanolaki, Z. S., Tigani, X., Siamatras, T., Bacopoulou, F., Tsartsalis, A., Artemiadis, A., Megalooikonomou, V., Vlachakis, D., Chrousos, G. P., & Darviri, C. (2019). Stress management in women with Hashimoto's thyroiditis: A randomized controlled trial. *Journal of Molecular Biochemistry, 8*(1), 3–12.

Mazzola, A., Calcagno, M. L., Goicochea, M. T., Pueyrredòn, H., Leston, J., & Salvat, F. (2009). EMDR in the treatment of chronic pain. *Journal of EMDR Practice and Research*, *3*(2), 66–79. https://psycnet.apa.org/doi/, https://doi.org/10.1891/1933-3196.3.2.66

Moons, W. G., Eisenberger, N. I., & Taylor, S. E. (2010). Anger and fear responses to stress have different biological profiles. *Brain, Behavior and Immunity, 24*(2), 215–219. https://doi.org/10.1016/j.bbi.2009.08.009

Müssig, K., Künle, A., Säuberlich, A. L., Weinert, C., Ethofer, T., Saur, R., Klein, R., Häring, H. U., Klingberg, S., Gallwitz, B., & Leyhe, T. (2012). Thyroid peroxidase antibody positivity is associated with symptomatic distress in patients with Hashimoto's thyroiditis. *Brain, Behavior and Immunity, 26*(4), 559–563. https://doi.org/10.1016/j.bbi.2012.01.006

Nery-Hurwit, M., Yun, J., & Ebbeck, V. (2018). Examining the roles of self-compassion and resilience on health-related quality of life for individuals with Multiple Sclerosis. *Disability and Health Journal, 11*(2), 256–261. https://doi.org/10.1016/j.dhjo.2017.10.010

Ott, J., Promberger, R., Kober, F., Neuhold, N., Tea, M., Huber, J. C., & Hermann, M. (2011). Hashimoto's thyroiditis affects symptom load and quality of life unrelated to hypothyroidism: A prospective case–control study in women undergoing thyroidectomy for benign goiter. *Thyroid, 21*(2), 161–167. https://doi.org/10.1089/thy.2010.0191

Pace, T. W., Negi, L. T., Adame, D. D., Cole, S. P., Sivilli, T. I., Brown, T. D., Issa, M. J., & Raison, C. L. (2009). Effect of compassion meditation on neuroendocrine, innate immune and behavioral responses to psychosocial stress. *Psychoneuroendocrinology, 34*(1), 87–98. https://doi.org/10.1016/j.psyneuen.2008.08.011

Porges S.W (2017) Vagal pathways: Portals to compassion. In Seppälä, E.M., Simon-Thomas, E., Brown, S.L., Worline, M.C. (Eds.). *The Oxford Handbook of Compassion Science* (pp. 189–202). Oxford University Press. https://doi.org/10.1093/oxfordhb/9780190464684.013.15

Rode, D., & Rode, M. M. (2018). The relationship between self-esteem, sense of self-efficacy and level of illness acceptance, and healthful behaviours in patients with long-term illnesses (type II diabetes, Hashimoto's disease). *Health Psychology Report, 6*(2), 158–170. https://doi.org/10.5114/hpr.2018.71635

Royle, L. (2008). EMDR as a therapeutic treatment for chronic fatigue syndrome (CFS). *Journal of EMDR Practice and Research, 2*(3), 226–232. https://doi.org/10.1891/1933-3196.2.3.226

Schubert, C. (2013). Psychoneuroimmunology of the life span: impact of childhood stress on immune dysregulation and inflammatory disease in later life. *Psychotherapie, Psychosomatik, Medizinische Psychologie, 64*(5), 171–180. https://doi.org/10.1055/s-0033-1357175

Skinta, M. D., Lezama, M., Wells, G., & Dilley, J. W. (2015). Acceptance and compassion-based group therapy to reduce HIV stigma. *Cognitive Behavioral Practice, 22*(4), 481–490. https://doi.org/10.1016/j.cbpra.2014.05.006

Sommers-Spijkerman, M. P. J., Trompetter, H. R., Schreurs, K. M., & Bohlmeijer, E. T. (2018). Compassion-focused therapy as guided self-help for enhancing public mental health: A randomized controlled trial. *Journal of Consulting and Clinical Psychology, 86*(2), 101–115. https://doi.org/10.1037/ccp0000268

Trindade, I. A., Pereira, J., Galhardo, A., Ferreira, N. B., Lucena-Santos, P., Carvalho, S. A., Oliveira, S., Skvarc, D., Rocha, B. S., Portela, F., & Ferreira, C. (2021). The LIFEwithIBD Intervention: Study protocol for a randomized controlled trial of a face-to-face Acceptance and Commitment Therapy and Compassion-Based Intervention tailored to people with inflammatory bowel disease. *Frontiers in Psychiatry, 12*, 699367. https://doi.org/10.3389/fpsyt.2021.699367

Uysal, H. B., & Ayhan, M. (2016). Autoimmunity affects health-related quality of life in patients with Hashimoto's thyroiditis. *The Kaohsiung Journal of Medical Sciences, 32*(8), 427–433. https://doi.org/10.1016/j.kjms.2016.06.006

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology, 54*(6), 1063–1070. https://doi.org/10.1037/0022-3514.54.6.1063