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Development of a person-centered conceptual model of perceived fatigability

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Abstract

Purpose Perceived fatigability, reflective of changes in fatigue intensity in the context of activity, has emerged as a potentially important clinical outcome and quality of life indicator. Unfortunately, the nature of perceived fatigability is not well characterized. The aim of this study is to define the characteristics of fatigability through the development of a conceptual model informed by input from key stakeholders who experience fatigability, including the general population, individuals with multiple sclerosis (MS), and individuals with fibromyalgia (FM).

Methods Thirteen focus groups were conducted with 101 participants; five groups with $n=44$ individuals representing the general population, four groups with $n=26$ individuals with MS, and four groups with $n=31$ individuals with FM. Focus group data were qualitatively analyzed to identify major themes in the participants' characterizations of perceived fatigability.

Results Seven major themes were identified: general fatigability, physical fatigability, mental fatigability, emotional fatigability, moderators of fatigability, proactive and reactive behaviors, and temporal aspects of fatigability. Relative to those in the general sample, FM or MS groups more often described experiencing fatigue as a result of cognitive activity, use of proactive behaviors to manage fatigability, and sensory stimulation as exacerbating fatigability.

Conclusions Fatigability is the complex and dynamic process of the development of physical, mental, and/or emotional fatigue. Trait- and state-like biological, psychological, social, and environmental moderators contribute to tremendous variability in fatigability (both between and within-person variability). Future research to further characterize fatigability across populations, test treatments for fatigability, and develop new measures of this construct are greatly needed.

Keywords Fatigue · Fatigability · Multiple sclerosis · Fibromyalgia · Aging

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Introduction

Fatigue—the intensity of perceived tiredness, lack of energy, or exhaustion—is a pervasive symptom in the general population [1] and in almost every acute, chronic, and relapsing clinical condition. There is also some evidence that aging is associated with fatigue [2], but in general this evidence is conflicting [1, 3–9]. One plausible explanation for the disparate findings on the age–fatigue association is a failure to account for fatigue within the context of activity level. For example, older individuals and those with chronic conditions may slow down, spread-out, or pace activities in order to keep fatigue at tolerable levels. A person who limits activity in order to keep fatigue at a tolerable level may report low fatigue intensity, but may tire out very easily if they attempt a more active lifestyle; consequently, examining fatigue intensity alone may not provide a complete picture of an individual's struggle with fatigue.

Attention has recently turned to the related concept of perceived *fatigability*, which reflects the association between subjective fatigue and activity level [10]; in other words, fatigability reflects how a person fatigues as a result of activity. Whereas fatigue reflects the experience or the sensation of a lack of energy, fatigability reflects the process of developing fatigue. Fatigability is conceptualized as having both subjective aspects, *perceived* fatigability (changes in self-reported fatigue in the context of activity), as well as objective aspects, *performance* fatigability (decrement in performance during activity) [10, 11]. Both aspects of fatigability reflect a "whole-person" construct that is distinct from studies of fatigability at a cellular or tissue level (e.g., muscle fatigability) [12, 13]. Because fatigability can be thought of as a ratio of perceived fatigue to activity level, individuals can be placed along a hierarchy ranging from high fatigability (high perceived fatigue/low activity) to low fatigability (low perceived fatigue/high activity) [10]. Fatigability has also been loosely conceptualized as having both physical and mental/cognitive aspects; physical and mental activities seemingly relate to the development of physical and/or mental fatigue. The concept of perceived fatigability has the potential to address the limitations of focusing solely on fatigue intensity by encompassing both the individual's experience of fatigue and functioning.

Despite recent progress, fatigability research is in its infancy. Additional work regarding the identification of fatigability phenotypes, mechanisms, and the most promising points for intervention is necessary. Lack of a formalized conceptual model poses a significant limitation in fatigability research. Furthermore, many unanswered questions remain regarding the very construct of fatigability. For instance, very little is known about the personal experiences of mental and physical fatigability, how these experiences relate to each other, and whether "mental" tasks can be physically fatiguing (or vice versa). Questions regarding aggravating or alleviating factors for fatigability, and how people attempt to prevent or manage fatigability, also remain. Finally, most research has focused on fatigability in older adults or those with multiple sclerosis [14–20]. Consequently, the experience of fatigability across the adult lifespan and clinical populations is understudied.

Limitations in the ability to assess perceived fatigability currently hinder progress in this field of study. Currently, two self-report measures of fatigability have been developed, the Situational Fatigue Scale (SFS) [21], and the Pittsburgh Fatigability Scale (PFS) [22]. Although these measures have advanced our thinking about measurement of perceived fatigability, they have similar weaknesses. Because these measures were not based on a person-centered conceptual model of fatigability, they are overly focused on development of fatigue in the context of a narrow range of activity, lacking breadth in terms of low-level physical activity and mentally intensive activities. This suggests they have limited relevance and sensitivity in more impaired populations or populations that experience fatigability in the context of a wide range of activities. Relatedly, neither measure offers the capability to compare fatigability across conditions or the lifespan; this is especially unfortunate as a measure with this capacity would help address questions about how changes in activity influence fatigue as people age or as clinical conditions progress.

The aim of this report is to define the nature and components of perceived fatigability through the development of a conceptual model informed by input from stakeholders who experience a broad range of fatigability, including a general sample of adults, and individuals with multiple sclerosis (MS) or fibromyalgia (FM). These three groups were selected to provide a diverse sample in terms of age, fatigability, and clinical presentation. The "general population" group is meant to represent the general population in terms of diversity of age and comorbid conditions, with the likely accumulation of morbidity with advancing age. In MS, a progressive neurological condition, fatigue is the most common and debilitating symptom [23], and it is one of the few conditions where fatigability—particularly performance fatigability—has been a construct of interest [14, 15, 17, 18, 20, 24]. In FM, fatigue is one of the most common symptoms, on par with pain in terms of symptom intensity and impact [25, 26] and qualitative findings suggest that people with FM experience high fatigability [27]. Data from these groups, in conjunction with review of the fatigability literature, and input from clinicians and researchers were used to develop a conceptual model; these methods correspond with the standards set by the Patient Reported Outcomes Measurement Information System [28] to define the underlying construct or domain in the process of developing a patient-reported outcome measure (the next aim of this study). Input from these three groups was incorporated to ensure that the model is "person-centered," or based on the accumulated knowledge from a wide range of people, outside of a clinical setting, in a way that acknowledges the complexity and individual nature of the human experience [29, 30]. This conceptual model both describes the construct of perceived fatigability and identifies the most important aspects of fatigability from the perspective of a diverse sample of individuals. A foundational conceptual model such as this is sorely needed to propel the field toward better understanding, assessment, and treatment of fatigability.

Research methods

Study participants

Prior to initiation of data collection, the Medical Institutional Review Board at the University of Michigan (UM) approved all study procedures. Study inclusion criteria were ≥ 18 years of age and ability to read and converse fluently in English. Participants with FM fulfilled the 2016 American College of Rheumatology survey criteria [31] and participants with MS had a physician-confirmed diagnosis. Exclusion criteria were acute illness within the past 2 weeks and MS relapse within 30 days of screening. Participants were recruited through flyers in the community and clinics, existing research participant registries, and advertising the study on a university-based recruitment website (http://www.UMHealthresearch.org). Purposive sampling was used to ensure sample diversity; this was done primarily by recruiting individuals from registries who were known to be older, with increased morbidity, and/or greater physical impairment. Volunteers were screened over the telephone, and eligible individuals provided verbal informed consent prior to study participation. A written copy of the consent form was provided to participants at the focus group. Data were collected 1/26/2017–05/26/2017.

Focus group procedures

Separate focus groups were held for each subgroup—"general population" ($n = 5$ groups), FM ($n = 4$ groups), and MS ($n = 4$ groups); general population groups included two groups with participants ages 18–59 ($n = 15$) and three groups with participants aged 60 years and up ($n = 29$). Group facilitators began each session by describing the purpose of the study and presenting group "ground rules" (e.g., maintaining confidentiality within the group); this was followed by an introduction to the concept of fatigability, with descriptions of distinctions between fatigue and fatigability. The concept and definition of fatigability presented to focus group participants was based on the seminal 2010 article by Eldadah [10] as well as by discussions among the investigators of the current study and of a working group consisting of awardees of a National Institutes of Health grant on measuring fatigability in older adults (RFA-AG-16-013). Facilitators began group discussion with an open-ended question ("How does fatigability relate to your day-to-day experience?") and participants discussed how various activities fatigue them, what the term "fatigability" means to them, what they believe to be the most important aspects of fatigability, how their fatigability has changed over time, and how they manage fatigability in daily life. As the discussion progressed, facilitators asked more targeted open-ended questions to probe fatigability in specific domains to ensure that a broad range of topics was covered (see Focus Group Guide in Supplemental Materials). Each focus group lasted approximately 60 min. After the focus group concluded, the participants completed a battery of demographic, clinical, and health-related quality of life surveys, which are not a focus of this paper.

Data coding and analysis

Data saturation, or the point at which no new information was observed in subsequent groups, was achieved by the third focus group within each subgroup; one to two additional groups per subgroup were held to ensure generalizability of results. Focus group recordings were transcribed verbatim and reviewed by two investigators (ALK and NEC) who developed a hierarchical taxonomy or "codebook" through an ongoing, iterative, deductive, and inductive analytical process. The aim of this thematic content analysis was to identify fatigability themes in the text [32–34]. After an initial draft of the codebook was developed, the full team of investigators, consisting of two clinical psychologists, a rheumatologist, a neurologist/MS specialist, and a doctoral-level occupational therapist—reviewed the transcripts and codebook. Edits, including additions, deletions, and clarification of theme definitions were made to the codebook with group consensus in order to create a finalized version of the codebook to be used in coding all transcripts.

All transcripts were then systematically and independently coded [35, 36] by two Masters-level raters, each of whom used the codebook to identify the themes in the focus group content, using QSR International's NVivo 11 [37] software to code the transcripts. Prior to initiating the coding, the two coders and a third expert coder (ALK) completed an inter-rater reliability exercise designed to ensure the consistent interpretation of the codebook (84% agreement). Raters then coded each focus group independent from one another and then reconciled discrepancies. In cases where an agreement could not be reached, the first author provided reconciliation. Once raters completed coding the transcripts independently, they worked together to create a single report of the themes. Theme reports generated with the NVIVO 11 software were examined by the team of investigators to ensure that the coded content matched theme definitions and fully captured the concepts of interest. Finally, a matrix analysis [34, 38] on the coded transcripts was conducted to facilitate the examination of similarities and differences in the fatigability themes between the groups of older adults, and adults with either MS or FM. For the matrix analysis, a theme report for each subgroup was generated allowing for side-by-side comparison of descriptions of fatigability themes between the groups.

Development of a fatigability conceptual model

The conceptual model was generated by the multidisciplinary group of investigators; this process leveraged the focus group findings, review of the literature, and clinical experience to formulate the final model, meant to provide a clear and comprehensive description of the full range of the experience of fatigability.

Results

Sample characteristics

Study sample descriptive statistics for the subgroups are shown in Table 1. Groups did not differ in terms of average age or distributions of sex or race. In terms of the sample as a whole, most (76.2%) of the participants were women. Mean age was 55.2 years (SD = 16.45). Most (85.1%) of the sample was identified as White/Caucasian. The average number of years since diagnosis was 9.3 years (SD = 7.1) for FM and 14.5 years (SD = 9.1) for MS. For those with MS, *n* = 25 had relapsing-remitting MS, *n* = 3 had secondary progressive MS, and *n* = 3 had primary progressive MS.

Qualitative themes

Seven major themes were identified in the focus group content: perceived fatigability (general), physical fatigability, mental fatigability, emotional fatigability, moderators of fatigability, proactive and reactive behaviors, and temporal aspects of fatigability. Major themes were present in all groups. These themes are summarized and illustrated with exemplary quotes below. Findings are also summarized in cases where group differences in themes were identified.

Fatigability (general), physical fatigability, mental fatigability, and emotional fatigability

Focus group participants provided descriptions of fatigability in their daily lives as the process of becoming fatigued as a result of activity. Most often, fatigability was described in general terms, with no specific mention of whether the experience reflected the process of developing physical, mental, or emotional fatigue. This was interpreted as a lack of precision when participants spoke spontaneously about fatigue rather than of an experience of developing "general fatigue" based on the fact that, when queried, participants consistently described fatigability in more specific terms. In some cases, participants did spontaneously describe fatigability in terms of developing specifically *physical* fatigue, *mental* fatigue, or *emotional* fatigue. Physical fatigue was described as a lack of physical energy, of feeling "weak" or "physical drained"; some descriptions of physical fatigue were specific to fatigue in certain parts of the body (e.g., Person with MS: "dragging my legs. I can hardly move down the street"). Mental fatigue was described as a lack of energy to think, feeling like "my brain wants to shut down," as "brain fog"

Table 1 Sample descriptive statistics by subgroup (*N* = 101)

Variable	FM *n* = 26	MS *n* = 31	General population *n* = 44	*P* value
Age				
Mean (SD)	54.5 (13.3)	52.4 (14.3)	57.5 (19.2)	0.41
Range	23–76 years	27–90 years	18–85 years	
Sex				
Female, % (*n*)	92.3 (24)	83.9 (26)	61.4 (27)	0.06
Race				
Asian, % (*n*)	0 (0)	3.2 (1)	0 (0)	0.50
Black, % (*n*)	7.7 (2)	6.5 (2)	9.1 (4)	
White, % (*n*)	84.6 (22)	90.3 (28)	81.8 (36)	
Multiracial, % (*n*)	7.7 (2)	0 (0)	9.1 (4)	

P values generated by Chi-square tests (for race and sex) and analysis of variance test (for age) or "fogginess," and as feeling "mentally tired" or "mentally drained." Emotional fatigue was described as developing a sense of being emotionally "overwhelmed," "empty," "exhausted," "burned out," "defeated," or having no more emotional energy (e.g., "nothing left to give"). Participants' experienced these subtypes of fatigue as being related yet distinct constructs. This was underscored in descriptions of preferences for certain subtypes of fatigue (e.g., Person with MS: "I think that mental fatigue is worst because you can't push through the fatigue like you can with physical [fatigue]"; Older Adult: "When I'm physically fatigued, it almost feels good because I can rest and it feels good to relax. Emotional fatigue sticks with you for a long time"), differential effects of sleep on subtypes of fatigue (e.g., Person with MS: "Poor sleep impacts my mental fatigue more than my physical fatigue"; Older Adult: "With sleep, it has more of an effect on mental fatigue than physical fatigue. Physical fatigability for me is more so because of aging and loss of muscle mass"), and differences in efforts to manage or cope with various types of fatigue (e.g., Young Adult: "It seems like physical fatigue is easier to get over than the mental fatigue"; Older Adult: "I think we have the tools to deal with physical fatigue. We know what to do. With mental fatigue or emotional fatigue, most of the time we don't

Table 2 Focus group quotes that exemplify the themes of general fatigability, physical fatigability, mental fatigability, and emotional fatigability

#		
General (non-specific) fatigability		
1	Person with FM	Those hours of study are as wearing on me as riding my bike or doing exercises
2	Older Adult	Another thing that fatigues me is…computer problems and being on tech support. I try to get help and once I get so frustrated with that, I become fatigued
3	Younger Adult	Just taking care of people I think is very, very draining, taking their problems and putting them on top of yours and having to deal with that
4	Person with MS	I would have an emotion and it would take me and I'd run off like we do, just human nature, be angry or sad or reactive in some way. And it—that would wear me out. It would wear me out with fatigue associated with sort of any emotion, negative or positive emotion, you know even excitement or happiness
5	Older Adult	I have knee issues and if I'm doing something that requires me to be stooping [down], that will fatigue me faster than a mile jogging
6	Person with MS	When you're thinking of a million things, I think that contributes a lot to fatigability. In fact, I have a list of things in my head that I want to get done in the house, work on, and get things done with the baby and my husband, and for myself whenever I get to it. It's constant just running, running, running in my head…that exhausts me a lot, just thinking about that
7	Person with FM	[Moderator: What represents your fatigability?] Processing simultaneous stimulation, like someone's trying to talk to you while you're trying to work with credit card machine. Like those kinds of things just make you want to just shut down
Physical fatigability		
8	Younger adult	Being…physically active or biking to class really does take a lot out of me physically but not mentally
9	Person with MS	I am physically exhausted after going for a walk and going more than a mile with a cane
Mental fatigability		
10	Young adult	I was a medical documentation specialist for 2 years and I was so mentally drained when I got home, I had barely any energy for my three kids
11	Person with FM	If I have a fight with my girlfriend, or I'm out in public and my anxiety is really bad, or I'm trying to read through something and fill something out for Social Security or something and it's really stressing me, then I get very mentally fatigued
12	Young adult	Something that's very mentally fatiguing with me is dealing with my children's stress, feeling like I'm being pelted with a Nerf [toy] gun with "Mommy this, Mommy that." That is very mentally fatiguing
Emotional fatigability		
13	Older adult	I get emotionally fatigued because I worked with people and their problems. And it's like I don't want to hear anything from anybody for the rest of the day. It's not that I wanted to sleep… I'm past knowing what to do. Emotionally fatigued
14	Person with MS	I have real challenges with my mother and I find her emotionally exhausting…spending time with her absolutely wipes me out. She'll frequently come and spend time and I'll just have to excuse myself… it is very draining

have the tools. We don't know what to do."). Exemplar focus group quotes for general, physical, mental, and emotional fatigability are shown in Table 2.

Moderators of fatigability

Considerable individual differences emerged in regard to which activities were considered to be fatiguing. These differences can be partially attributed to relatively stable moderators of the activity/fatigue association, such as disease severity, physical fitness, medication regimens, sleep disorders, comorbidities, and age. Of the relatively stable moderators, personality appeared to exert a strong influence on what activities a person identified as fatiguing. This was particularly apparent in terms of social activities, which extroverts identified as energizing, whereas introverts identified as fatiguing. Participants also noted variability in their fatigability that was attributed to a number of relatively variable moderating factors, including sleep quality, interest/motivation, emotional state, diet, weather, fluctuations in other symptoms (e.g., pain), environmental context (e.g., noisy), social context, and acute illness. Select focus group quotes reflecting the theme of moderators of fatigability are shown in Table 3.

Proactive and reactive behaviors

Participants described behaviors that were either meant to proactively manage fatigability or the impact of fatigability on their life, or behaviors that were reactive to fatigability (e.g., recovery). Giving up certain activities, including relying more on others for help, pacing activities, conserving energy, and carefully planning activities were proactive behaviors described by those who recognized their fatigability and took action to mitigate the increase of fatigue or the decline in functioning as a result of relatively high fatigability. Resting was discussed as a behavior that was sometimes used proactively, to prevent further development of fatigue, and sometimes used to recover from extreme fatigue. Select quotes from this theme are shown in Table 4.

Temporal aspects of fatigability

Fatigability was described as changing (Table 5) across short (within-day, day-to-day, week-to-week; quote 31) and long time frames (years, life stages; quotes 32 and 33). A number of older adults reported that their fatigability changed for the better when they retired (quotes 34–36). Participants explained that even though they are as active or more active during retirement than when working, that they are less fatigable.

Group differences in fatigability themes

Comparison of themes across the groups revealed notable differences, with discussions in the two clinical groups being relatively more similar to each other than to the general samples. In terms of group differences in the descriptions of fatigability, accounts of cognitive activities causing fatigue were commonly mentioned in the FM and MS groups, but rarely discussed in the general population groups (see Table 2, quotes 6 and 7). In terms of group differences in moderators of fatigability, the topic of sensory over-stimulation augmenting the development of fatigue was mentioned in the MS and FM groups (see Table 3, quotes 20 and 21). Participants in the clinical groups also talked about proactively managing fatigability. Those in the FM groups talked frequently about breaking up tasks into smaller pieces and

Table 3 Focus group quotes that exemplify the theme of moderators of fatigability

#		
15	Person with FM	I'm also an introvert and just being around people sucks the life out of me
16	Older adult	I have to be out, going out, meeting my friends, being with my friends or family. Anyway, people energize me. But that's part of being an extrovert…they energize me, they do not tire me
17	Older adult	I think if you're really, really interested in something, you don't even think about getting tired. I take ceramics and I get into class and I do hand building, and I can stand and work and move around, just moving clay from one part of the room to the other. Sometimes I can do that from 9:00 in the morning until 4:00 in the afternoon and never sit and never get tired… I can go through about five pages of The New York Times… if it's something I'm interested in, I don't get fatigued
18	Younger adult	So with me it's all the interest level so if I'm really interested in it there's not fatigue with it but if I'm not interested in it then there's a high amount of fatigue
19	Older adult	In the summer and especially in August with humidity and that kind of thing, I have to walk when it's cool. I have to walk before 10:00 AM or after 7:00 PM. I will become fatigued if I—can't walk that same distance with that same energy. So weather actually affects it more
20	Person with MS	It's sensory stuff—like you walk into a place and there's patterns on the carpet or the lights are different or it's too bright… or there's too many people around and…this is part of what is exhausting about having MS
21	Person with FM	A crowd makes you tired. I think it might have to do with all the noise

Table 4 Focus group quotes that exemplify the theme of proactive and reactive behaviors

#	Group	Quote
22	Person with FM	I have to work my day around it [fatigability] pretty much. I work fulltime and I commute, and so I build time into my day to rest
23	Person with FM	If you have the doctor's appointment 1 day then the next day you don't want to schedule anything because you're going to need to rest
24	Older Adult	When I go out back and start planting or digging, I notice that I can't—I don't last too long. So I sit down is what I do. I don't go and nap, I just sit down and rest and then revitalize
25	Person with MS	This is your new situation and this is how you have to adjust. You can't rake your leaves in the backyard for an hour. Now you have to do 15-min spurts
26	Person with MS	I have to limit what I do and I have to rely on my husband to do some of it
27	Person with MS	I have to plan each minute, so like when I go back to work on thursday, I will basically be doing nothing tomorrow after 2:00, because I know I have to save up all that energy to get up like at 3:30 in the morning
28	Person with MS	I have to plan that that's going to wear me out, so I'll either say no, that's too much so I won't do it. Like certain events that I used to go to I won't go to anymore or I know I have to plan
29	Person with FM	My fatigue can plan a couple of days for me. I've had to rearrange things for a couple days just based on one day
30	Person with FM	I don't do an hour of almost anything. I break it up into smaller pieces

Table 5 Focus group quotes that exemplify the theme of temporal aspects of fatigability

#	Group	Quote
31	Person with FM	For my fatigability, I sometimes can get more done—I get these wonderful spurt days
32	Person with FM	Walking from one end of the house to the other, I have to sit down and it wasn't like that a year ago
33	Older adult	I do notice that I get tired more quickly than I did when I was younger
34	Older adult	I don't have the mental fatigue because I don't have the challenge with as much with the job and I have just enjoyment throughout the day because you make your own decisions pretty much
35	Older adult	I know when I retired it took me a couple of months to get over the fatigue of having been working. I didn't realize how stressful and fatiguing my job was until I wasn't doing it
36	Older adult	When you're working or you're raising children… commitments are made by other people for you and you can't get out of them. So I think it's also less tiring because you're not having to do so many things that you don't really want to do or that's not the time that you want to do them

about planning their daily activities to manage fatigability. Both FM and MS groups talked extensively about using rest to manage fatigability (see Table 4).

Fatigability conceptual model

The person-centered conceptual model of perceived fatigability is shown in Fig. 1. As described by participants, activities are generally experienced as being simultaneously comprised of physical, mental, and social/emotional facets. Engaging in activities can result in the development of physical, mental, and/or emotional fatigue; this process is fatigability. Fatigability can cross activity/fatigue domains; for instance, an activity that is defined as having a primarily mental component (e.g., filling out tax forms) may result in the development of physical fatigue as well as mental fatigue. The perception of fatigability is moderated by both trait- and state-like individual factors, highlighting that fatigability is very individual, and specific to time and context. As fatigue develops, it impacts subsequent activity (fatigue impact). People engage in a wide range of behaviors meant to prevent (proactive) and/or cope with (reactive) increases in fatigue—such as rest, avoidance of activities, delegation of tasks, pacing of activities/energy conservation, planning activities, or other alterations in typical activity. This model of fatigability does not depict a static situation, but rather a constantly and dynamically evolving process where activities that are antecedent causes of fatigue can later be affected by the fatigue that develops.

Discussion

This study provides new evidence as to the complex experience of fatigability as reported by individuals representing a range of fatigability severity. To date, the study of fatigability has been mainly constrained to a few populations—older age adults [10, 22, 39] and those with MS [14–20] and has prioritized examinations of performance fatigability and physical fatigability [11, 22, 40–42]. This

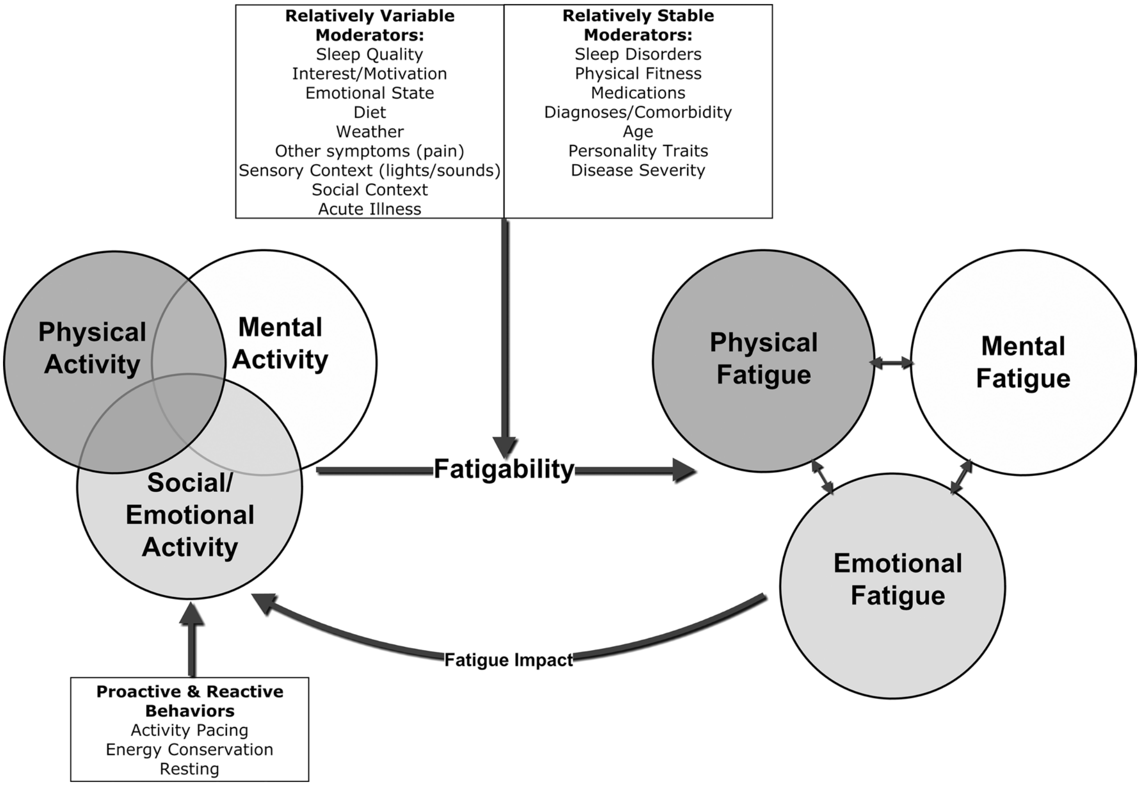

Fig. 1 Person-centered conceptual model of perceived fatigability

study fills a gap in terms of providing a comprehensive examination of perceived fatigability across the adult lifespan and clinical populations. An emphasis on fatigability as a more informative outcome measure, as compared to fatigue intensity, highlights the potential for fatigability to be an important clinical construct across populations in both the clinical and research realms [10]. However, substantial growth in the field of fatigability research is stymied by a number of limitations, including a lack of comprehensive measures of the experience of fatigability, that are applicable across multiple populations. This study offers a much-needed person-centered conceptual model of the experience of fatigability informed by clinicians, researchers, the extant literature on fatigability, and, importantly, by those who experience fatigability in their daily life.

Despite fatigability being an unfamiliar concept to most, the lay people who participated in this study were able to describe, with vivid detail and notable insight, how they experience fatigability in their lives. Their accounts substantiated many of the assumptions of fatigability researchers. For instance, as people age, some experience an increase in physical fatigability and therefore pace themselves more than when they were younger [10]. Participant accounts are also consistent with objective lab-based findings in osteoarthritis on cognitive [43] and physical tasks [42] that indicate increases in fatigue and decreases in physical activity associated with activity.

Perhaps more importantly, the accounts of focus group participants provide unexpected insights about fatigability that can ensure that future fatigability research is relevant to those impacted most by fatigability. One of the most crucial insights is that while there are many stable contributors to an individual's fatigability, fatigability exhibits large within-person variability due to myriad moderators that affect fatigability at any moment. Although we are not aware of any studies looking at moderators of perceived fatigability, in research on performance fatigability, a small body of literature, showing personality factors which are related to metabolic rate, aerobic activity, muscle strength, and walking limitations in older age [44–46], hints at the importance of considering biopsychosocial contributors to fatigability. For many in the fatigability field, there is a desire to define fatigability as a stable biomarker that could reliably phenotype a person's functional status [e.g., frailty; 47, 48]. However, when considering fatigability as a "whole-person" construct, it is essential to fully consider the range of the biological, psychological, social, and environmental contributors to fatigability. The variability in fatigability that emerges from this perspective has both clinical and measurement implications.

In terms of clinical implications, identifying contributors to fatigability could effectively open many doors for intervention. Conceptualizing fatigability from a single perspective (e.g., biomedical, psychological, or social) presents limited treatment options. In contrast, recognizing the full range of factors that may impact fatigability, such as inflammation, muscle strength, stress, posture, exercise, sleep, diet, mood, and physical and social environment opens up many more opportunities for intervention, with potential contributions from a diverse team of clinicians.

In terms of measurement implications, the variability in fatigability presents numerous challenges that must be addressed in future work. For self-report measures, it is not likely adequate to simply ask a person's level of physical fatigue after heavy gardening for 1 h or level of mental fatigue after participating in a social activity, as in currently available self-report measures [21, 22, 49, 50], due to myriad influential contextual factors. However, designing a practicable survey measure that accounts for all possible contextual contributors is unwieldy. Performance-based measures of fatigability are also likely to be subject to the influences of moderators of fatigability. For example, the researcher who measures how a person's walking speed declines over the course of a task (i.e., performance fatigability) may need to consider factors such as: How interested is the participant? How hot is the testing room? Did the participant sleep well? Is the participant on any medications? Did the participant just start a new exercise regimen? etc. Indeed, some studies of muscle fatigability have concluded that central nervous system and psychological factors, such as motivation and tolerance for discomfort, impact performance fatigability [12, 13]. Therefore, the extent to which performance fatigability is about physiology while perceived fatigability is about psychology is an open question that warrants examination, rather than a foregone conclusion [12]. Work to design better measures of both performance and perceived mental and physical fatigability is currently ongoing; any "whole-person" measure of fatigability (i.e., a measure of fatigability of the person as a whole, not of any individual cell, muscle, etc.) will benefit from considering and incorporating the impact from multiple inputs to fatigability. This may call for a profile approach to measuring fatigability, where perceived or performance fatigability is measured concurrent with measures of other person- and environmental-level factors.

Fatigability may be an especially important construct to supplement fatigue intensity in clinical trials [10]. For example, clinical trials that measure fatigue intensity as a primary outcome may be deemed effective, but may improve fatigue by way of reducing activity; the net effect of such an intervention would be that patient function did not improve [51]. Conversely, a treatment that increases fatigue symptom intensity and also increases activity might be deemed ineffective and abandoned when the net outcome is improved patient functioning. Use of a fatigability outcome measure would provide a clearer picture of the impact of an intervention on fatigue symptom burden as well as activity and functioning.

Existing conceptual models of fatigue detail the characteristics and disabling impact of fatigue in fibromyalgia [27, 52] and of the personal, cognitive/behavioral, and pathophysiological contributors to fatigue in rheumatoid arthritis [53]. This conceptual model of fatigability builds on these models of fatigue intensity by highlighting the role of physical, emotional, and mental activities in the process of developing fatigue, the distinct and yet overlapping types of perceived fatigue, and of the likelihood that fatigue, like fatigability, has both stable and variable within-person characteristics.

Better measures of fatigability will also present greater opportunities to understand the mechanisms of fatigue. Despite years of investigation, the biological pathways of fatigue have yet to be determined [54]. If, as we propose, fatigability is a precursor of the experience of fatigue, this construct may better align temporally with proposed biological underpinnings. For example, numerous functional magnetic brain imaging studies of fatigue have uniformly employed fatigue severity as their measure of interest [55, 56]. Since these imaging methods capture real-time data, the potential temporal disconnect between imaging and self-report fatigue severity (designed to capture data over larger timeframes) may, in part, explain variability in published data in this field. Designing such studies around the fatigability construct could provide insights that are more useful.

The construct of fatigability is of especially keen interest to those who treat and study aging individuals. Our findings suggest that in addition to age, health status and major life stressors are important contributors to fatigability. This is illustrated, in part, by the decrease in fatigability with age, as described by some focus group participants. Personal accounts reflecting this "retirement effect" suggest that a sense of more control over activities and increased engagement in self-care and preferred activities (versus obligatory activities during working years) contribute to a perception of decreased fatigability in retirement relative to when they were employed. It is important to note that the positive effects of retirement were described by individuals who were relatively healthy and who did not have substantial caregiver responsibilities. For these individuals, even though they have aged since their working years, they perceive an increase in endurance due to lower stress and decreased obligations. However, older individuals with significant medical conditions or who were in a stressful caregiving situation reported experiencing increased fatigability with age. These findings are consistent with prior research in older adults with osteoarthritis showing that fatigability was associated with poorer health, as indicated by high body mass index, advanced osteoarthritis, and weak knee strength [39]; notably, no association between fatigue intensity and measures of physical health was found in this study. Taken together, these findings suggest that advancing age may impart increased fatigability in part due to a natural accumulation of comorbid conditions with age and/or stressful caregiver responsibilities.

Strengths and limitations

Although this study represents the first attempt to develop a person-centered conceptual model of fatigability in an effort to support future fatigability research and clinical care, there are a number of limitations that should be mentioned. Given our focus on FM, MS, and the general population, the generalizability of these results to other clinical conditions is uncertain; future research that examines the fit of this conceptual model to other populations is warranted. In addition, the majority of study participants were female (which is somewhat reflective of the FM and MS populations that are predominantly female [57–59]), well-educated, and the sample was predominantly Caucasian. More work is needed to confirm the generalizability of these findings to both males (especially those with chronic conditions), as well in minority subgroups. Also, all of the focus group participants were sufficiently well and energetic to participate in the in-person focus group. Therefore, the perspectives of those with the most severe fatigability may not be reflected in these data. The data collection and analysis strategy, while providing a rich and comprehensive perspective of fatigability, does not allow for quantification of findings or quantitative comparison of which themes were more or less important to the groups. Consequently, findings of differences for the clinical groups warrant replication.

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Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to declare.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Lerdal, A., et al. (2005). Fatigue in the general population: A translation and test of the psychometric properties of the Norwegian version of the fatigue severity scale. *Scandinavian Journal of Public Health, 33*(2), 123–130.
2. Avlund, K., Damsgaard, M. T., & Schroll, M. (2001). Tiredness as determinant of subsequent use of health and social services among nondisabled elderly people. *Journal of Aging and Health, 13*(2), 267–286.
3. Cheng, H., Gurland, B. J., & Maurer, M. S. (2008). Self-reported lack of energy (anergia) among elders in a multiethnic community. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 63*(7), 707–714.
4. Beutel, M. E., et al. (2004). Age-related complaints in women and their determinants based on a representative community study. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 117*(2), 204–212.
5. Beutel, M. E., et al. (2002). Complaints of the ageing male based on a representative community study. *European Urology, 41*(1), 85–92.
6. Liao, S., & Ferrell, B. A. (2000). Fatigue in an older population. *Journal of the American Geriatrics Society, 48*(4), 426–430.
7. Junghaenel, D. U., et al. (2011). Demographic correlates of fatigue in the US general population: Results from the patient-reported outcomes measurement information system (PROMIS) initiative. *Journal of Psychosomatic Research, 71*(3), 117–123.
8. Fuhrer, R., & Wessely, S. (1995). The epidemiology of fatigue and depression: A French primary-care study. *Psychological Medicine, 25*(5), 895–905.
9. Bardel, A., et al. (2009). Age-specific symptom prevalence in women 35–64 years old: A population-based study. *BMC Public Health, 9*, 37.
10. Eldadah, B. A. (2010). Fatigue and fatigability in older adults. *PM&R, 2*(5), 406–413.
11. Kluger, B. M., Krupp, L. B., & Enoka, R. M. (2013). Fatigue and fatigability in neurologic illnesses: Proposal for a unified taxonomy. *Neurology, 80*(4), 409–416.
12. Enoka, R. M. (1995). Mechanisms of muscle fatigue: Central factors and task dependency. *Journal of Electromyography and Kinesiology, 5*(3), 141–149.
13. Stokes, M. J., Cooper, R. G., & Edwards, R. H. (1988). Normal muscle strength and fatigability in patients with effort syndromes. *BMJ, 297*(6655), 1014–1017.
14. Aldughmi, M., Bruce, J., & Siengsukon, C. F. (2017). Relationship between fatigability and perceived fatigue measured using the neurological fatigue index in people with multiple sclerosis. *International Journal of MS Care, 19*(5), 232–239.
15. Aldughmi, M., et al. (2016). The relationship between fatigability and sleep quality in people with multiple sclerosis. *Multiple Sclerosis Journal–Experimental, Translational and Clinical, 2*, 2055217316682774.
16. Hameau, S., et al. (2017). Adaptations of fatigue and fatigability after a short intensive, combined rehabilitation program in patients with multiple sclerosis. *Journal of Rehabilitation Medicine*. https://doi.org/10.2340/16501977-2277.
17. Harrison, A. M., Nair, R., & Moss-Morris, R. (2017). Operationalising cognitive fatigability in multiple sclerosis: A Gordian knot that can be cut? *Multiple Sclerosis Journal, 23*(13), 1682–1696.

18. Loy, B. D., et al. (2017). Relationship between perceived fatigue and performance fatigability in people with multiple sclerosis: A systematic review and meta-analysis. *Journal of Psychosomatic Research, 100*, 1–7.
19. Seamon, B. A., & Harris-Love, M. O. (2016). Clinical assessment of fatigability in multiple sclerosis: A Shift from perception to performance. *Frontiers in Neurology, 7*, 194.
20. Zijdewind, I., Prak, R. F., & Wolkorte, R. (2016). Fatigue and fatigability in persons with multiple sclerosis. *Exercise and Sport Sciences Reviews, 44*(4), 123–128.
21. Yang, C. M., & Wu, C. H. (2005). The situational fatigue scale: A different approach to measuring fatigue. *Quality of Life Research, 14*(5), 1357–1362.
22. Glynn, N. W., et al. (2015). The Pittsburgh Fatigability scale for older adults: Development and validation. *Journal of the American Geriatrics Society, 63*(1), 130–135.
23. Krupp, L. B., et al. (1988). Fatigue in multiple sclerosis. *Archives of Neurology, 45*(4), 435–437.
24. Severijns, D., Van Geel, F., & Feys, P. (2017). Motor fatigability in persons with multiple sclerosis: Relation between different upper limb muscles, and with fatigue and the perceived use of the arm in daily life. *Multiple Sclerosis and Related Disorders, 19*, 90–95.
25. Mease, P. J., et al. (2008). Identifying the clinical domains of fibromyalgia: Contributions from clinician and patient Delphi exercises. *Arthritis Care & Research: Official Journal of the American College of Rheumatology, 59*(7), 952–960.
26. Bennett, R. M., et al. (2007). An internet survey of 2,596 people with fibromyalgia. *BMC Musculoskeletal Disorders, 8*, 27.
27. Mease, P., et al. (2009). Fibromyalgia fatigue-development of a conceptual model based on qualitative patient interviews. *Value in Health, 12*(7), A232–A232.
28. PROMIS. (2013). *PROMIS(R) instrument development and validation scientific standards*. Retrieved August 20, 2018, from http://www.healthmeasures.net/images/PROMIS/PROMISStandards_Vers2.0_Final.pdf.
29. Morgan, S., & Yoder, L. H. (2012). A concept analysis of person-centered care. *Journal of Holistic Nursing, 30*(1), 6–15.
30. Lines, L. M., Lepore, M., & Wiener, J. M. (2015). Patient-centered, person-centered, and person-directed care: They are not the same. *Medical Care, 53*(7), 561–563.
31. Wolfe, F., et al. (2016). 2016 revisions to the 2010/2011 fibromyalgia diagnostic criteria. *Seminars in Arthritis and Rheumatism, 46*(3), 319–329.
32. Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualtiative Research in Psychology, 3*(2), 77–101.
33. Hsieh, H. F., & Shannon, S. E. (2005). Three approaches to qualitative content analysis. *Qualitative Health Research, 15*(9), 1277–1288.
34. Miles, M. B., Huberman, A. M., & Saldana, J. (2014). *Qualitative data analysis: A methods sourcebook* (3rd edn.). Thousand Oaks: Sage Publications.
35. Strauss, A., & Corbin, J. (2008). *Basics of qualitative research: Techniques and procedures for developing grounded theory* (3rd edn.). Thousand Oaks: Sage Publications.
36. Basch, C. E. (1987). Focus group interview: An underutilized research technique for improving theory and practice in health education. *Health Education Quarterly, 14*(4), 411–448.
37. QSR International Pty Ltd. (2012). *NVivo qualitative data analysis software*.
38. Averill, J. B. (2002). Matrix analysis as a complementary analytic strategy in qualitative inquiry. *Qualitative Health Research, 12*(6), 855–866.
39. Murphy, S. L., & Smith, D. M. (2010). Ecological measurement of fatigue and fatigability in older adults with osteoarthritis. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences, 65*(2), 184–189.
40. Murphy, S. L., Kratz, A. L., & Schepens Niemiec, S. L. (2017). Assessing fatigability in the lab and in daily life in older adults with osteoarthritis using perceived, performance, and ecological measures. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences, 72*(1), 115–120.
41. Severijns, D., et al. (2017). The assessment of motor fatigability in persons with multiple sclerosis: A systematic review. *Neurorehabilitation and Neural Repair, 31*(5), 413–431.
42. Schepens, S. L., Kratz, A. L., & Murphy, S. L. (2012). Fatigability in osteoarthritis: Effects of an activity bout on subsequent symptoms and activity. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences, 67*(10), 1114–1120.
43. Kratz, A. L., Schepens, S. L., & Murphy, S. L. (2013). Effects of cognitive task demands on subsequent symptoms and activity in adults with symptomatic osteoarthritis. *American Journal of Occupational Therapy, 67*(6), 683–691.
44. Terracciano, A., et al. (2013). Personality, metabolic rate and aerobic capacity. *PLoS ONE, 8*(1), e54746.
45. Tolea, M. I., et al. (2012). Associations between personality traits, physical activity level, and muscle strength. *Journal of Research in Personality, 46*(3), 264–270.
46. Tolea, M. I., et al. (2012). Personality and reduced incidence of walking limitation in late life: Findings from the health, aging, and body composition study. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 67*(6), 712–719.
47. Simonsick, E. M., et al. (2016). Fatigued, but not frail: Perceived fatigability as a marker of impending decline in mobility-intact older adults. *Journal of the American Geriatrics Society, 64*(6), 1287–1292.
48. Fried, L. P., et al. (2001). Frailty in older adults: evidence for a phenotype. *The Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences, 56*(3), M146–M156.
49. Avlund, K., et al. (1996). Item bias in self-reported functional ability among 75-year-old men and women in three Nordic localities. *Scandinavian Journal of Social Medicine, 24*(3), 206–217.
50. Tiesinga, L. J., Dassen, T. W., & Halfens, R. J. (1998). DUFS and DEFS: Development, reliability and validity of the Dutch Fatigue Scale and the Dutch Exertion Fatigue Scale. *International Journal of Nursing Studies, 35*(1–2), 115–123.
51. Hadley, E. C., et al. (2017). Report: NIA workshop on measures of physiologic resiliencies in human aging. *The Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences, 72*(7), 980–990.
52. Humphrey, L., et al. (2010). Fatigue in fibromyalgia: A conceptual model informed by patient interviews. *BMC Musculoskeletal Disorders, 11*, 216.
53. Hewlett, S., et al. (2011). Fatigue in rheumatoid arthritis: Time for a conceptual model. *Rheumatology, 50*(6), 1004–1006.
54. Norheim, K. B., Jonsson, G., & Omdal, R. (2011). Biological mechanisms of chronic fatigue. *Rheumatology, 50*(6), 1009–1018.
55. Filippi, M., et al. (2002). Functional magnetic resonance imaging correlates of fatigue in multiple sclerosis. *Neuroimage, 15*(3), 559–567.
56. Cook, D. B., et al. (2007). Functional neuroimaging correlates of mental fatigue induced by cognition among chronic fatigue syndrome patients and controls. *Neuroimage, 36*(1), 108–122.
57. Queiroz, L. P. (2013). Worldwide epidemiology of fibromyalgia. *Current Pain and Headache Reports, 17*(8), 356.
58. Ramagopalan, S. V., et al. (2010). Sex ratio of multiple sclerosis and clinical phenotype. *European Journal of Neurology, 17*(4), 634–637.
59. Orton, S. M., et al. (2006). Sex ratio of multiple sclerosis in Canada: A longitudinal study. *The Lancet Neurology, 5*(11), 932–936.