

## **Supplementary Material**

### **Sub-grouping somatic symptom disorder: an analysis based on the Diagnostic Criteria for Psychosomatic Research**

#### **Materials and Methods**

##### *Participants and Procedure*

The Institutional Review Board of National Taiwan University Hospital (NTUH) approved this study design. This study was performed in NTUH, Yun-Lin Branch in 2016–2017. All subjects were patients with somatic symptom disorder (SSD) who visited the psychiatric outpatient department of NTUH, Yun-Lin Branch. The SSD diagnosis was confirmed by a board-certified psychiatrist according to DSM-5 criteria [1]. Patients with the following conditions were excluded from the study: (1) age younger than 20 or older than 70; (2) psychotic symptoms or a reality disturbance; (3) inability to complete the questionnaires of the present study or having overt cognitive impairment; (4) a terminal physical illness. Data from the subjects were gathered after they completed informed consent.

Demographic data, long-term personality traits, recent psychological states, DSM-5 diagnoses, and Diagnostic Criteria for Psychosomatic Research (DCPR) diagnoses were gathered and analyzed in this study. We used the Tridimensional Personality Questionnaire (TPQ) to measure personality features. Psychological states

included somatic symptoms and health anxiety, as well as comorbid emotional disturbance within the previous weeks to months. The assessment of somatic symptoms and health anxiety consisted of the Patient Health Questionnaire-15 (PHQ-15), Health Anxiety Questionnaire (HAQ), Scale for the Assessment of Illness Behavior (SAIB), Cognitions About Body and Health Questionnaire (CABAH). The emotional disturbance assessment included the Beck Depression Inventory-II (BDI-II), Beck Anxiety Inventory (BAI), and the Penn State Worry Questionnaire (PSWQ). In addition to SSD, three common comorbid DSM-5 diagnoses were also taken into account: major depressive disorder (MDD), generalized anxiety disorder (GAD), and panic disorder. These were confirmed by a board-certified psychiatrist via a DSM-5–based diagnostic interview (an unstructured clinical interview because there is currently no structured Traditional Chinese tool based on DSM-5). DCPR diagnoses were made according to a standardized interview based on the Chinese DCPR. Collecting the above data took about 1.5 hours.

Most subjects visited the psychiatric clinic because: (1) their physical problems had been evaluated by other specialists and seemed to be medically unexplained; (2) although some physical etiology had been found, the symptoms showed limited improvement with non-psychiatric management and were considered to be related to psychological factors. Some patients came directly to the psychiatric out-patient

department because of somatic symptoms or health anxiety. A total of 114 individuals met the eligibility criteria. Five people were unwilling to join the study, and two did not complete the DCPR structured interview; therefore, data from 107 subjects were analyzed in this study. Among them, 27 patients were recruited during their first psychiatric visit, and 80 had visited psychiatric clinics in the past. Seventy-five individuals had at least one psychiatric diagnosis before enrollment, and 19 had been diagnosed as having somatoform (or somatic symptom and related) disorders. The duration of having visited psychiatric clinics for those who were not first visitors was between 2 months and 10 years (median: 1 year). In addition to SSD (n=107), MDD (n=17), GAD (n=39), panic disorder (n=33), and other DSM-5 psychiatric diagnoses in our subjects included obsessive-compulsive disorder (n=3), persistent depressive disorder (n=2), agoraphobia (n=4), and social anxiety disorder (n=2). The most common physical comorbidities were: hypertension (n=13), peptic ulcer (n=13), hepatitis B (n=5), reflux esophagitis (n=5), and gout (n=3).

#### *DCPR Diagnoses*

The DCPR, developed by Fava et al. [2] in 1995, are diagnostic systems with 12 psychosomatic constructs. The DCPR include diagnostic criteria and a standardized interview which can be performed by trained medical staff. DCPR diagnoses can be separated into five categories: abnormal illness behavior (including health anxiety,

disease phobia, thanatophobia, illness denial), somatization syndromes (including functional somatic symptoms secondary to a psychiatric disorder (FSS), persistent somatization, conversion symptoms, anniversary reaction), irritability (including type A behavior, irritable mood), demoralization, and alexithymia [3]. The DCPR have been applied extensively in psychosomatic research; their association with physical diseases and psychiatric disorders has been investigated [4, 5]. The Chinese version of the DCPR were translated by Huang and Liao [6], have shown good reliability and validity, and were used in the present study.

### *Psychological Measurements*

Three categories of questionnaires were used in this study to measure aspects of SSD, comorbid emotional problems, and personality traits.

We used four inventories to measure the somatic and psychological aspects of SSD. The PHQ-15 was used to evaluate the severity of somatic distress and is similar to the concept of SSD criterion A. The original version of the PHQ-15 was developed by Kroenke et al. [7]. It has 15 questions that use a 3-point Likert scale. The psychometric data of the Chinese version of the PHQ-15 have been examined by Liao et al. [8]; its Cronbach's alpha is 0.86 and it can be divided into three factors: cardiovascular, pain-fatigue, and gastrointestinal. The psychological aspects of SSD (criterion B) can be evaluated with the HAQ, SAIB, and CABA. The HAQ

measures overall health anxiety, whereas the SAIB and CABA focus on behavioral and cognitive aspects, respectively. The HAQ was constructed by Lucock and Morley [9] and has 21 questions that are scored from 0 to 3. In our sample, its Cronbach's alpha was 0.96. The SAIB and CABA were developed by Rief et al. [10, 11]. They adopted a 4-point Likert scale and included 25 and 39 items, respectively. Their Cronbach's alphas were both 0.87 in our sample.

We used three inventories to measure comorbid anxiety and depression. The BDI-II and BAI were both developed by Beck [12, 13]. Each of them has 21 questions with scoring between 0 and 3 (higher scores indicating higher severity). The BDI-II measures vegetative and cognitive/affective depressive symptoms, whereas the BAI focuses on the somatic aspect of anxiety. The Chinese versions of the BDI-II and BAI have appropriate reliability and validity (Cronbach's alpha around 0.94–0.95) [14, 15]. The PSWQ evaluates cognitive worry, a construct similar to the psychopathology of GAD. It has 16 items scored on a five-point Likert scale [16]. Psychometric data of its Chinese version have been published (Cronbach's alpha = 0.81–0.89) [17].

We used the TPQ to measure personality features. The TPQ is composed of 100 yes/no questions and has three major dimensions: novelty seeking, harm avoidance, and reward dependence, corresponding to behavioral activation, behavioral inhibition, and drive to maintain social interaction, respectively [18]. A sub-dimension of reward

dependence (persistence) was found to be independent, so it was usually not included in reward dependence scores. Our scoring was based on this principle. The Chinese version of the TPQ was translated by Chen et al. [19], who also determined its validity and reliability.

### *Statistical Analysis*

Sub-grouping was done with a two-step cluster analysis. The sub-typing was based on data from 11 DCPR diagnoses (anniversary reaction was not included because this diagnosis was not present in our sample), which are all categorical variables. The log-likelihood method was adopted for distance measurement and Schwarz's Bayesian Criterion was the clustering criterion. After the clusters were generated, we used Chi-square analysis (categorical variables, including part of the demographic data; DCPR and DSM diagnoses) and ANOVA (continuous variables, including part of the demographic data; the questionnaire scores for somatic symptoms; health anxiety and comorbid emotional disturbance; personality traits) to compare data among different clusters. For factors with significant inter-group difference, post-hoc analysis (the Scheffe method for ANOVA) was adopted for further clarification. We also performed another cluster analysis with regard to DSM-5 diagnoses (considering seven DCPR diagnoses with greater influence on subgrouping as shown in Supplementary Figure SF1 and three DSM-5 diagnoses:

panic disorder, MDD, GAD). SPSS 19 (IBM, USA) software was used for analysis.

## **Secondary Results**

The important DCPR diagnoses for clustering (predictor importance > 0.4) were irritable mood, demoralization, health anxiety, type A behavior, disease phobia, persistent somatization, and FSS. Detailed information is shown in Supplementary Figure SF 1.

Supplementary Table ST 1 shows the demographic data of the five clusters. There were no significant inter-group differences in age, gender, educational level, occupational, or marital status. This implies that the sub-typing was actually based on DCPR diagnoses and not biased by demographic variables.

The results of cluster analysis based on both DCPR and DSM-5 diagnoses (shown in Supplementary Table ST2) can be compared with the original findings in Table 1. In general, new clusters 1-4 were similar to the original ones. There were still high proportions of health anxiety and moderate/severe SSD in the new cluster 2. The new cluster 3 showed GAD and FSS. All subjects in the new cluster 4 had irritable mood; there were more DCPR comorbidities in this sub-group. The new cluster 1 still showed fewer feature; however, considering the increased number of individuals and the higher proportion of demoralization, some people in the original cluster 5 might

enter this sub-group. The main features of the new cluster 5 were panic disorder (100%), coexistent health anxiety (100%), and FSS (52.9%).

### **Limitations**

Several limitations of this study should be mentioned. First, the sample size of 107 was not very large because performing DCPR interviews and completing many types of questionnaires required the participants' cooperation. The small sample size caused several less frequent diagnoses to have limited meaning on sub-typing. In addition, the sample size was less than the optimal number for cluster analysis suggested by some scholars, although similar sample size and variable numbers are not uncommon in the literature [20, 21]. Moreover, we considered only the severity of SSD and common DSM-5 comorbid diagnoses in the between-group comparison. Because of the low numbers of other DSM-5 diagnoses, a quantitative analysis for a similar purpose was not performed. Finally, all subjects were recruited from a psychiatric outpatient department. It is possible that SSD patients in consultation–liaison situations and those visiting other specialists have different DCPR features, which could not be examined in the present study.

### **Extended References**



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**SUPPLEMENTARY TABLE 1 Demographic data of the five clusters**

	<b>Cluster 1</b>	<b>Cluster 2</b>	<b>Cluster 3</b>	<b>Cluster 4</b>	<b>Cluster 5</b>	<b>Statistics</b>	
	<b>(1, n = 24)</b>	<b>(2, n = 21)</b>	<b>(3, n = 27)</b>	<b>(4, n = 18)</b>	<b>(5, n = 17)</b>		
	<b>mean/n</b>	<b>mean/n</b>	<b>mean/n</b>	<b>mean/n</b>	<b>mean/n</b>	<b>F/<math>\chi^2</math></b>	<b>p value</b>
	<b>(<math>\pm</math> SD/%)</b>	<b>(<math>\pm</math> SD/%)</b>	<b>(<math>\pm</math> SD/%)</b>	<b>(<math>\pm</math> SD/%)</b>	<b>(<math>\pm</math> SD/%)</b>		
<b>Age (years)</b>	47.21 ( $\pm$ 14.37)	49.67 ( $\pm$ 11.77)	44.26 ( $\pm$ 12.12)	46.56 ( $\pm$ 11.77)	46.35 ( $\pm$ 8.90)	0.604	0.661
<b>Gender (male)</b>	9 (37.5%)	9 (42.9%)	10 (37.0%)	7 (38.9%)	5 (29.4%)	0.749	0.945
<b>BMI (kg/m<sup>2</sup>)</b>	22.68 ( $\pm$ 3.35)	22.74 ( $\pm$ 3.00)	23.02 ( $\pm$ 4.66)	23.30 ( $\pm$ 3.43)	22.42 ( $\pm$ 2.49)	0.159	0.959
<b>Educational level (years)</b>	13.67 ( $\pm$ 3.46)	12.57 ( $\pm$ 2.77)	13.26 ( $\pm$ 2.97)	13.50 ( $\pm$ 2.85)	12.76 ( $\pm$ 2.41)	0.549	0.700
<b>Employment (employed)</b>	13 (54.2%)	10 (47.6%)	16 (59.3%)	12 (66.7%)	10 (58.8%)	1.598	0.809
<b>Marital status (married)</b>	18 (75.0%)	19 (90.5%)	19 (70.4%)	11 (61.1%)	13 (76.5%)	4.830	0.305
<b>Exercise hours (hours/day)</b>	0.33 ( $\pm$ 0.43)	0.36 ( $\pm$ 0.57)	0.25 ( $\pm$ 0.48)	0.23 ( $\pm$ 0.40)	0.00 ( $\pm$ 0.00)	1.929	0.111
<b>Cigarette smoking</b>	2 (8.3%)	1 (4.8%)	3 (11.1%)	2 (11.1%)	2 (11.8%)	0.833	0.934
BMI, body mass index							

**SUPPLEMENTARY TABLE 2** Five clusters generated by cluster analysis based on both DCPR and DSM-5 (MDD, GAD, panic disorder) diagnoses. TABLE 1 was based on only DCPR diagnoses.

	New Cluster 1 (1, n = 37) mean/n (± SD/%)	New Cluster 2 (2, n = 16) mean/n (± SD/%)	New Cluster 3 (3, n = 14) mean/n (± SD/%)	New Cluster 4 (4, n = 23) mean/n (± SD/%)	New Cluster 5 (5, n = 17) mean/n (± SD/%)	Statistics		
						F/ $\chi^2$	p value	Comparison
<i><b>DCPR diagnoses</b></i>								
<b>Health anxiety</b>	15 (40.5%)	14 (87.5%)	1 (7.1%)	10 (43.5%)	17 (100.0%)	37.705	< 0.001***	5>1,3,4; 2>1,3
<b>Disease phobia</b>	1 (2.7%)	8 (50.0%)	0 (0%)	3 (13.0%)	3 (17.6%)	23.603	< 0.001***	2>1,3
<b>Thanatophobia</b>	1 (2.7%)	3 (18.8%)	0 (0%)	4 (17.4%)	5 (29.4%)	11.021	0.026*	5>1
<b>Illness denial</b>	1 (2.7%)	0 (0%)	0 (0%)	2 (8.7%)	0 (0%)	4.287	0.369	-
<b>FSS</b>	2 (5.4%)	1 (6.3%)	11 (78.6%)	7 (30.4%)	9 (52.9%)	36.168	< 0.001***	3>1,2,4; 5>1,2
<b>Persistent somatization</b>	9 (24.3%)	14 (87.5%)	6 (42.9%)	19 (82.6%)	8 (47.1%)	28.713	< 0.001***	2,4>1
<b>Conversion symptoms</b>	1 (2.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1.910	0.752	-
<b>Type A behavior</b>	13 (35.1%)	8 (50.0%)	7 (50.0%)	13 (56.5%)	6 (35.3%)	3.606	0.462	-
<b>Irritable mood</b>	2 (5.4%)	0 (0%)	1 (7.1%)	23 (100.0%)	6 (35.3%)	75.025	< 0.001***	4>1,2,3,5; 5>1
<b>Demoralization</b>	11 (29.7%)	15 (93.8%)	3 (21.4%)	17 (73.9%)	5 (29.4%)	30.880	< 0.001***	2>1,3,5; 4>1,3
<b>Alexithymia</b>	1 (2.7%)	2 (12.5%)	0 (0%)	1 (4.3%)	0 (0%)	4.751	0.314	-
<i><b>DSM-5 diagnoses</b></i>								
<b>Moderate/severe SSD<sup>+</sup></b>	17 (45.9%)	12 (75.0%)	5 (35.7%)	13 (56.6%)	11 (64.7%)	6.537	0.162	-
<b>MDD</b>	8 (21.6%)	2 (12.5%)	0 (0%)	7 (30.4%)	0 (0%)	10.545	0.032*	#
<b>GAD</b>	7 (18.9%)	9 (56.3%)	12 (85.7%)	9 (39.1%)	2 (11.8%)	26.829	<0.001***	3>1,5
<b>Panic disorder</b>	13 (35.1%)	0 (0%)	0 (0%)	3 (13.0%)	17 (100.0%)	55.235	<0.001***	5>1,2,3,4

### *Psychological states*

<b>PHQ-15</b>	10.97 (± 5.83)	14.88 (± 4.69)	13.86 (± 6.29)	15.52 (± 4.79)	11.82 (± 5.49)	3.240	0.015*	#
<b>HAQ</b>	23.41 (± 13.31)	32.19 (± 10.98)	21.14 (± 13.05)	32.43 (± 12.75)	29.82 (± 13.71)	3.285	0.014*	#
<b>SAIB</b>	37.62 (± 11.50)	46.19 (± 11.14)	36.93 (± 9.87)	37.09 (± 14.13)	38.29 (± 6.84)	2.047	0.093	-
<b>CABAH</b>	60.57 (± 12.52)	70.44 (± 10.71)	60.29 (± 17.23)	64.26 (± 10.83)	59.88 (± 9.68)	2.331	0.061	-
<b>PSWQ</b>	52.43 (± 12.18)	61.63 (± 9.93)	55.36 (± 9.27)	61.87 (± 10.99)	51.29 (± 10.46)	4.445	0.002**	4>1
<b>BDI-II</b>	15.70 (± 8.58)	26.06 (± 12.14)	13.43 (± 6.76)	29.22 (± 13.36)	14.41 (± 5.46)	11.247	<0.001***	2,4>1,3,5
<b>BAI</b>	16.35 (± 10.45)	21.63 (± 9.55)	18.71 (± 11.55)	26.43 (± 11.82)	17.18 (± 11.00)	3.470	0.011*	4>1

### *Personality traits*

<b>Novelty seeking</b>	14.78 (± 3.77)	12.81 (± 3.82)	13.50 (± 4.05)	13.65 (± 3.17)	15.00 (± 5.77)	1.011	0.405	-
<b>Harm avoidance</b>	20.32 (± 5.50)	25.81 (± 4.55)	21.50 (± 5.23)	23.61 (± 6.32)	19.94 (± 6.35)	3.665	0.008**	2>1
<b>Reward dependence</b>	12.89 (± 3.45)	12.25 (± 2.93)	13.64 (± 2.62)	12.04 (± 3.44)	13.35 (± 3.10)	0.804	0.525	-
<b>Persistence</b>	5.49 (± 1.61)	4.88 (± 1.63)	5.43 (± 1.79)	6.30 (± 1.69)	4.88 (± 1.76)	2.450	0.051	-

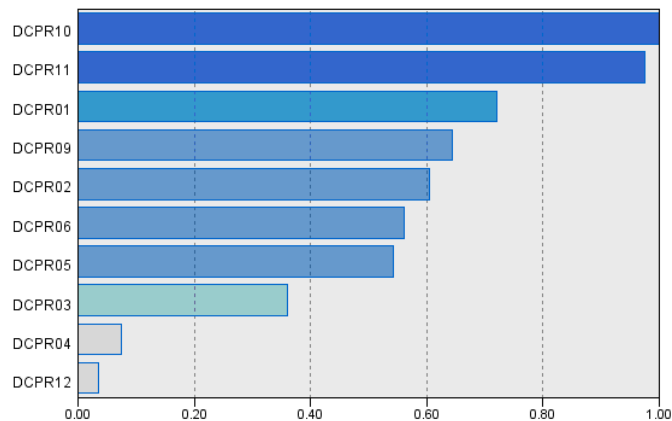
\*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001

# No significant difference using the Bonferroni (for Chi-square) or Scheffe (for ANOVA) method

<sup>+</sup>According to the severity specifiers of DSM-5 somatic symptom disorder. Because only three subjects had severe SSD, the numbers or moderate and severe SSD patients were summed

DCPR, Diagnostic Criteria for Psychosomatic Research; DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; FSS, functional somatic symptoms secondary to a psychiatric disorder; SSD, somatic symptom disorder; MDD, major depressive disorder; GAD, generalized anxiety disorder; PHQ-15, Patient Health Questionnaire-15; HAQ, Health Anxiety Questionnaire; SAIB, Scale for the Assessment of Illness Behavior; CABAH, Cognitions about Body and Health Questionnaire; PSWQ, Penn State Worry Questionnaire; BDI-II, Beck Depression Inventory-II; BAI, Beck Anxiety Inventory

**SUPPLEMENTARY FIGURE 1 Predictor importance for the clustering of 107 patients with somatic symptom disorder. Predictor importance is a quantitative index for estimating the influence of variables on clustering. Its value is between 0-1; a higher value indicates greater importance. The common cutoff for an obvious influence is 0.4. The most important DCPR diagnoses for sub-grouping are irritable mood, demoralization, and health anxiety.**



DCPR, Diagnostic Criteria for Psychosomatic Research; DCPR10, irritable mood; DCPR11, demoralization; DCPR01, health anxiety; DCPR09, type A behavior; DCPR02, disease phobia; DCPR06, persistent somatization; DCPR05, functional somatic symptoms secondary to a psychiatric disorder; DCPR03, thanatophobia; DCPR04, illness denial; DCPR12, alexithymia