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Similar but different

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Document Version

Publisher's PDF, also known as Version of record

Publication date:

2019

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Joustra, M. L. (2019). *Similar but different: Implications for the one versus many functional somatic syndromes discussion*. [Thesis fully internal (DIV), University of Groningen]. Rijksuniversiteit Groningen.

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Summary

SUMMARY

Clusters of somatic symptoms with no detectable well-defined structural organic pathology can be classified as functional somatic syndromes (FSS). Many functional somatic syndromes (FSS) exist, and every medical specialty seems to have at least one. The exact etiology that underlies the different FSS is not fully understood, but it is assumed to be multifactorial involving biological, psychological, social, and healthcare factors. The phenomenon that FSS are known for substantial clinical and diagnostic overlap has resulted in the so-called lumpers-splitter discussion. Lumpers believe that all FSS result from the same etiology, while splitters take the approach that every separate FSS has its own specific background. The aim of this thesis was to investigate the validity of FSS diagnoses, and to examine to which degree these diagnoses are able to identify separate groups of patients. A large part of this thesis is based on data of the LifeLines cohort study, a multi-disciplinary, prospective cohort study, examining health in the general population.

Since FSS are symptom-based diagnoses, we first examined the most clinically relevant assessment time frame for somatic symptoms in **chapter 2**. We defined relevance as the time frame that best reflects subjective symptom burden in daily life, in terms of quality of life and health anxiety. Our results indicate that the time frame of 4 weeks provided the measure of subjective somatic symptom burden that is clinically most relevant. Furthermore, somatic symptom questionnaires using the 4 weeks' time frame had the best psychometric properties, in terms of internal reliability. This finding may be important, since self-report questionnaires are useful tools to assess symptom burden in patients with an FSS.

We examined the idea that FSS are less serious health conditions than well-defined medical diseases (MD) in **chapter 3**. The aim was to compare functional limitations, defined as quality of life and work participation, in the three main FSS compared to MD. Our study revealed that functional limitations in patients with an FSS are comparable to those in patients with an MD. Patients with an FSS and patients with an MD had a reduced quality of life compared to controls. Controls, patients with an FSS, and patients with an MD reported a comparable frequency of work participation, but working patients with an FSS or an MD worked less hours per week and reported higher sick leave compared to controls.

Thus, functional limitations in patients with an FSS are common, and as severe as those in patients with an MD.

In **chapter 4**, we investigated whether FSS are different names for the same problem by examining networks of the symptoms that compose the diagnostic criteria for chronic fatigue syndrome (CFS), fibromyalgia syndrome (FMS), and irritable bowel syndrome (IBS). Different findings emerged from this study. First, we found that all diagnostic symptoms were connected, either directly or via other symptoms. Second, the network density between diagnoses was in most cases slightly lower than within diagnosis, but differences were small. Main symptoms were important in connecting the different FSS diagnoses. Lastly, clustering of symptoms in the general population revealed a general, musculoskeletal, abdominal, and other symptom cluster. This study suggests that symptom clusters reflecting the different FSS can be identified, but also that these symptom clusters are strongly related.

The validity and the diagnostic overlap between the three main FSS diagnoses based on the official diagnostic criteria was examined in **chapter 5**. Two key findings emerged from this study. First, the diagnostic overlap between the FSS was much higher than would be expected by chance. The diagnostic overlap substantially increased when FSS were more chronic and serious in nature. Second, participants who met the criteria for a specific FSS frequently reported symptoms that were included in the diagnostic criteria of other FSS. This chapter also suggests that the different FSS diagnoses are related.

The hypothesis that FSS are the result of psychological distress, defined as mood or anxiety disorders, was examined in **chapter 6**. We found that patients with CFS, FMS, and IBS suffer from mood and anxiety disorders more often than individuals without FSS, however, in most of them we did not find any indications for psychiatric disorders.

Cognitive symptoms are part of the diagnostic criteria of both CFS and FMS. We therefore examined objective and subjective cognitive functioning in patients with CFS and FMS in **chapter 7**. We revealed that subjective cognitive symptoms are more prevalent in patients with CFS and patients with FMS compared to controls and patients with an MD. We found small differences in objective cognitive

impairments in patients with CFS compared to controls on the domains of visual learning, working memory, and visual attention. These differences could not be explained by comorbid mood or anxiety disorders or the severity of symptoms.

The role of physical activity and sleep in patients with CFS and FMS was examined in **chapter 8**. Our study suggested a role of physical activity and sleep duration in CFS and FMS. We found that Patients with CFS and patients with FMS were significantly less physically active than controls. Patients with CFS reported longer sleep duration than patients with FMS and controls. Both relatively high and low physical activity levels were associated with higher symptom severity in patients with CFS and FMS; this was also true for both relatively long and short sleep duration.

A systematic review and meta-analysis was carried out to examine vitamin and mineral status in patients with CFS and FMS in **chapter 9**. We found little evidence to support our hypothesis that vitamin and mineral deficiencies play a role in the pathophysiology of both CFS and FMS, or that use of nutritional supplements is effective in these patients. Poor study quality and considerable heterogeneity in most studies was found, which makes it difficult to reach a final conclusion.

In **chapter 10**, all findings were summarized and discussed. In this thesis, we found evidence to support both the lumpers' and splitters' perspective. Arguments in favor of the lumpers perspective are the diagnostic overlap, the overlap in reported symptoms, and patient characteristics such as sex, age, lifestyle factors, and functional limitations. Arguments in favor of the splitters perspective include symptom clusters reflecting FSS diagnoses, differences in symptoms between patients with different FSS, and indications for differences in contributing factors. In summary, we can state that, although there is overlap in case definitions, the differences between FSS cannot be ignored. We suggest that FSS may reflect the same underlying syndrome with different subtypes. These subtypes may have their own unique manifestation of specific symptom patterns based on symptoms' bodily systems and share both common as well as unique factors. This underlying syndrome should be more extensively investigated in the future to establish valid and generally accepted diagnostic criteria across medical specialties.

