RESEARCH ARTICLE

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The Reliability and Validity of the Dutch Version of the Composite Autonomic Score and the Relationship with Pupillometry in Chronic Pain Patients

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ABSTRACT

Background: Functional disorders of the Autonomic Nervous System (ANS) are associated with chronic pain syndromes. The COMPASS 31 score is a validated measure of the severity of autonomic impairment. Pupillometry is a rapid, non-invasive, and valuable indicator of autonomic nervous system function.

Objectives: The present study aimed to develop and evaluate the reliability of the Dutch version of the COMPASS-31 and to determine whether pupillometry is related to the autonomic scores of the COMPASS-31.

Methods: A retrospective study of all chronic pain patients who had Pupillometry and completed the COMPASS-31 score in Pain Clinic De Bilt in the period from January 2025 to May 2025 (n=62). We explored the reliability of the COMPASS-31 test by determining Cronbach's alpha and Intra-Class Correlation Coefficients (ICC agreement). We also calculated the Spearman correlation coefficients among the six domains of the COMPASS-31 and pupillometry observations and among the items of the COMPASS-31 and pupillometry values.

Results: This study examined 62 pain patients using the patient-reported outcome measure COMPASS-31 after it was translated into Dutch and utilized a pupillometer. We calculated the correlations between the COMPASS-31 items and the pupillometry values. These correlations reveal a clear relationship between pupillometry and the COMPASS-31 items that assess autonomic symptoms related to the light perception reaction of the eyes, as well as the response after standing up and experiencing a dry mouth.

Conclusion: The COMPASS-31 is a moderately reliable patient-reported outcome questionnaire looking at multidimensional autonomic domains. The significant relationship between the COMPASS-31 and pupillometry demonstrates construct validity. Objective measurements, such as pupillometry, are not superior to subjective measurements like the patient-reported outcome COMPASS-31.

Keywords: Autonomic Nervous System, Chronic pain syndromes, Pupillometry, Cronbach 's alpha, COMPASS-31, Intra-Class Correlation Coefficients, Spearman correlation.

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INTRODUCTION

Functional disorders of the Autonomic Nervous System (ANS) are associated with chronic pain syndromes, especially in fibromyalgia, neck and back pain, and complex regional pain syndrome[1,2]. Sympathetic activity demonstrates significant positive associations with widespread pain and the severity of symptoms[1].

Patient-Reported Outcome Measures (PROMs) quantify the subjective experiences of patients or populations regarding a health condition and its treatment. The Composite Autonomic Symptom Score (COMPASS-31) is a thirty-one-item survey that indicate the quality of life related to neurodegenerative disorders. This abbreviated COMPASS-31 is a refinement of the Autonomic Symptom Profile (ASP), which contains 169 questions[3]. The COMPASS-31 encompasses six subclasses: Orthostatic Intolerance (OI), Vasomotor (VM), Secretomotor (SM), Gastrointestinal (GI), Bladder (BL), and Pupillomotor (PM). The OI assessment includes four questions, the VM domain includes three questions, the SM domain includes four questions, the GI domain includes twelve questions, the BL domain includes three questions, and the PM domain includes five questions. The raw scores of the items are adjusted using a scoring algorithm. The answers are recorded in categories that vary from two to seven. The domains are weighted with 10 points for OI, 6 points for VM, 7 points for SM, 28 points for GI, 9 points for BL, and 15 points for PM. The investigator calculates a separate score for each item on the COMPASS-31 (**Table 1**) and a total score for each domain. The COMPASS-31 has been translated into Italian[4,5], Croatian, Serbian[6,7], Indian[8], Korean[9], German[10], Norwegian[11], and Turkish[12]. We translated the 31 items of the COMPASS-31 into Dutch according to the generally accepted rules for translating non-Dutch questionnaires[13-15].

Pupillometry is a rapid, non-invasive, and valuable indicator of autonomic nervous system function[16]. It assesses the basal pupil diameter and components of the pupillary light reflex (PLR). The pupil muscles receive opposed stimulation from the sympathetic and parasympathetic ANS. Hence, measurements of separate sections of the PLR can be used to indicate sympathetic or parasympathetic modulation[17]. The present study aimed to develop and evaluate the reliability of the Dutch version of the COMPASS-31 and to determine whether pupillometry is related to the autonomic scores of the COMPASS-31.

METHODS

Design

This study includes all chronic pain patients who had Pupillometry and completed the COMPASS-31 score twice, with a period of 30 minutes between the two completions in Pain Clinic De Bilt in the period from January 2025 to May 2025 (n=62). The Ethics Committee Amsterdam (Amsterdam, the Netherlands) admitted our study (2025.0614).

Data assessment

The information obtained included gender, age, serial measurements with quantitative Pupillometry, and information on the 31 items of the COMPASS-31 questionnaire.

Quantitative Pupillometry

Using an automated pupillometer, two operators performed serial measurements with quantitative Pupillometry (NeuroLight Algiscan, ID-MED, Marseille, France). Each eye of the patient was measured twice, with five minutes between the measurements. Baseline Pupil Diameter (BPD (mm), Latency of Constriction (LC) (msec), pupillary constriction rate (i.e., the difference between BPD and the post-stimulation pupil diameter, as percentage of constriction from the BPD) (PCR), Maximum Constriction Amplitude (MCA) (mm), and Maximal Constriction Velocity (MCV) (mm/sec) were measured.

COMPASS-31 questionnaire

Two certified bilingual translators independently translated the thirty-one items of the COMPASS-31 into Dutch, adhering to the accepted guidelines for translating non-Dutch questionnaires[13]. Two clinicians reviewed the two translated versions and resolved any differences through revisions. A certified English translator, who is a native speaker, then back-translated the Dutch version of the COMPASS-31 into English. The two clinicians compared this back-translation with the original English version of the COMPASS-31 and refined the Dutch translation to enhance its exactness

Statistics

We used IBM SPSS Statistics for Windows, Version 26.0, Armonk, NY: IBM Corp.. We explored the validity of the COMPASS-31 test by determining Cronbach ‘s alpha

Table 1: Calculation of COMPASS-31 score.

Score	Sum of items	Multiplies by
Orthostatic Intolerance-score	1-4	4
Vasomotor score	5-7	0.8333
Secretomotor score	8-11	2.1428571
Gastrointestinal score	12-23	0.8928571
Bladder-score	24-26	1.111
Pupillomotor score	27-31	0.333
COMPASS-31-score	Sum of all six domain scores	

and intra-class correlation coefficients (ICC agreement). To measure test-retest similarity for each domain of the COMPASS-31, the standard error of measurement (SEM similarity) was determined with the error variance from the ICC formula[18]. We also calculated the Spearman correlation coefficients among the six domains of the COMPASS-31 and pupillometry observations and the Spearman correlation coefficients among the items of the COMPASS-31 and pupillometry values. We calculated the difficulty of the items relative to the pain population of persons who were administered the COMPASS-31. The difficulty of the items was determined by dividing the mean item score by the maximum item score. We assessed the discrimination of the items by measuring the correlation between the item scores of the domains.

RESULTS

We present the details of the patients in (**Table 2**). All patients complained of pain, with females outnumbering males. The mean age was 57 years (SD = 14). The pupillometry values were comparable to our former study's[16]. OI was seen in 66% of the patients. VM symptoms were seen in 27% of the patients. Excessively dry eyes feelings were seen in 26% of the cases, and excessively dry mouth feelings were seen in 24% as a symptom of the SM domain. Bouts of diarrhoea were complained of in 45% of the patients, and constipation in the past year was seen in 36%. In the past year, 39% of the patients lost occasional control of their bladder function. Bright light frequently bothered the eyes in 27% of the patients. Focusing the eyes gave problems occasionally, in 42% of the patients.

We present measures of reliability calculated from repeated measurements of the COMPASS-31 domains **(Table 3)**. Reliability refers to the reproducibility of a measurement. Cronbach's alpha is a reliability parameter that is not based on two repetitive measurements. The Cronbach's alpha across the domains was 0.69 or lower. The calculation of Cronbach's alpha excludes patients with missing values, including those who could not fill in certain items. This reduces the value of Cronbach's alpha. These items are locally dependent, violating local independence. The Cronbach's alpha for the VM domain was zero because the variance of item six was zero, indicating that this item did not contribute to the variance. The Intraclass Correlation Coefficient (ICC) points out the inter-observer reliability of two measurements. We selected a two-way random effects model that emphasizes absolute agreement. We focus on absolute agreement rather than consistency (ranking) in medicine. Reliability was excellent, with Intraclass Correlation Coefficient measures exceeding 0.85. We calculated the standard error of measurement (SEM agreement) for each domain of COMPASS-31 as an indicator of test-retest agreement for repeated measurements. This standard error of measurement, expressed in the unit of measurement, is low.

The calculated difficulties of the items range from 0 to 1 **(Table 4)**. Items with high difficulty values indicate that patients have more severe autonomic symptoms. The first item on OI was the most challenging in this area. Items 2 and 4 in this domain shared the same level of difficulty, as both pertained to complaints over time. The items in the SM domain displayed nearly identical difficulty, suggesting that these items reflect comparable symptom severity for pain patients. The items in the GI domain exhibited a wide range of difficulty, from 0.09 to 0.65. The low difficulty was linked to item 14 regarding vomiting after a meal, while the highest difficulty corresponded to item 22, which addressed the severity of constipation episodes. Items with the same difficulty should be reviewed to determine if any can be eliminated; for example, items 16 and 17 discuss bouts of diarrhoea over time. The BL domain items showed almost equal difficulty, underscoring the need to explore more severe autonomic symptoms related to bladder function. From the PM domain, the symptoms of bright light bothering the eyes (item 27) and difficulty focusing the eyes (item

Table 2: Patient characteristics and pupillometry values.

Characteristics	Number of patients	%	Mean	SD
Male	27	43.5		
Female	35	56.5		
Age (years)			57	14
Baseline pupil diameter (mm) of the eye			3.8	0.82
Maximum constriction amplitude (MCA) (mm) of the eye			0.97	0.61
Maximum constriction velocity (MVC) (mm/sec) of the eye			2.9	1.29
Latency constriction (LC) (msec) of the eye			267.8	71.26

Table 3: Results of the analysis of the COMPASS-31 domains.

COMPASS-31 domains	Orthostatic intolerance	Vasomotor	Secreto-motor	Gastro-intestinal	Bladder	Pupillomotor	Sum score
Mean score (SD)	12.4 (10.4)	0.71 (1.2)	3.1 (3.7)	6.1 (5.2)	1.7 (2.0)	1.8 (1.4)	25.7 (16.4)
Cronbach 's alpha	0.6	0	0.58	0.69	0.69	0.69	0.5
Intra-class correlation coefficient (agreement)	0.94	0.99	0.92	0.98	0.96	0.97	0.96
Standard error of measurements (agreement)	2.54	0.1	1	0.67	0.38	0.24	3.33

Table 4: The difficulty of the items of the COMPASS-31.

Item	N	Maximum score	Mean	Item difficulty
Orthostatic 1	62	1	0.66	0.66
Orthostatic 2	41	3	1.15	0.38
Orthostatic 3	41	3	1.44	0.48
Orthostatic 4	41	3	1.1	0.37
Vasomotor 1	62	1	0.27	0.27
Vasomotor 2	15	2	1	0.5
Vasomotor 3	16	3	1.31	0.44
Secretomotor 1	61	2	0.33	0.17
Secretomotor 2	61	1	0.26	0.26
Secretomotor 3	62	1	0.24	0.24
Secretomotor 4	58	3	0.66	0.22
Gastrointestinal 1	61	2	0.56	0.28
Gastrointestinal 2	62	2	0.79	0.395
Gastrointestinal 3	62	2	0.18	0.09
Gastrointestinal 4	62	2	0.74	0.37
Gastrointestinal 5	62	1	0.45	0.45
Gastrointestinal 6	28	3	1.29	0.43
Gastrointestinal 7	28	3	1.86	0.62
Gastrointestinal 8	28	3	1.36	0.45
Gastrointestinal 9	62	1	0.4	0.4
Gastrointestinal 10	23	3	1.48	0.49
Gastrointestinal 11	22	3	1.95	0.65
Gastrointestinal 12	23	3	1.09	0.36
Bladder 1	62	3	0.48	0.16
Bladder 2	62	3	0.44	0.15
Bladder 3	62	3	0.58	0.19
Pupillomotor 1	62	3	1.08	0.36
Pupillomotor 2	37	3	1.97	0.66
Pupillomotor 3	62	3	1.03	0.34
Pupillomotor 4	40	3	1.82	0.61
Pupillomotor 5	61	3	1.07	0.36

29) were equally severe for the patients. The items (28 and 30) discussing the severity of these complaints exhibited the highest symptom seriousness in this domain.

The discrimination index for an item represents a correlation, with values ranging from -1 to 1 **(Table 5)**. Discrimination indicates how consistent an item is with other items in a domain. The correlations were positive and significant. The correlation for item 5 could not be calculated because the answers were constant. The scoring algorithm causes this. Both parts of the body (hands and feet) get the same code (one). The recording of item 5 should be changed to two different codes.

We computed correlations between COMPASS-31 items and pupillometry measurements **(Table 6)**. The BPD refers to the diameter before the light stimulus is activated, while the MCV is the highest speed of pupil constriction during the light stimulus. We present only the significant correlations among the 31 items. Patients disturbed by bright light in their eyes (item 27) exhibited higher BPD. Patients who reported faintness, dizziness, feeling goofy, and difficulty concentrating shortly after standing up from a sitting or lying position (item 2) had lower MCV. Patients reporting infrequent constipation (item 21) and experiencing mild episodes of constipation with improving symptoms had higher PCR and lower MCA. Patients with excessive dry mouth (item 10) exhibited higher LC values.

DISCUSSION

This study examined 62 pain patients using the patient-reported outcome measure COMPASS-31 after it was translated into Dutch and utilized a pupillometer. We calculated the correlations between the COMPASS-31 items and the pupillometry values, which included BPD and MCV. These correlations reveal a clear relationship between pupillometry and the COMPASS-31 items that assess autonomic symptoms related to the light perception reaction of the eyes, as well as the response after standing up and experiencing a dry mouth.

Cronbach's alpha values were moderate, while the intra-class correlation coefficients were high. This contradiction results in conflicting conclusions about reliability. The intra-class correlation coefficient might be influenced by the short duration of 30 minutes between observations and the two repetitive measurements of the COMPASS-31, which could have enhanced memory for responding to the items.

We calculated the difficulty and discrimination of the items, which are concepts related to item analysis in Classical

Table 5: The discrimination of the items of the COMPASS-31.

Item	N	Pearson Correlation	Sig. (2-tailed)
Orthostatic 1	62	0.86	0
Orthostatic 2	41	0.76	0
Orthostatic 3	41	0.84	0
Orthostatic 4	41	0.76	0
Vasomotor 1	62	0.95	0
Vasomotor 2	15	a*	
Vasomotor 3	16	0.95	0
Secretomotor 1	61	0.47	0
Secretomotor 2	61	0.65	0
Secretomotor 3	62	0.65	0
Secretomotor 4	58	0.91	0
Gastrointestinal 1	61	0.38	0.02
Gastrointestinal 2	62	0.54	0
Gastrointestinal 3	62	0.49	0
Gastrointestinal 4	62	0.64	0
Gastrointestinal 5	62	0.64	0
Gastrointestinal 6	28	0.42	0.03
Gastrointestinal 7	28	0.61	0
Gastrointestinal 8	28	0.46	0.02
Gastrointestinal 9	62	0.63	0
Gastrointestinal 10	23	0.54	0.01
Gastrointestinal 11	22	0.45	0.03
Gastrointestinal 12	23	0.79	0
Bladder 1	62	0.56	0
Bladder 2	62	0.88	0
Bladder 3	62	0.89	0
Pupillomotor 1	62	0.82	0
Pupillomotor 2	37	0.58	0
Pupillomotor 3	62	0.85	0
Pupillomotor 4	40	0.76	0
Pupillomotor 5	61	0.76	0

a* Cannot be computed because at least one of the variables is constant.

Table 6: Correlations between pupillometry and COMPASS-31 scores.

COMPASS-31 items	Pupillometry	Baseline pupil diameter (mm)	Maximum constriction amplitude (MCA) (mm)	Pupillary constriction rate (PCR) (%)	Maximum constriction velocity (mm/sec) (mm/sec	Latency constriction (LC) (msec)
Orthostatic Intolerance score 2	Pearson Correlation				-0.32	
	Sig. (2-tailed)				0.041	
	N				41	
Secretomotor score score 3	Pearson Correlation					0.294
	Sig. (2-tailed)					0.021
	N					62
Gastro-intestinaal score 10	Pearson Correlation			-0.436		
	Sig. (2-tailed)			0.038		
	N			23		
Gastro-intestinaal score 11	Pearson Correlation			-0.416		
	Sig. (2-tailed)			0.054		
	N			22		
Gastro-intestinaal score 12	Pearson Correlation		0.427	-0.503		
	Sig. (2-tailed)		0.042	0.014		
	N		23	23		
Pupillomotor score 1	Pearson Correlation	0.298				
	Sig. (2-tailed)	0.019				
	N	62				

Test Theory (CTT), even though these calculations are not a formal part of CTT[18]. The item discrimination was good, and the item difficulty provided valuable clues for reconsidering certain items.

The BPD reflects the balance between the iris sphincter muscle, which narrows the pupil, and the dilatory pupillary muscle, which widens the pupil. The dynamics of the PLR consist of four stages: response latency, maximum constriction, a fast dilatation of the pupil, and a slow dilatation where the pupil recovers to its original size[19]. Response latency refers to the delay in pupil constriction after a light stimulus. A rapid constriction of the pupil follows the latency period until it reaches the MCV. The MCA is the distinction between the baseline and minimum pupil diameter. The PCR is calculated as the ratio of MCA to BPD, eliminating the leverage of the BPD. The BPD is firstly driven by sympathetic activity, while the latency, amplitude, and velocity of pupil contraction indicate parasympathetic activity[17,20,21]. Reduced parasympathetic activity is reflected by a longer LC, slower MCV, and smaller MCA.

The COMPASS 31 score is a validated measure of the severity of autonomic impairment[20]. The COMPASS-31 holds six subclasses: OI, VM, SM, GI, BL, and PM functions. In our study, we found that PM function correlated with BPD, which is an indicator of sympathetic activity. OI correlated inversely with MCV, the SM score correlated with LC, and the GI core correlated inversely with PCR and directly with MCA. We conclude that the PM score of the COMPASS 31 reflects sympathetic activity, while the scores for OI, SM, GI domains of the COMPASS 31 indicate the parasympathetic activity of the patient.

Abnormal pupillary function is associated with the earnestness of autonomic symptoms, as observed through the Compass-31 questionnaire[20]. The PM weighted COMPASS 31 sub-score correlated with BPD, suggesting an association between high sympathetic tone and the severity of PM symptoms. The center of the sympathetic nervous system is located at the locus coeruleus[22]. Activity of the locus coeruleus represses the Edinger–Westphal (EW) nucleus, leading to the inhibition of the pupil's constricting muscle and pupil dilation. Changes in pupil diameter correlate directly with changes in locus coeruleus activity.

The scores for OI, SM, GI domains of the COMPASS 31 reflect the patient's parasympathetic activity. Longer constriction latency, slower MCV, and smaller constriction amplitude indicate primarily parasympathetic dysfunction. Parasympathetically linked pupillary constriction is driven by the EW nucleus (22). Central sympathetic neurons of the reticular activating system of the brainstem inhibit the parasympathetic neurons at the EW nucleus.

Autonomic dysfunction is often observed in various painful conditions[1,2]. Sympathetic activity shows significant positive associations with widespread pain and symptom severity[1]. We also found that the PM weighted COMPASS 31 sub-score correlated with the BPD, indicating a relationship between high sympathetic tone and the severity of PM symptoms. We conclude that pain can enhance the activity of the locus coeruleus, affecting pupil diameter via the EW nucleus and co-activating the noradrenergic system.

Our readers should interpret our findings while considering several limitations of our study. The overall number of patients and the retrospective study plan introduce meaningful restrictions. We recommend conducting a prospective study with a larger patient cohort. Additionally, we should include patients' post-therapy and those with other conditions, such as tinnitus.

We analyze the COMPASS-31 using Classical Test Theory (CTT). CTT has several assumptions, not all of which are met by the COMPASS-31. Although the COMPASS-31 is a multidimensional scale, the measured construct should be unidimensional. For this reason, researchers must interpret the COMPASS-31's sum score with care. Another assumption is that the items should be unrelated or independent; responding to one item should not interfere with answering another. However, the items in the COMPASS-31 are related, as an answer to one item may lead the patient to another, excluding responses to the items in between (for instance, items 1 and 5).

CONCLUSION

The COMPASS-31 is a moderately reliable patient-reported outcome questionnaire looking at multidimensional autonomic subclasses, including OI, VM, SM, GI, BL and PM functions. The significant relationship between the COMPASS-31 and pupillometry demonstrates construct validity. Objective measurements, such as pupillometry, are not superior to subjective measurements like the patient-reported outcome COMPASS-31.

CONFLICTS OF INTEREST AND SOURCE OF FUNDING

The authors declare no conflict of interest.

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