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EFFICACY OF NIJMEGEN QUESTIONNAIRE IN RECOGNITION OF THE HYPERVENTILATION SYNDROME

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Abstract—The pattern of complaints of patients with the hyperventilation syndrome (HVS) was studied on the basis of the Nijmegen HVS Questionnaire (van Doorn, Colla, Folgering). This list was completed by 75 patients with the clinical diagnosis HVS. Non-metric principal components analysis (NMPCA) showed that the structure was three-dimensional, the dimensions being labelled: Shortness of breath (HVS-I), Peripheral tetany (HVS-II), Central tetany (HVS-III).

The questionnaire's differentiating ability was investigated by comparing HVS patients with non-HVS persons (80 persons employed in health care). All three components had an unequivocally high ability to differentiate between HVS and non-HVS. Application of linear analysis of discriminance to HVS-I, HVS-II and HVS-III together yielded 93% correct classifications. Statistical double cross-validation resulted in 90 and 94% correct classifications. The sensitivity of the Nijmegen Questionnaire in relation to the clinical diagnosis was 91% and the specificity 95%.

It is concluded that the questionnaire is suitable as a screening instrument for early detection of HVS, and also as an aid in diagnosis and therapy planning.

INTRODUCTION

QUITE a lot has been written about the syndrome of chronic, habitual or acute hyperventilation (HVS) [1–4]. This syndrome is regarded as the determinant of a multiplicity of physical complaints. Recognition is considered important because it increases the chance of appropriate treatment. This can prevent the complaints becoming chronic and disabling.

An obstacle to early recognition is the fact that clinically a large number of complaints is ascribed to HVS. A common element is that the complaints can be generated by provoking rapid breathing: Hyperventilation Provocation Test (HVPT) [3,5].

Particularly as regards the early recognition of HVS, an instrument for investigation is needed, based on a unequivocal and circumscribed definition of HVS. A first step in this direction has been taken by a research group at the University of Nijmegen, The Netherlands, who published a list with 16 complaints for HVS [6]. The list was tested on 263 patients who were referred to a lung function laboratory with suspected HVS, and was found capable of discriminating between those with a positive HVPT and those who did not have HVS according to the HVPT. The questionnaire classified 83% correctly in the first instance and 79% after statistical cross-validation [7]. This provides empirical support for the possibility of a circumscribed definition of HVS.

A second step would be to investigate the dimensional structure of the questionnaire. If the list is not unidimensional, but contains several components, the subgroups of items should be compared as to differentiating ability and also be related to relevant elements of the clinical picture. Another step is to assess the qualities of the questionnaire as a screening instrument. For that purpose it is necessary to investigate

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whether it differentiates between healthy persons and HVS patients. As HVS may be considered as one extreme of a continuum of more or less normal stress reactions, it is important to determine to what extent it can be distinguished from the other, least stressful extreme.

Formulated more specifically, the research questions are: What is the complexity of the Nijmegen Questionnaire for HVS complaints? Does the Nijmegen Questionnaire have the ability to differentiate HVS patients from non-HVS ('normals')? If so, to what extent?

MATERIAL AND METHODS

Subjects

Eligible for this study were HVS patients who in 1981–1983 underwent breathing and relaxation therapy in the Biofeedback Department of St Joannes de Deo Hospital, Haarlem, or the Breathing Therapy Practice, Amersfoort, The Netherlands. The HVS diagnosis was made on the basis of the complaints pattern (a) by the referring general practitioner or specialist, and (b) by the therapist. Exclusion criteria were (1) patients in whom a somatic disorder could explain the complaints and (2) patients in whom no irregularity in breathing was found which fitted in with hyperventilation (high thoracic, rapid and irregular respiration, frequent sighing, etc.) [3,4]. Doubtful cases were decided by applying the hyperventilation provocation test or left out of the study. Seventy-five patients were found eligible for the study (22 men, 53 women; mean age 36.6 yr, SD 9.8 yr; mean duration of the complaints 4.1 yr).

The reference group (non-HVS) consisted of persons who for professional reasons attended the lessons on breathing therapy given by the first author. The great majority of them were physiotherapists or yoga teachers by profession. They were chosen as a reference group on the assumption that they would have little chance to suffer from stress complaints and HVS. However, absence of HVS could not be confirmed for all of them. The lessons were held in the context of a refresher programme for physiotherapists and a course in a rehabilitation centre and in the Breathing Therapy practice. Questionnaires utilizable for statistical analysis were obtained from 80 persons (28 men, 52 women; mean age 31.9 yr, SD 11.8 yr).

Procedure

The patients (HVS) completed the questionnaire at the time of the first interview as part of the intake procedure, in the presence of the therapist. The non-HVS persons completed the questionnaire as a group during a short pause in the lecture or course which was provided for the purpose. They were told beforehand that a scientific study was being made of respiratory symptoms. Afterwards they were told the real purpose of the study.

Questionnaire

The Nijmegen Questionnaire consists of 16 complaints whose frequency of incidence can be indicated on a five-point ordinal scale (1 = never, 5 = very frequently). The complaints relate to different systems: (a) cardiovascular, e.g. 'palpitations'; (b) neurological, e.g. 'dizzy spells', 'tingling fingers'; (c) respiratory, e.g. 'shortness of breath'; (d) gastro-intestinal, e.g. 'bloated abdominal sensation'; (e) psyche, e.g. 'tense'. The item 'anxiety' was omitted. This phenomenon should be seen rather as a cause or background feeling than as being inherent in the symptoms of HVS.

Methods of analysis

Non-Metric Principal Components Analysis (NMCPA): This method makes it possible to detect the dimensional structure of the variables under study, i.e. the underlying relation between the variables is tracked down in a parsimonious model. The structure is rotated according to the VARIMAX-criterion. In addition, the technique gives the correlations of the individual variables with the detected components (component loadings). These provide an indication of the relational importance of the variables as regards the components which have been extracted.

NMPCA is essentially a generalized classical principal components analysis, in that the latter method is used for variables at the numerical level (the variables are of an interval nature, e.g. age or temperature), whereas NMPCA can also be applied to variables at other levels, at the ordinal level (the variables have a ranking order), the nominal level (the variables do not have an order) and combinations of the two. The computer algorhythm for NMPCA is 'PRINCALS' [8–10]. In this study NMPCA has been used to variables declared at ordinal and numerical level. The structure turned out to be quite similar. Because of the very ordinal character of the level of the variables, the structure of this is presented.

In the present study NMPCA was used to explore the dimensional structure of hyperventilation complaints, the method being applied to the Nijmegen Questionnaire as completed by the HVS patients. The group of non-HVS is not considered for this analysis, because it is only the HVS group who may be expected to exhibit the typical clinical picture of the Hyperventilation syndrome, to be reflected in the questionnaire.

Once the structure of the questionnaire has been determined the sum scores of the two groups (HVS and non-HVS) on the components were calculated.

Linear Analysis of Discriminance: This method is used to discriminate optimally between two or more categories of subjects. In the present study there are two categories: HVS and non-HVS. By means of this method predictor variables are selected which have discriminating values as regards HVS and non-HVS. The mathematical objective is to weigh and combine variables linearly in such a manner that the two groups are distinguished from one another statistically in an optimal way. The method selects the predictor variables stepwise and determines the coefficients for each variable selected. The procedure is as follows. A single variable is to be selected which has the highest value on the selection criterion. The first variable selected is then paired with each of the remaining variables one at a time. The combination which has the highest value on the selection criterion is selected, and so on. This process continues until all variables or combination of variables which meet the criterion have been selected. A variable which has been selected might later be removed, because other variables or combinations of variables may have greater discriminating power. Similarly, a variable which is excluded might be re-entered at a later step in the selection procedure. The criteria used for inclusion and exclusion are $F \geqslant 1.00$ and $F \leqslant 0.95$ respectively. In this analysis Wilks Lambda (λ) is used. This test takes into consideration the differences between the centroids (i.e. means) and the cohesion (i.e. homogeneity) within groups. Relevant literature on linear analysis of discriminance is given, among others, by Cooley and Lohnes, van der Geer, Tatsuoka [11–13].

One of the pitfalls in linear analysis of discriminance is multicollinearity [14]. This occurs when two variables in a matrix are perfectly (or near perfectly) correlated and when they show a similar pattern of correlations with the other variables. In order to prevent this pitfall the items are subjected to NMPCA; and then the scores on the components extracted are used as variables in subsequent analysis. That is the reason why we have relinquished the idea to apply discriminant analysis on the fifteen individual items.

RESULTS

Formulated in operational terms the first research question is: What is the dimensional structure of the Nijmegen questionnaire? NMPCA shows that the questionnaire contains three components. Table I gives the loadings (correlations) of the variables on the components.

TABLE I.—DIMENSIONAL STRUCTURE OF HYPERVENTILATION COMPLAINTS

		Components		
		I	II	III
		Shortness of breath	Peripheral Tetany	Central Tetany
8	Constricted chest	0.81	0.16	−0.23
7	Shortness of breath	0.81	0.28	−0.12
6	Accelerated or deepened breathing	0.81	0.15	−0.01
11	Unable to breath deeply	0.76	0.16	0.04
1	Chest pain	0.53	−0.13	−0.52
2	Feeling tense	0.48	−0.13	0.15
15	Palpitations	0.41	−0.22	0.29
13	Tightness around the mouth	0.02	−0.73	−0.07
12	Stiffness of fingers or arms	0.06	−0.72	−0.15
14	Cold hands or feet	0.10	−0.58	0.08
10	Tingling fingers	0.16	−0.57	−0.16
9	Bloated abdominal sensation	0.13	−0.03	−0.67
4	Dizzy spells	0.25	−0.06	0.62
3	Blurred vision	0.04	−0.11	0.55
5	To be confused, losing touch with environment	0.47	−0.08	0.54

*Figures represent loadings, i.e. correlations of the items with the components.

The first component is formed by seven items in total. Four of them, with the highest correlations,—'constricted chest' (item no. 8), 'shortness of breath' (7), 'accelerated or deepened breathing' (6), and 'unable to breathe deeply' (11)—have to do with difficulties with breathing. They constitute the core of HVS: complaints arise from a (subjective) impediment to breathing. Also with high loadings on this component are 'chest pain' (1), 'feeling tense' (2), 'being confused' (5) and 'palpitations' (15). The relation of chest pain and heightened perception of heart action to this impediment to breathing, or shortness of breath, may well be understood by way of the location in the thorax. Evidently, 'feeling tense' is related to the inability to breathe freely. The item 'being confused' however, does correlate with this component but more so with the third component. As the latter relation is also better understood clinically, this item is subsumed under the third component and left out of this component, which is labelled: 'Shortness of Breath'.

This second component is formed by four items: 'tightness around the mouth' (13), 'stiffness of fingers or arms' (12), 'cold hands or feet' (14) and 'tingling fingers' (10). These phenomena can all be seen as specific consequences of excessive ventilation in relation to the metabolism of the moment: the carbon dioxide level drops (hypocapnia and respiratory alkalosis); this leads to instability of the cell membrane in the central and autonomic nervous system and hence, to phenomena which can be summarized under a pathophysiological concept, tetany [15]. The peripheral manifestations of this tetany (paraesthesia, stiff muscles, vasoconstriction) are evidently relatively independent of the respiratory difficulties and of the central manifestations. In other words, 'Peripheral Tetany' is a proper name for this component.

The third component comprises five items in total, namely: 'dizzy spells' (4), 'blurred vision' (3), 'being confused' (5), and, in the reverse direction, 'bloated abdominal sensation' (9) and 'chest pain' (1). This dimension is bipolar. A person who is troubled by a bloated sensation in the abdomen is not troubled by dizzy spells. The first three items can be viewed as the central nervous phenomena of hypocapnia and are well-known hyperventilation complaints. Therefore, the component is labelled 'Central Tetany'.

The connection between a bloated abdominal sensation and chest pain could be understood as a consequence of aerophagia. The swallowing of air into the stomach causes pressure on both abdomen and chest. These two items diverge in their correlation on the first component. Only bloated abdominal sensation has a low correlation, like the other items of the third component, and can be truly considered part of Central Tetany. However, its negative relation is not easy to interpret.

If a loading of 0.40 is taken as a limit, only two items are found to belong to more than one component. These components are mutually independent, i.e. a HVS patient will not necessarily have a high score on all three components.

In our view the conclusion is justified that the complaints pattern of HVS patients unmistakably has a three-dimensional structure. The components can be labelled as follows: 'Shortness of Breath' (HVS-I), 'Peripheral Tetany' (HVS-II) and 'Central Tetany' (HVS-III).

The second research question was: To what extent does the Nijmegen questionnaire have the ability to differentiate HVS-patients from non-HVS ('normals')? The average scores of the two groups on the HVS components were calculated. The differences

between groups are significant for each of the three components (HVS-I: $F(1,153)=257.0$, $p \ll 0.0001$; HVS-II: $F(1,153)=121.3$, $p \ll 0.0001$; HVS-III: $F(1,153)=64.7$, $p \ll 0.0001$). This means that HVS patients score discernably higher at the average than non-HVS on Shortness of Breath (HVS-I), Peripheral Tetany (HVS-II) and Central Tetany (HVS-III).

The extent of the questionnaires ability (i.e. of the three components jointly) to differentiate between the two groups was investigated by means of a stepwise linear analysis of discriminance. The differentiation is highly significant (Wilks $\lambda=0.278$; $\chi^2=193.8$, df $=3$, $p \ll 0.001$). The stability of the discriminant function was investigated by means of a statistical double cross-validation, i.e. both HVS and non-HVS were divided at random into two groups, as far as possible of equal size (I and II). The discriminant function coefficients of group I were estimated and the subjects of group II were then classified on the basis of these coefficients. An identical procedure was used for group II, but in the reverse order, i.e. the discriminant function coefficients of group II were estimated and the subjects of group I were then classified. The respective percentages of correct classifications were 90 and 94. The conclusion is justified that this questionnaire is highly robust.

TABLE II.—CLASSIFICATION MATRIX OF HVS VS NON-HVS ON THE BASIS OF DISCRIMINANT ANALYSIS

Criterion	Assignment		On the basis of discriminant analysis	
	HVS	non-HVS	HVS	non-HVS
HVS ($n=75$)	a	b	68	7
non-HVS ($n=80$)	c	d	4	76

	Classification rates (%)	Statistical double cross-validation (%)
Correct classification	**93**	**92**
Sensitivity $\frac{a}{a+b}$	**91**	**89**
Specificity $\frac{d}{c+d}$	**95**	**94**
True positive prediction $\frac{a}{a+c}$	**94**	**93**
True negative prediction $\frac{a}{d+b}$	**92**	**90**

The classification results are given in Table II, from which it can be seen that the three HVS components together were capable of classifying 144 of the 155 subjects (93%) correctly. The specificity of the questionnaire is greater than the sensitivity, i.e. the number of non-HVS persons who were classified as HVS patients (False Positives) was smaller than the number of HVS patients who were classified as healthy (False Negatives). Seven of the 75 HVS patients were classified as non-HVS. Therefore, the questionnaire is not capable of detecting all HVS patients (negative predictive value is 92%). More important for purposes of screening and early detection however,

is that few people were classified wrongly as HVS patients (positive predictive value is 94%) [16]. It can be concluded that the differentiating ability of the Nijmegen questionnaire is high and that it can be used as a screening instrument.

DISCUSSION

Analysis of the Nijmegen questionnaire, completed by HVS patients shows a clear and clinically meaningful pattern in the complaints. In this analysis the reference group was omitted, first, because they would not contribute to an understanding of the clinical pattern of the syndrome, second, because the HVS patients turned out to vary considerably in the severity of complaints and to cover almost the whole range of the questionnaire. That is the reason why 7 of the 75 could not be distinguished from the reference group. The results support the concept of HVS as a well-defined syndrome, as well as the conclusion of Lum: 'that the habitually unstable breathing is the prime cause of symptoms' [3]. The complaints picture comprises on the one hand a breathing disturbance, in the sense of a subjective impediment to breathe freely, which results on the other hand in the tendency to excessive breathing which produces the symptoms of tetany, due to hypocarbia and respiratory alkalosis. It means that a clinician or investigator, when trying to assess the presence of HVS, has to explicitly ask questions with respect to the three dimensions of the Nijmegen questionnaire. As far as these complaints are sufficient to identify HVS one can speak of 'primary' HVS or HVS in a strict sense, to distinguish the syndrome from the cases where other psychic or somatic problems are also present and often dominate the clinical picture [17]. The three dimensions correspond with the classical triad of acute hyperventilation: dyspnoe, paraesthesia and syncope. Thus, the same kind of symptoms appear in chronic, habitual hyperventilation but in a mitigated form.

The questionnaire turns out to have high differentiating qualities for the detection of HVS. Discriminant analysis was done, using the scores on the three components, instead of the individual items jointly, for two reasons. First, successful differentiation shows the clinical relevance of the three components and their ability to identify HVS. Second, the pitfall of collinearity is avoided (see under methods of analysis). When linear analysis of discriminance was done with all the items individually, however, the result was the same: 93% of correct classifications, with 3 false positives and 8 false negatives.

Successful differentiation of HVS patients and healthy controls with the same characteristics of age and sex, shows that HVS complaints are not part of the minor disturbances that commonly occur and are part of normal life. In other words, the two extremes of what may be viewed as a 'continuum of stress complaints' hardly overlap with respect to hyperventilation complaints. This is of special importance when screening is attempted for HVS among non-patients or among patients with unrelated disorders, for instance in sports medicine, or when occurrence of HVS in the population is investigated in an epidemiological study. In this situation the risk of false positives, who would be wrongly labelled as HVS should be minimal, and true positive prediction maximal.

Nevertheless, differentiation was not complete. Of the 80 persons in the reference group 4 were classified as HVS. Although this group was assumed to have minimal chance for HVS or stress-related complaints, a shortcoming of this study is that the

absence of HVS could not be confirmed. Therefore, the possibility cannot be ruled out that they are *not* false positives. The Nijmegen questionnaire showed them to have several complaints and it may very well be that they are HVS patients. If this reasoning is correct, the positive predictive value of the questionnaire could become even higher in a future study, supporting its value as a screening instrument.

The sensitivity of the questionnaire (91%) is not maximal. It means that 9% of the patients is not detected among 'normals'. One reason for this might be that the questionnaire is incomplete in the sense that complaints inherent in HVS are not included, for instance, fatigue and behavioral disturbances. Another reason may be that certain patients do not perceive their own 'physical functioning' adequately, i.e., they simply do not notice or do not wish to notice the symptoms ('faking good'). Therefore, when the questionnaire is used in diagnosis, a low score cannot be taken as a strong argument against HVS. When a person is suspected of HVS and has a low score, it is recommended to seek additional information and to apply the provocation test. On the other hand, a high score confirms the clinicians suspicion that HVS is present, or suggests HVS as a possibility to be seriously considered.

Further research is needed to determine the occurrence of false positives and false negatives among different groups of patients. The purpose is to study the utility of the Nijmegen questionnaire as an aid in diagnosis, in such a way that a higher score indicates increasing probability of HVS. The reference group of this study may serve as an anchor point for lowest probability and the patients with confirmed HVS indicate the range with higher probability.

The differentiating qualities of the Nijmegen questionnaire might vary dependent on symptomatology and complaints of different disorders. Therefore it is recommended to test the qualities of the questionnaire in e.g. a general practice, or an outpatient clinic for cardiology, neurology, internal medicine, psychiatry, lung disease, etc. Also, in each of these situations different items may have to be added to achieve adequate differentiation. Lastly, follow-up is necessary in order to determine how many patients with the initial diagnosis of HVS will turn out to have an organic cause for the complaints later on, and how these patients could have been identified in the first place.

REFERENCES

1. Christopher B. Hyperventilation syndrome. *Med J Australia* 1961; **48:** 81–86.
2. Lewis BI. Mechanism and management of hyperventilation syndromes. *Biochem Clin* 1964; **4:** 89–96.
3. Lum LC. Hyperventilation and anxiety state. *J R Soc Med* 1981; **71:** 1–4.
4. Rice RL. Symptom pattern of the hyperventilation syndrome. *Am J Med* 1950; **95:** 691–700.
5. Folgering H, Colla P. Some anomalies in the control of PA-CO2 in patients with a hyperventilation syndrome. ***Bull Europ Physiopath Resp*** 1978; **14:** 503–512.
6. Van Doorn P, Colla P, Folgering H. Control of end-tidal PCO2 in the hyperventilation syndrome: effects of biofeedback and breathing instructions compared. *Bull Europ Physiopath Resp* 1982; **18:** 829–836.
7. Van Doorn P, Colla P, Folgering H. Een vragenlijst voor hyperventilatieklachten. *De Psycholoog* 1983; **18:** 573–577.
8. Kruskal JB, Shepherd RN. A nonmetric variety of linear factor analysis. *Psychometrika* 1974; **39:** 123–157.
9. Young FW. Quantitative analysis of qualitative data. ***Psychometrika*** 1981; **46:** 357–388.
10. Gifi A. *Nonlinear Multivariate Analysis.* Leiden: Dept Data Theory, Leiden University, 1981.
11. Cooley WW, Lohnes PL. Multivariate data analysis, New York: Wiley, 1971.
12. Van der Geer JP. *Introduction to Multivariate Analysis in the Social Sciences.* San Francisco: Freeman, 1971.

13. TATSUOKA MM. *Multivariate Analysis.* New York: Wiley, 1971.
14. TABACHNIK BG, FIDELL LS. *Using Multivariate Statistics.* New York: Harper and Row, 1983.
15. DROOGLEEVER FORTUYN J, GROENEVELD W, KLAVER-KRÒL E, LEENSTRA-BORSJES H, TEELKEN AW. Studies over het hyperventilatiesyndroom III. Pathofysiologie. *Ned T Geneeskunde* 1976; **120:** 878–80.
16. GRINER PF, MAYENSKI RJ, MUSHLIN I, GREENLAND P. Selection and interpretation of diagnostic tests and procedures. *Ann Intern Med* 1981; **94:** 533–96.
17. WEIMANN G. *Das Hyperventilationssyndrom.* München: Urban und Schwarzenburg, 1968.