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Correlation between Breath Hold Time and Nijmegen Questionnaire scores among patients referred to respiratory physiotherapy practice for Hyperventilation Syndrome – a retrospective study

Grégoire Passard, PT, [1,2] **and Bertrand Selleron, PT,** [1]

[1]Private Respiratory Physiotherapy Clinic, Saint Jean de la Ruelle, France, [2]University School of Physiotherapy, Orleans University, Orléans, France

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ABSTRACT

Background: While there is an increasing interest given to Hyperventilation Syndrome (HVS), there is also a lack of consistency in the literature concerning its diagnosis and treatment. Breath Holding Time (BHT) is a simple, feasible clinical test already used in other conditions. Currently, there is limited evidence demonstrating its utility in identifying HSV. **Objective**: The primary aim of this study was to assess the correlation between NQ scores and subscores and the Breath-Holding Time (BHT) in patients seeking consultation with a physiotherapist for HVS. **Method**: We conducted a retrospective study in an ambulatory respiratory physiotherapy practice. Nijmegen Questionnaire (NQ) scores and BHT were extracted from patient's files attending their first physiotherapy session between march 2018 and march 2022. Correlation between NQ scores and BHT was calculated using Pearson's test. Optimal cut-off for BHT was calculated with a Receiver Operating Characteristic curve and BHT sensitivity and specificity were calculated. **Results**: 109 patients files meeting inclusion criteria were included. A low negative correlation (-0.302) between BHT and NQ total score was found. Sensitivity and specificity, using an NQ score $\geq$ 23 as the case definition, were 0.558 and 0.714, respectively. **Conclusion**: These preliminary results show a low negative correlation between BHT and HVS symptoms.

KEYWORDS: breath Holding, hyperventilation, physical examination

Introduction

Background

Hyperventilation syndrome (HVS) can be defined as an inappropriate ventilation leading to a large range of symptoms [1]. It is prevalent among the general population, with an estimated prevalence of 8% in a general adult population [2], and it can reach 30% to 58% among individuals with asthma [3, 4]. However, HVS remains a challenging condition due to a substantial lack of knowledge concerning its pathophysiology, diagnosis and treatment.

In terms of pathophysiology, it is believed that an increased respiratory rate leads to a decrease in arterial partial pressure of carbon dioxide ($PaCO_2$), which is known to trigger various symptoms, including but not limited to tremors, dizziness, dyspnea, and paresthesia. The underlying mechanisms explaining the persistence of these symptoms remain unclear. Several authors have explored the potential influence of both automatic (brainstem-mediated) and voluntary (cortically controlled) respiratory regulation in the development of HVS. Some studies have examined whether chemosensitivity to CO_2 is altered in individuals with confirmed HVS, by assessing ventilatory responses to the inhalation of gas mixtures with varying concentrations [5, 6]. Although these investigations did not provide conclusive evidence regarding the role of CO_2 sensitivity, they revealed that breath-holding times differed significantly between HVS patients and healthy controls. As CO_2 sensitivity alone did not appear to account for these differences, researchers have proposed that a dysfunction in cortical regulation of breathing may offer a more plausible explanation [7].

The diagnostic process for HVS remains controversial, with no estab-

Corresponding author:
Grégoire Passard, 50 rue Léon Foucault, 45140 Saint Jean de la Ruelle, France e-mail: gregoire.passard@gmail.com

lished consensus or clinical guidelines. Among the most frequently used tools, the Nijmegen Questionnaire (NQ)—a 16-item self-administered survey assessing hyperventilation-related symptoms—has gained notable attention. In addition, a hyperventilation provocation test, which involves voluntarily increasing the breathing rate to induce hypocapnia and reproduce symptoms, has been proposed. However, its interpretation is debated: while some researchers focus on symptom reproduction, others emphasize changes in end-tidal CO_2 ($PetCO_2$) [8]. Notably, the association between hypocapnia and symptoms has been questioned, as similar symptoms can occur under isocapnic conditions during the same test [9]. Alternatively, measuring Breath Holding Time (BHT) is promising since Jack et al. showed that it differed significantly between HVS patients and healthy controls [5]. In healthy subjects, this test is a valid and reproducible tool [10]. Its utility has been studied in patients with cardiac, respiratory, or neurological conditions [11, 12]. BHT demonstrates a low positive correlation with the 6-minute walk test in Chronic Obstructive Pulmonary Disease patients, suggesting that similar mechanisms are at play during both the breath-holding test and exercise [13]. It also has demonstrated a strong correlation with exercise parameters, including VO_2 at the anaerobic threshold, in a small group of patients with cystic fibrosis [14].

In the context of our target population, specifically patients with Dysfunctional Breathing (DB), the BHT has been investigated only to a limited extent. Courtney et al. investigated the relationship between BHT and various DB measurements in both healthy individuals and those with abnormal spirometry in the absence of a confirmed medical diagnosis. Their study found no correlation between BHT and NQ scores [15].

Aims

The primary aim of this study was to assess the correlation between NQ score and subscores and the Breath-Holding Time (BHT) in patients seeking consultation with a physiotherapist for HVS.

The secondary aim of this study was to establish the validity of the BHT test in identifying HVS compared to the NQ.

Methods

Study design and Population

This retrospective study was conducted at an outpatient respiratory physiotherapy practice in Saint Jean de la Ruelle, France. Patient records from individuals who attended physiotherapy sessions for the rehabilitation of HVS between March 2018 and March 2022 were retained if they met inclusion criteria, which were being over 18 years of age and having a medical referral for HVS rehabilitation. In accordance with French law, patients were contacted to be informed about the study, and assurance was provided that no data allowing their identification would be disclosed. Files were excluded if individuals refused the use of their data or if relevant data was missing.

Data collection

Data were extracted from patients' records. Individuals presenting with HVS at the practice had typically undergone a systematic assessment during their initial evaluation. This assessment included:

(1) Completion of the NQ by the patient.

(2) Clinical tests, such as measurements of respiratory rate and BHT measurement. Both of these tests are conducted with the patient in a semi-seated position, following a brief rest period.

All patient records referred to the private practice for HVS between March 1, 2018, and March 1, 2022, were examined and assessed for inclusion. For each patient, demographic data including age at inclusion, gender, height, and weight were recorded.

Outcomes

(1) Symptoms: To address the primary aim of the study, we obtained patient-reported outcome measures for symptoms using the total score and subscores of the NQ. For each item, the frequency of the mentioned symptom is rated among five possibilities: never (0), rarely (1), sometimes (2), often (3), or very often (4). The total score, which can range from 0 to 64, is divided into four subscores named psychological, dyspnea, peripheral, and central scores as described by Courtney et al. [16]. This questionnaire was initially developed to screen for hyperventilation in the general population, demonstrating a sensitivity of 91% and a specificity of 95% [17].

(2) BHT: The methodology for BHT assessment is not consistently described and varies among different studies. To streamline the procedure in our clinical practice, the test was commonly performed as follows: patient is positioned semi-seated and instructed to take a deep breath to reach total lung capacity, then holds breath for as long as possible. The time is recorded from the end of the last breath until exhalation.

(3) Breath-Hold Time Test Validity.

Statistical analysis

Normality of distribution was assessed with the Shapiro-Wilk test. The correlation between BHT and NQ scores was evaluated using Pearson or Spearman correlation tests, depending on the data distribution. Statistical analyses were performed using JAMOVI software.

A Receiver Operating Characteristic (ROC) curve was constructed, and the area under the curve was calculated. The optimal cut-off value for the BHT test was determined using the Youden method. A 4x4 contingency table was created, and standard metrological criteria were calculated for the BHT test, including sensitivity (true positives / [true positives + false negatives]), specificity (true negatives / [true negatives + false positives]), positive predictive value (true positives / [true positives + false positives]), negative predictive value (true negatives / [true negatives + false negatives]), positive likelihood ratio (sensitivity / [1 - specificity]) and negative likelihood ratio ([1 - sensitivity] / specificity). The 95% confidence interval for these parameters was computed using the Wald method.

A true positive result was defined as a patient with a NQ score equal to or above 23 [18] and a BHT below or equal to the optimal cut-off determined from the ROC curve. A true negative result was when a patient with a NQ score below 23 had a BHT above or equal to the optimal cut-off. A false positive result occurred when a patient with a NQ score below 23 had a BHT below the optimal cut-off, and a false negative result was observed when a patient with a NQ score equal to or above 23 had a BHT below the optimal cut-off. The statistical significance threshold was set at 0.05.

Results

Among the 113 patients referred to the practice for HVS from March 2018 to March 2022, two were excluded because they were under 18 years old, and two were excluded because they did not consent to the use of their data, resulting in a total of 109 patients who met the inclusion criteria. Women were the predominant gender (n=85). The mean age of the sample was 51 years. The mean total NQ score was 27 ($\pm$10), and the mean maximal BHT was 28 seconds ($\pm$20). Descriptive data for the sample are presented in Table 1. No missing data were observed, except for height and weight, which were not consistently recorded for every patient but do not impact the statistical analysis.

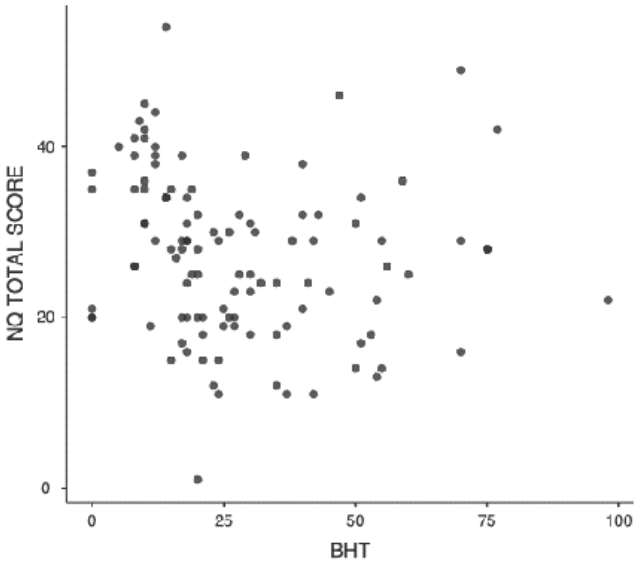

Figure 1 Scatter plot showing the relationship between Nijmegen Questionnaire (NQ) scores and Breath Holding Time (BHT). Each dot represents a patient.

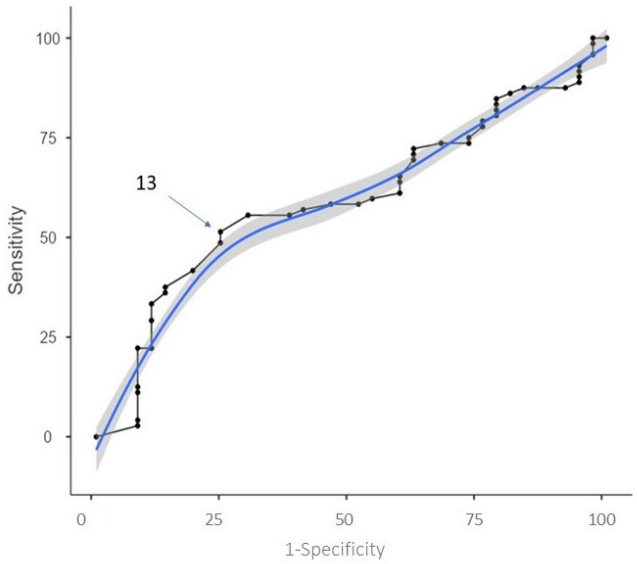

Figure 2 ROC curve analysis of Breath Holding Time (BHT) for predicting Nijmegen Questionnaire (NQ) scores $\geq$ 23. The blue line represents the local regression, and the grey area indicates the standard error.

Table 1 Descriptive data. Variables are expressed by means (± standard deviation). NQ = Nijmegen Questionnaire; BHT = Breath Holding Time

Variables	**Females** (n =85)	**Males** (n =24)	**Total** (n=109)
Age (years)	52 (± 16)	50 (± 21)	51 (± 17)
NQ total score	28 (±10)	26 (± 9)	27 (± 10)
NQ psychological subsocre	8 (± 3)	8 (± 3)	8 (± 3)
NQ central subscore	6 (± 3)	6 (± 4)	6 (± 3)
NQ peripheral subscore	5 (± 4)	3 (± 3)	5 (± 4)
NQ dyspnea subscore	9 (± 3)	9 (± 3)	9 (± 3)
Respiratory rate (cycles/min)	17 (± 6)	15 (± 6)	16 (± 6)
BHT	26 (± 18)	35 (± 24)	28 (± 20)

For the primary objective, the distribution of breath-holding time (BHT), peripheral score, central score, and respiratory rate was non-normal ($p < 0.05$), so a Spearman test was conducted. The correlation matrix is shown in Table 2. A low negative correlation was observed between the BHT and the total NQ score, with a Spearman rho of -0.302 ($p < 0.01$). Figure 1 presents a scatter plot illustrating this relationship.

Regarding the secondary objective, the area under the curve was 0.65682. The optimal cutoff for end-inspiratory breath-hold time was calculated using the Youden method and set at 13 seconds. The ROC curve is represented in Figure 2. A contingency table was then constructed, using a NQ score equal to or greater than 23 as a reference for suspecting HVS and is represented in Table 3. The sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio were 0.548 (95% CI: 0.383-0.713), 0.714 (95% CI: 0.564-0.864), 0.800 (95% CI: 0.689-0.911), 0.431 (95% CI: 0.304-0.558), 1.918 (95% CI: 0.960-3.835), and 0.633 (95% CI: 0.376-1.064), respectively.

Discussion

BHT shows a low negative correlation with symptoms assessed by the NQ. However, while this correlation is statistically significant, it remains low with a coefficient of -0.302, explaining only 9% of the variance between the two variables. The clinical significance of this correlation is uncertain. If confirmed, this relationship could provide a basis for initial evaluation of HVS and monitoring treatment efficacy.

One potential explanation for this low correlation is that breath holding is a multifaceted phenomenon, involving biomechanical, biochemical, and psychological components [19]. Furthermore, BHT is a one-time measure sensitive to contextual factors (e.g., stress, fatigue, time of day), whereas the NQ reflects perceived health over several days, potentially reducing the impact of isolated events. Another justification stems from the NQ itself. The NQ was designed to screen for HVS, but its ability to quantify symptom severity remains uncertain, potentially explaining the low correlation. In addition, methodological issues exist—particularly the variability of cut-off values across studies. We used the original cutoff of 23 [18], though others have proposed thresholds of 19 [20] or 20 [21]. It is important to note that among the patients referred by pulmonologists, 37 had NQ scores below 23. This may be due to symptom reduction following a single educational session [22] or to the broad use of "Hyperventilation Syndrome" to describe varied dysfunctional breathing patterns. Some patients experience symptoms like air hunger without actual hyperventilation, which may explain the absence of typical signs (e.g., numbness, tingling). Given this heterogeneity, the validity and metrological properties of the NQ should be reconsidered in light of current knowledge.

Regarding the secondary aim of this study, we reported a sensitivity of 0.548 and a specificity of 0.714. This notably low sensitivity, indicating a high rate of false negatives, should raise concerns about the use of this test as a screening tool. This result is likely influenced by the comparison with the NQ, which is commonly regarded as a screening tool and a first-line evaluation method.

Currently, the diagnosis of HVS is considered a diagnosis of exclusion, meaning that other organic causes of the symptoms must first be considered and ruled out. Once these have been excluded, an HVS diagnosis can

Table 2 Correlation matrix. NQ = Nijmegen Questionnaire; BHT = Breath Holding Time; RR = Respiratory Rate. *p<0.05; **p<0.01; ***p<0.001

	Total NQ score	Psychological score	Central score	Peripheral Score	Dyspnea score	BHT	RR
Total NQ score	-						
Psychological score	0.617***	-					
Central score	0.768***	0.349***	-				
Peripheral score	0.669***	0.311**	0.572***	-			
Dyspnea score	0.554***	0.280**	0.286**	0.124	-		
BHT	-0.302**	-0.111	-0.245*	-0.247**	-0.245	-	
RR	-0.028	-0.180	-0.058	-0.015	0.027	-0.193*	-

be made. The lack of a test with high specificity capable of confirming this diagnosis remains a major limitation in defining HVS cases.
This is not the first study to explore the relevance of assessing breath-hold time in individuals with HVS. Kiesel et al. developed a clinical screening tool that examined various aspects of HVS with similar findings to ours including a comparable sensitivity (0,54). Their BHT cutoff was 20 seconds, slightly higher than the cutoff we calculated using the Youden method [23]. However, other results in their study, such as specificity, significantly differed from our findings. It is worth noting that the protocol for measuring BHT in the Kiesel study was slightly different, possibly due to a different measurement protocol starting at functional residual capacity and ending at the first involuntary respiratory muscle contraction, which may affect BHT values.

Table 3 Contingency table. Values are expressed as number of subjects. NQ = Nijmegen Questionnaire; BHT = Breath Holding Time; TP = True positive; FP = False positive; False negative; TN = True negative

	Total NQ $\geq$ 23	Total NQ <23
BHT $\leq$ 13	37 (TP)	9 (FP)
BHT >13	35 (FN)	28 (TN)

Our results should be interpreted with caution due to their limitations, and further research is necessary to confirm this link between BHT and symptom scores. Firstly, regarding the procedure: due to the retrospective nature of the data, we were unable to standardize the measurement of BHT. In routine practice, the test is typically performed in a semi-seated position after a 5-minute rest period, during which patients are instructed to hold their breath starting from total lung capacity. The instruction is usually formulated as follows: "*When you feel ready, take a maximal inspiration and hold your breath for as long as you can.*" The measurement begins at the end of inspiration and ends at the onset of exhalation (i.e., at the end of the apnea). Standardizing the BHT assessment would likely improve both the reproducibility and the validity of the measurement. For example, in the case of our study, some patients may not have reached total lung capacity, as this parameter was not objectively verified during the test, potentially leading to underestimated BHT values.
Secondly, our study is limited by incomplete characterization of the population—particularly regarding respiratory comorbidities such as COPD or interstitial lung disease, which may reduce BHT. Subgroup analyses would be valuable. In addition, the diagnosis of HVS remains imprecise. Participants were referred for suspected HVS by general practitioners or pulmonologists, but no standardized criteria were applied. Although tools like capnography exist, their use is inconsistent. Given the variability of clinical presentations, these conditions are increasingly grouped under the broader term "dysfunctional breathing." A precise definition of the diagnostic process for Hyperventilation is necessary to enhance population selection for future studies. Cardiopulmonary exercise testing, when combined with other criteria, may help identify exercise-induced hyperventilation by reproducing symptoms in realistic conditions. Typical findings include elevated VE/VCO_2 and reduced $PETCO_2$ [24]. The test also helps exclude other causes of dyspnea and supports patient education. However, its limited availability and inability to detect some dysfunctional breathing patterns (e.g., irregular breathing, sighing without hypocapnia) remain notable limitations.

Conclusion

This retrospective study, conducted in an ambulatory respiratory physiotherapy practice, aimed to investigate the correlation between BHT and NQ scores, and to establish metrological parameters for BHT in patients referred to physiotherapy for HVS. Our results suggest that there is a statistically significant low negative correlation between these variables. The sensitivity and specificity of BHT, with an optimal cut-off of 13 seconds, were 0.548 and 0.714, respectively, based on a diagnostic criterion of an NQ score equal to or greater than 23. While our data indicate limited relevance for this test in individuals suffering from HVS, further investigation is warranted, given the lack of consensus on clinical tests and paraclinical evaluations for identifying HVS.

Statement and declaration

Authors' contribution

Grégoire Passard was involved in conception of the work; or the acquisition, analysis, interpretation of data for the work and drafting the work. Bertrand Selleron was involved in acquisition and interpretation of data for the work and revising it critically for important intellectual content.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing Interests

The authors declare not to have any conflicts of interest that may be considered to influence directly or indirectly the content of the manuscript.

Artificial intelligence involvement

During the preparation of this manuscript, the authors used ChatGPT to perform a final grammatical and orthographic proofreading. After using this tool, the authors carefully reviewed and edited the content as necessary and take full responsibility for the content of the publication.

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