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What good old breath-holding tests really show?

or

Good old breath-holding test does not reflect the state of the cardiorespiratory system, but the ability of volitional inhibition of inspiratory neurons

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Abstract:

Background. The breath-holding tests of Stange (after a deep inspiration) and Guenchi (after a normal expiration) have been used in clinical and sports practice for more than a century as simple bedside markers of cardio-respiratory reserve. Their physiological meaning, however, has never been firmly established, and the literature has alternated between treating the test as an index of lung capacity, of haemodynamic efficiency or of CO₂ tolerance. **Objectives.** We aimed to verify whether the duration of voluntary apnoea really reflects the state of the cardiorespiratory system, or whether — as we hypothesised — it reflects mainly the capacity of supraspinal structures to inhibit the bulbar inspiratory generator. **Material and methods.** Forty-four adult patients with chronic pyelonephritis and cholecystitis in remission (34 men aged 23–70 years; 10 women aged 33–76 years) were examined twice — on admission and after 7–10 days of standard balneotherapy at Truskavets' Spa (Naftussya bioactive water, ozokerite, mineral baths). At each examination Stange's and Guenchi's tests were performed together with submaximal cycle-ergometer PWC₁₅₀, echocardiographic haemodynamics, heart rate variability (HRV), 16-lead resting EEG, faecal microbiota, urinary syndrome, gall-bladder cholekinetics, urinary and serum electrolytes, immunogram and phagocytic activity of neutrophils, giving a total of 88 paired observations. Correlation, multiple regression and canonical correlation analyses were applied. **Results.** Stange and Guenchi durations were entirely uncorrelated with each other ($r = -0.02$; Fig. 1) and only marginally with PWC₁₅₀. Classical haemodynamic parameters (cardiac output, ejection fraction, blood pressure, peripheral resistance, contractile-activity indices) failed to predict either test ($|r| \leq 0.18$ throughout). In contrast, both apnoea durations were tightly linked to neural variables: Stange's test was determined by Baevskiy's Activity Regulation Systems Index, pNN₅₀, θ -power in central loci and α -rhythm frequency ($R = 0.911$; $R^2 = 0.830$; $p < 10^{-6}$), while Guenchi's test depended on serum urea, %CD22 B-lymphocytes, frontal δ -power, occipito-temporal α -power, HF-band of HRV and β -index ($R = 0.723$; $R^2 = 0.523$; $p < 10^{-5}$). **Conclusions.** The duration of a voluntary breath-hold does not measure pulmonary or cardiac reserve. It measures the central nervous capacity to override the chemoreflex — that is, the strength of cortical and autonomic inhibition of the bulbar inspiratory generator. Stange and Guenchi tests, although superficially similar, tap two largely independent neural circuits and should not be used interchangeably as markers of cardiorespiratory fitness.

Keywords: breath-holding test, Stange test, Guenchi test, volitional apnoea, heart rate variability, EEG, neuro-endocrine-immune complex, Truskavets' Spa.

Introduction

Holding the breath after a deep inspiration (Stange's test, 1914) or after a normal expiration (Guenchi's test, also rendered Genchi or Genchi-Sabrazès) is one of the oldest functional manoeuvres in clinical medicine. Both tests are simple, cheap and require no equipment, which is why they have survived in occupational screening, sports medicine and pulmonology for more than a hundred years (Biletsky & Gozhenko, 2007; Trembach & Zabolotskikh, 2017; Berezhna et al., 2024). In the post-Soviet tradition, the two tests are still routinely included in school medical examinations and in the assessment of candidates for the army, divers, pilots and athletes, where they are interpreted as direct measures of "cardiorespiratory endurance" (Belotserkovskiy, 1986; Mishchenko, 1990).

The persistence of this interpretation is somewhat surprising. As early as the 1960s respiratory physiologists pointed out that the duration of a voluntary apnoea is determined by the breaking point — the moment at which the inspiratory drive generated by rising PaCO_2 and falling PaO_2 exceeds the conscious effort to inhibit it (Mithoefer, 1965; Lin, 1982). Trained free-divers can hold their breath for more than ten minutes (Schagatay, 2010; Bain et al., 2018), a feat that has nothing to do with lung volumes or cardiac output and everything to do with central tolerance of hypercapnia. Modern functional MRI studies confirm that the breaking point coincides with activation of prefrontal, insular and anterior cingulate cortices and with descending inhibition of the pre-Bötzinger inspiratory generator (Macey et al., 2017; Trembach & Zabolotskikh, 2019; Faull et al., 2022).

Despite this evidence, no large clinical study has directly compared the classical Stange and Guenchi tests with simultaneously recorded haemodynamic, autonomic, electroencephalographic, metabolic and immune parameters. Such a comparison is the only way to answer the question that gives the title to the present paper: what do good old breath-holding tests really show? In our recent series of studies on patients undergoing balneotherapy at Truskavets' Spa we have systematically registered, in the same persons and on the same days, parameters of the cardiovascular system, HRV, 16-lead EEG, immunogram, gut microbiota and physical working capacity (Popovych et al., 2022; Korda et al., 2024; Żukow et al., 2024). Adding both breath-holding tests to this battery gives a unique opportunity to test, on a single sample, the competing hypotheses about their physiological meaning.

We hypothesised that (i) Stange and Guenchi durations will be uncorrelated with each other, because they are performed at opposite ends of the respiratory cycle and engage different afferent inputs to the brainstem; (ii) neither test will be predicted by classical

cardiorespiratory variables such as PWC₁₅₀, cardiac output or peripheral resistance; and (iii) both tests will be predicted, although by different sets of variables, by parameters reflecting central nervous activity and the neuro-endocrine-immune complex. The aim of the study was therefore to determine which physiological systems actually contribute to the duration of voluntary apnoea in adult patients with chronic somatic pathology in remission.

Material & methods

Participants.

The objects of the study were patients with chronic pyelonephritis and cholecystitis in remission, verified by clinical, laboratory and instrumental criteria. The study included 34 men aged 23–70 years and 10 women aged 33–76 years. Inclusion criteria: chronic pyelonephritis in remission, no exacerbation for at least 3 months before balneotherapy, preserved nitrogen-excreting kidney function (serum creatinine level within normal limits) and functional renal reserve (Gozhenko et al., 2015). Exclusion criteria: acute urinary-tract infection, history of gout or hyperuricaemia, intake of uricolytic or uricosuric drugs within 3 months before the study, decompensated cardiovascular disease, diabetes mellitus, or oncological disease. All patients signed an informed consent to participate in the study. The protocol was approved by the local ethics committee in accordance with the principles of the Declaration of Helsinki.

Testing was performed twice — on admission and after 7–10 days of standard balneotherapy at Truskavets' Spa (drinking of Naftussya bioactive water, applications of ozokerite, mineral baths) (Chebanenko et al., 1997; Ivassivka SV et al., 1999; Ruzhylo et al., 2003; Popovych IL & Barylyak LG, 2009; Lukovych et al., 2015).

Procedure / test protocol / measurements / instruments.

The battery of tests was designed in line with the concepts of the functional-metabolic continuum (Gozhenko, 2016) and the neuro-endocrine-immune complex (Popovych et al., 2022; Korda et al., 2024).

The day before, samples of morning urine and faeces were collected, in which the levels of leukocyturia, erythrocyturia and bacteriuria and the composition of intestinal microbiota were determined, respectively, by unified methods. Urinary syndrome was assessed by the quantitative and quantitative-qualitative levels of bacteriuria, leukocyturia and erythrocyturia (Popovych et al., 2003; Gozhenko et al., 2015). For a qualitative grading of pyelonephritis manifestations the single-point Popovych's scale, built on the basis of Harrington's desirability function (Harrington, 1965), was used.

Then daily urine was collected, in which the concentrations of uric acid (uricase method), creatinine (Jaffe's colour reaction by Popper's method) and urea (urease method, reaction with phenol-hypochlorite) as well as the electrolytes calcium (arsenase III), magnesium (colgamite), phosphates (phosphate-molybdate method), chloride (mercury-rhodanidine method), sodium and potassium (flame photometry) were measured. The analysis followed the manual of Goryachkovskiy (1998). The same metabolic parameters were determined in serum.

Measurements used a flame spectrophotometer "CΦ-46" and analysers "Reflotron" (Germany) and "Pointe-180" (USA) with the corresponding reagent sets.

Next day systolic (Ps) and diastolic (Pd) blood pressure and heart rate (HR) were measured (tonometer "Omron M4-I", Netherlands) in the sitting position, and Stange's and Guenchi's breath-holding tests were carried out (Biletsky & Gozhenko, 2007). We determined also the electrokinetic index (EKI) as rate of electronegative nuclei of buccal epithelium by intracellular microelectrophoresis on the device "Biotest" (produced by VN Karazin Kharkiv National University), according to the method described (Shakhbazov et al., 2000).

Hemodynamic parameters were then determined (echocamera "Toshiba-140", Japan): ejection time (ET), end-diastolic (EDV) and end-systolic (ESV) volumes of the left ventricle; from these the general peripheral vessels resistance (GPVR), cardiac output (CO) and heart work per minute (HWM) were calculated by the classic formulas (Schiller & Osipov, 1993; Bobrov et al., 1997; Ruzhylo et al., 2003; Popovych et al., 2005):

$$GPVR = 80 \cdot (0.67 \cdot Pd + 0.33 \cdot Ps) / HR \cdot (EDV - ESV);$$

$$CO = (EDV - ESV) \cdot HR;$$

$$HWM = 0.1332 \cdot 1.055 \cdot (0.67 \cdot Pd + 0.33 \cdot Ps) \cdot (EDV - ESV) \cdot HR.$$

In addition, the contractile-activity index of the left ventricle was calculated by Sagawa (1981):

$$SCAI = Ps / ESV$$

and by Ruzhylo & Popovych (Popovych et al., 2005):

$$RPCAI = 0.1332 \cdot (0.67 \cdot Pd + 0.33 \cdot Ps) \cdot (EDV - ESV) / EDV \cdot ET.$$

To assess heart rate variability (HRV) the electrocardiogram was recorded during 7 min in lead II (hardware-software complex "CardioLab+HRV", "KhAI-Medica", Kharkiv, Ukraine). The following HRV parameters were used. Baevskiy's parameters: mode (Mo), amplitude of mode (AMo), variational scope (MxDMn), Baevskiy's Stress Index (BSI = AMo / 2 · Mo · MxDMn) and Baevskiy's Activity Regulatory Systems Index (BARS) (Baevsky & Chernikova, 2017). Time-domain methods: HR, SDNN, RMSSD, pNN₅₀, triangular index

(TNN). Frequency-domain methods: power spectral density (PSD) of HRV in the bands high-frequency (HF, 0.4–0.15 Hz), low-frequency (LF, 0.15–0.04 Hz), very-low-frequency (VLF, 0.04–0.015 Hz) and ultra-low-frequency (ULF, 0.015–0.003 Hz). Classical indices were calculated: LF/HF, LFnu = $100 \cdot \text{LF} / (\text{LF} + \text{HF})$, centralisation index $(\text{VLF} + \text{LF})/\text{HF}$ (Heart Rate Variability, 1996; Berntson et al., 1997; Shaffer & Ginsberg, 2017).

Simultaneously the EEG was recorded with the hardware-software complex "NeuroCom Standard" (KhAI Medica, Kharkiv, Ukraine) monopolarly in 16 loci (Fp1, Fp2, F3, F4, F7, F8, C3, C4, T3, T4, P3, P4, T5, T6, O1, O2) according to the 10-20 international system, with reference electrodes A and Ref on the earlobes. Two minutes after the eyes had been closed, 25 s of artefact-free EEG were collected. The analysed options included average EEG amplitude (μV), average frequency (Hz), frequency deviation (Hz), index (%), coefficient of asymmetry (%), absolute ($\mu\text{V}^2/\text{Hz}$) and relative (%) PSD of basic rhythms: β (35–13 Hz), α (13–8 Hz), θ (8–4 Hz) and δ (4–0.5 Hz) in all loci, according to the device instructions. Additionally, the coefficient of asymmetry (As) and laterality index (LI) for the PSD of each rhythm were calculated using formulas:

$$\text{As, \%} = 100 \cdot (\text{Max} - \text{Min}) / \text{Min}; \quad \text{LI, \%} = \Sigma [200 \cdot (\text{Right} - \text{Left}) / (\text{Right} + \text{Left})] / 8.$$

For each EEG locus the entropy (h) of the normalised PSD was computed using Popovych's formulas (Popadynets' et al., 2020; Gozhenko et al., 2021; Popovych et al., 2022), based on the classical Shannon (1948) entropy:

$$h_{\text{EEG}} = -[\text{PSD}\alpha \cdot \log_2 \text{PSD}\alpha + \text{PSD}\beta \cdot \log_2 \text{PSD}\beta + \text{PSD}\theta \cdot \log_2 \text{PSD}\theta + \text{PSD}\delta \cdot \log_2 \text{PSD}\delta] / \log_2 4.$$

Blood samples were then taken for biochemical (see above) and immune tests.

Immune status was evaluated as described in the manual of Lapovets' & Lutsyk (2004). Phenotyping of lymphocyte subpopulations used rosette formation with sheep erythrocytes coated with monoclonal antibodies against receptors CD3, CD4, CD8, CD22 and CD56 ("Granum", Kharkiv), visualised under a light microscope with immersion. Humoral immunity was judged by serum concentrations of immunoglobulins G, A and M (ELISA, "Immunochem", USA) and circulating immune complexes (polyethylene-glycol precipitation).

Phagocytic function of neutrophils was estimated as described by Kulchynskiy et al. (2016). The objects of phagocytosis were 24-h cultures of *Staphylococcus aureus* (ATCC 25423 F49) as a typical Gram-positive specimen and *Escherichia coli* (O55 K59) as a typical Gram-negative specimen. The following parameters were used: phagocytic activity (Hamburger's Phagocytic Index, PhI), intensity (Microbial Count, MC, or Right's Index) and completeness (Killing Index, KI).

Next, the tone and motility of the gall-bladder were evaluated by its volume on an empty stomach and 5, 15 and 30 min after ingestion of a cholekinetic (50 mL of 40 % xylitol). Echoscopy (echocamera "Radmir") was used. To quantify cholekinetics, the area between the cholecystovolumogram and the basal line was calculated (Marfiyan et al., 2015).

Finally, physical working capacity (PWC) was assessed on a bicycle ergometer "Tunturi" (Finland). The first load was 0.5 W/kg at a pedalling frequency of 60–75 rpm. The second load (after 3 min), following the recommendations for the gentle version of the PWC test and taking into account the age of the subjects (Belotserkovskiy, 1986), was chosen so that the heart rate at the end of the load was close to that calculated as $HR = (220 - \text{Age}) \cdot 0.87$, which corresponds to current recommendations for ergometer testing in occupational medicine (Trappe & Löllgen, 2000; Finger et al., 2013; Chatterjee & Schmeißer, 2017). Submaximal PWC₁₅₀ was calculated as mechanical power in Watt per kilogram of body weight (W/kg) as an indicator of cardiorespiratory fitness (Finger et al., 2013).

Statistical analysis.

Statistical analysis was performed with "Microsoft Excel" and "Statistica 6.4" (StatSoft Inc., Tulsa, OK, USA). For each variable Pearson correlation coefficients with both breath-holding tests were calculated; multivariate stepwise regression and canonical correlation analyses were then applied to identify the sets of predictors that best account for Stange and Guenchi durations. The critical value of $|r|$ for $n = 88$ was 0.212 ($p < 0.05$), 0.251 ($p < 0.02$), 0.279 ($p < 0.01$) and 0.356 ($p < 0.001$).

Study limitations.

Several limitations should be acknowledged. (i) The sample, although homogeneous in terms of underlying pathology and treatment, is moderate in size and consists of patients in remission; results may not be fully generalisable to healthy adults or to athletes. (ii) Breath-holding duration was timed by the operator with a stopwatch — a method universally accepted in this tradition (Stange 1914, Guenchi 1923) but inherently dependent on the subject's motivation; we therefore reported each test twice (on admission and after 7–10 days) and used the total $n = 88$. (iii) End-tidal CO₂, SpO₂ and intra-thoracic pressure were not monitored during apnoea; future work should integrate transcutaneous capnography. (iv) The EEG analysis was limited to 25 s of resting record after eye closure; longer recordings with task-related paradigms would allow finer dissection of cortical inhibitory networks.

Results

The first finding is illustrated in Fig. 1: the durations of the two classical breath-holding tests are not related to each other ($r = -0.02$). Subjects who held their breath for a long time

after a deep inspiration (Stange) did not necessarily perform well after a normal expiration (Guenchi), and vice versa. The scatter is broad and homogeneous over the whole range of values.

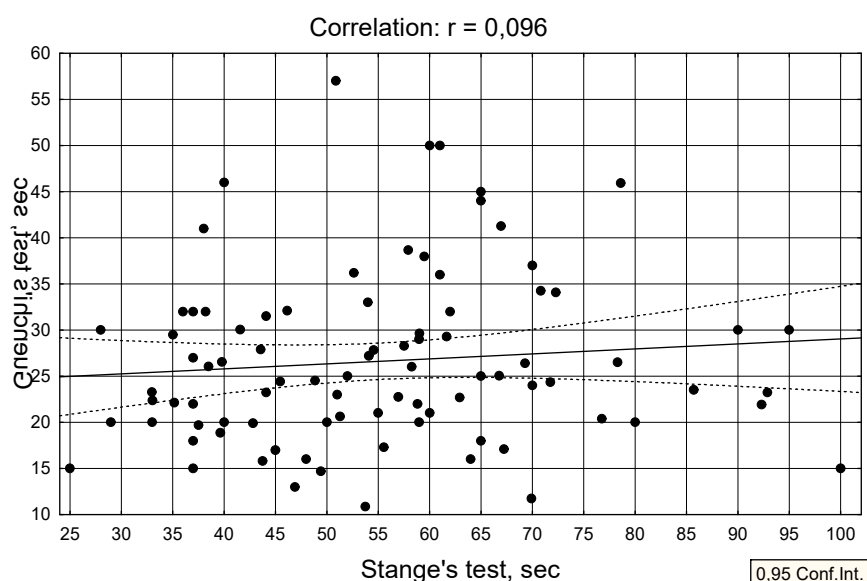


Fig. 1. Absence of correlation between both breath-holding tests

Table 1 lists Pearson correlation coefficients of both tests with 33 simultaneously measured variables ($n = 88$). Two facts stand out. First, classical haemodynamic and somatic descriptors — blood pressure, ejection fraction, cardiac output, stroke volume, contractile-activity indices, body-mass index, sex, ejection time, peripheral resistance — fail to reach the critical value of 0.212 for either test. Second, the few significant coefficients (bold in Table 1) cluster around two different axes: for Stange, the buccal-epithelium electrokinetic index, age, BMI and the cholecystokinetic index; for Guenchi, PWC_{150} in absolute and relative units. The two tests therefore tap two independent populations of correlates.

Table 1. Correlation matrix for breath-holding tests and some variables

Variables ($n=44 \cdot 2$)	**Stange**	**Guenchi**
PWC_{150} , W	-0.126	-0.214
PWC_{150} , W/kg	-0.016	-0.217
Electrokinetic Index of buccal epithelium, %	0.368	-0.020
Age, years	-0.358	0.077
Body Mass Index, kg/m^2	-0.245	-0.061
Cholecystokinetic Index, units	-0.225	0.077
Gall-bladder Basal Volume, mL	0.132	0.049

Sex Index (M=1; W=2)	0.141	-0.128
Ejection Time, msec	-0.027	0.176
General Peripheral Vessels Resistance, kPa·s/m ³	0.069	-0.159
Ejection Fraction, %	-0.154	0.025
Cardiac Output, L/min	0.055	0.142
Heart Work, kJ/min	0.046	0.129
Stroke Volume of Left Ventricle, mL	-0.121	0.073
Blood Pressure Systolic, mmHg	-0.110	-0.024
End-diastolic Volume of Left Ventricle, mL	-0.096	0.094
Blood Pressure Diastolic, mmHg	-0.088	0.088
End-systolic Volume of Left Ventricle, mL	0.044	0.058
Ruzhylo & Popovych's Contractile Activity Index, kPa/s	-0.049	-0.029
Sagawa's Contractile Activity Index, mmHg/mL	-0.022	-0.040
<i>Lactobacilli</i> feces, lg CFU/g	-0.007	0.197
<i>E. coli attenuated</i> feces, %	-0.051	-0.190
<i>Bifidobacteria</i> feces, lg CFU/g	-0.002	0.186
<i>E. coli hemolytica</i> feces, %	0.050	0.122
<i>Klebsiella & Proteus</i> feces, %	0.065	0.050
<i>E. coli common</i> feces, lg CFU/g	0.023	0.015
Leukocyturia, lg Leukocytes/mL	-0.004	-0.172
Leukocyturia, points	0.002	-0.136
Erythrocyturia, lg Erythrocytes/mL	-0.038	0.069
Erythrocyturia, points	0.006	0.057
Bacteriuria, points	0.054	0.045
Bacteriuria, lg CFU/mL	0.018	0.004

Note. According to the formula: $|r| = \{\exp[2t/(n-1.5)^{0.5}] - 1\} / \{\exp[2t/(n-1.5)^{0.5}] + 1\}$, for a sample of $n = 88$ the critical value of $|r|$ is **0.212** at $p < 0.05$ ($t > 2.00$); **0.251** at $p < 0.02$ ($t > 2.39$); **0.279** at $p < 0.01$ ($t > 2.66$); **0.356** at $p < 0.001$ ($t > 3.46$).

Even the weak haemodynamic dependence of Stange's test on PWC₁₅₀ (the textbook claim) is not confirmed in our material. Fig. 2 shows the corresponding scatterplot — a uniform

cloud with r close to zero. By contrast, Guenchi's test shows a weak but significant negative dependence on PWC_{150} (Fig. 3); the better the cardiorespiratory fitness, the shorter — not the longer — the post-expiratory apnoea. This counter-intuitive finding will be returned to in the Discussion.

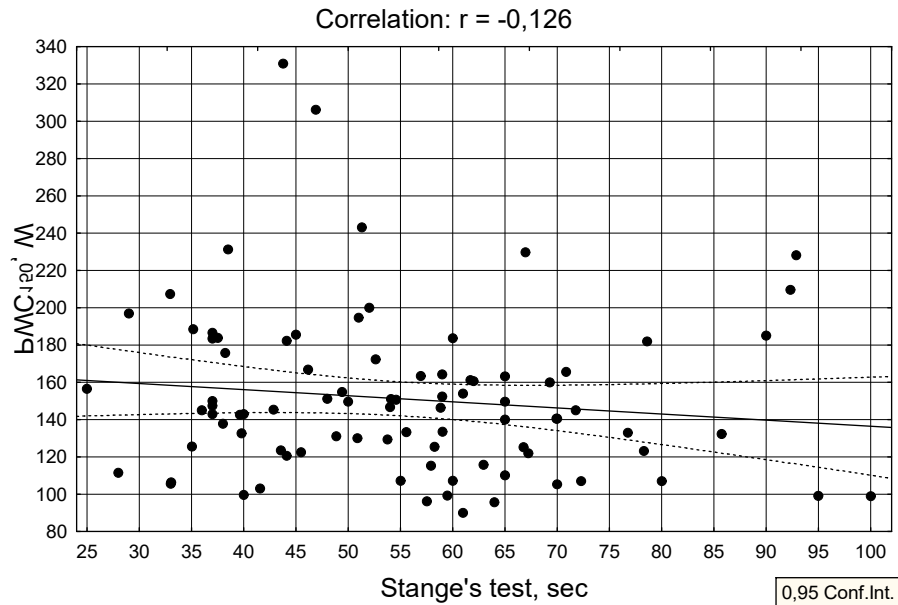


Fig. 2. Absence of correlation between Stange's test and PWC_{150}

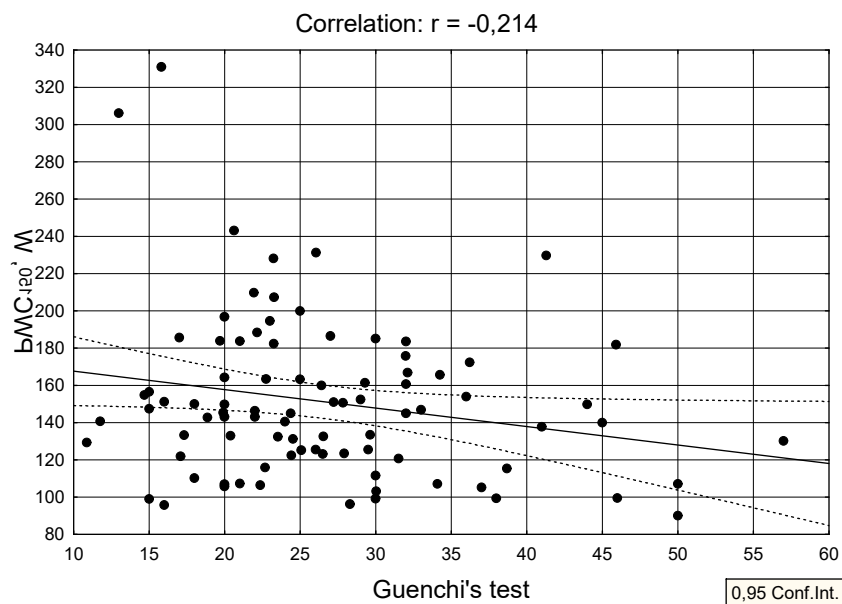


Fig. 3. Correlation between Guenchi's test and PWC_{150}

Multivariate stepwise regression confirms the picture (Tables 2 and 3). When PWC_{150} and faecal Lactobacilli are entered as predictors of Guenchi's test, the model explains only 8 % of variance (Table 2). Adding neuro-endocrine-immune variables raises the explained variance to 52 % (Table 3): serum urea, percentage of CD22 B-lymphocytes, frontal δ -power, occipito-

temporal α -power, HF-band of HRV and β -index together describe Guenchi's duration far better than any haemodynamic parameter.

Table 2. Regression summary for Guenchi test vs. PWC & LacBac

$R = 0.289$; $R^2 = 0.083$; Adjusted $R^2 = 0.062$; $F(2,9) = 3.9$; $p = 0.025$; $SE = 9$ sec

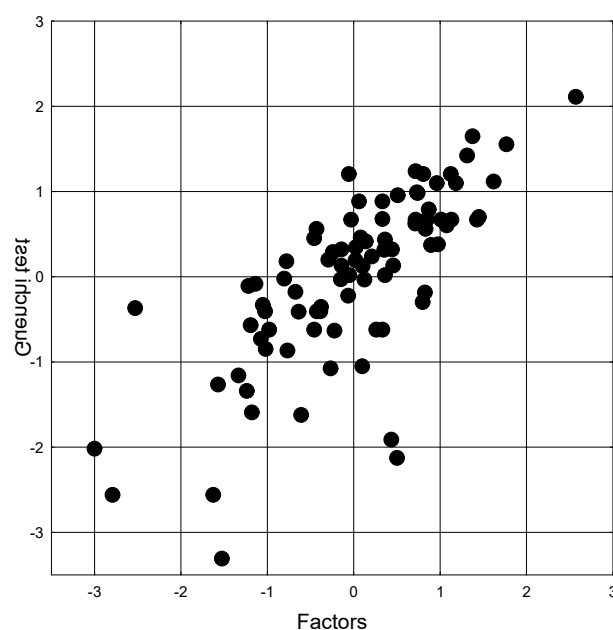
N = 2·44	r	Beta	St. Err. of Beta	B	St. Err. of B	t(85)	p-level
Intercept				25.9	5.8	4.46	10^{-4}
PWC ₁₅₀ , W/kg	-0.217	-0.211	0.104	-3.853	1.895	-2.03	0.045
<i>Lactobacilli</i> feces, lg CFU/g	0.197	0.191	0.104	1.264	0.687	1.84	0.069

Table 3. Regression summary for Guenchi test vs. neuro-immune-metabolic variables

$R = 0.723$; $R^2 = 0.523$; Adjusted $R^2 = 0.475$; $F(8,8) = 10.8$; $p < 10^{-5}$; $SE = 6.7$ sec

N = 2·44	r	Beta	St. Err. of Beta	B	St. Err. of B	t(79)	p-level
Intercept				3.25	9.01	0.36	0.719
Urea Serum, mM/L	0.355	0.402	0.080	3.263	0.647	5.04	10^{-5}
CD22 B-lymphocytes, %	0.310	0.350	0.082	0.708	0.166	4.27	10^{-4}
SPD Fp1- δ , %	0.240	0.301	0.100	0.133	0.044	2.99	0.004
SPD T5- δ , $\mu V^2/Hz$	0.226	0.206	0.088	0.003	0.001	2.34	0.022
SPD HF band, msec ²	0.223	0.238	0.081	0.004	0.001	2.94	0.004
Index- β , %	-0.290	-0.260	0.082	-0.197	0.062	-3.16	0.002
SPD O1- α , %	-0.273	-0.390	0.159	-0.185	0.075	-2.46	0.016
SPD T5- α , %	-0.222	0.366	0.161	0.214	0.094	2.27	0.026

Canonical-correlation analysis (Fig. 4) summarises the relationship: when the linear combination of the same eight neuro-immune-metabolic factors is treated as the X-line and Guenchi duration as the Y-line, R rises to 0.723; $\chi^2(8) = 64$; $p < 10^{-6}$; Wilks' Λ -prime = 0.456.



$$R = 0.723; R^2 = 0.523; \chi^2(8) = 64; p < 10^{-6}; \Lambda\text{-prime} = 0.456$$

Fig. 4. Scatterplot of canonical correlation between some factors (X-line) and Guenchi test (Y-line)

For Stange's test the picture is different. The buccal-epithelium electrokinetic index and the cholecystokinetic index together account for 15 % of variance (Table 4), but the addition of central-nervous variables — Baevskiy's ARSI, pNN_{50} , θ -power in central loci (C3, C4), α -power in frontal and parietal loci, α -rhythm frequency, electrolyte excretion — increases R^2 to 0.830 (Table 5). The strongest single predictors of Stange duration are Baevskiy's ARSI (a global index of autonomic regulation; $r = 0.592$) and the frequency of the α -rhythm ($r = -0.489$).

Table 4. Regression summary for Stange test vs. EKI & CCKI

$$R = 0.391; R^2 = 0.153; \text{Adjusted } R^2 = 0.133; F(2,9) = 7.7; p = 0.0009; SE = 15 \text{ sec}$$

N = 2·44	r	Beta	St. Err. of Beta	B	St. Err. of B	t(85)	p-level
Intercept				44.6	10.8	4.12	10^{-4}
Electrokinetic Index, %	0.368	0.332	0.104	0.455	0.142	3.21	0.002
Cholecystokinetic Index, units	-0.225	-0.136	0.104	-0.016	0.012	-1.31	0.193

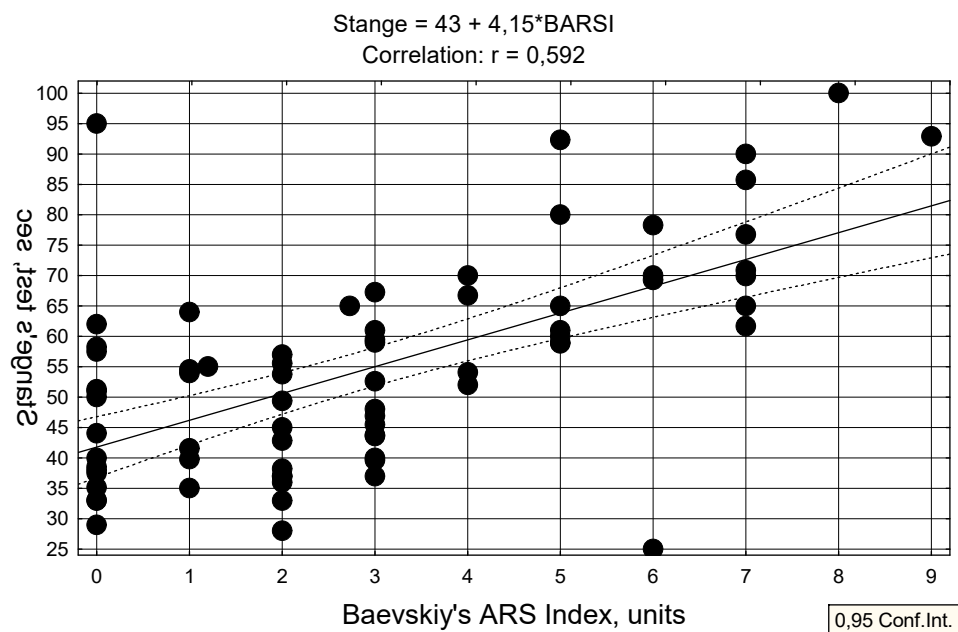


Fig. 5. Scatterplot of correlation between Baevskiy's ARS Index (X-line) and Stange's test (Y-line)

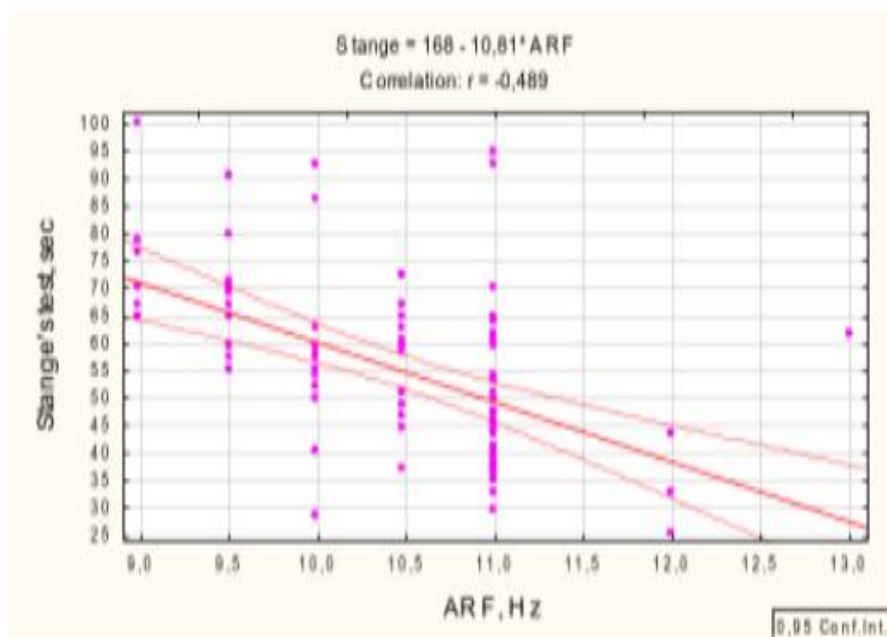
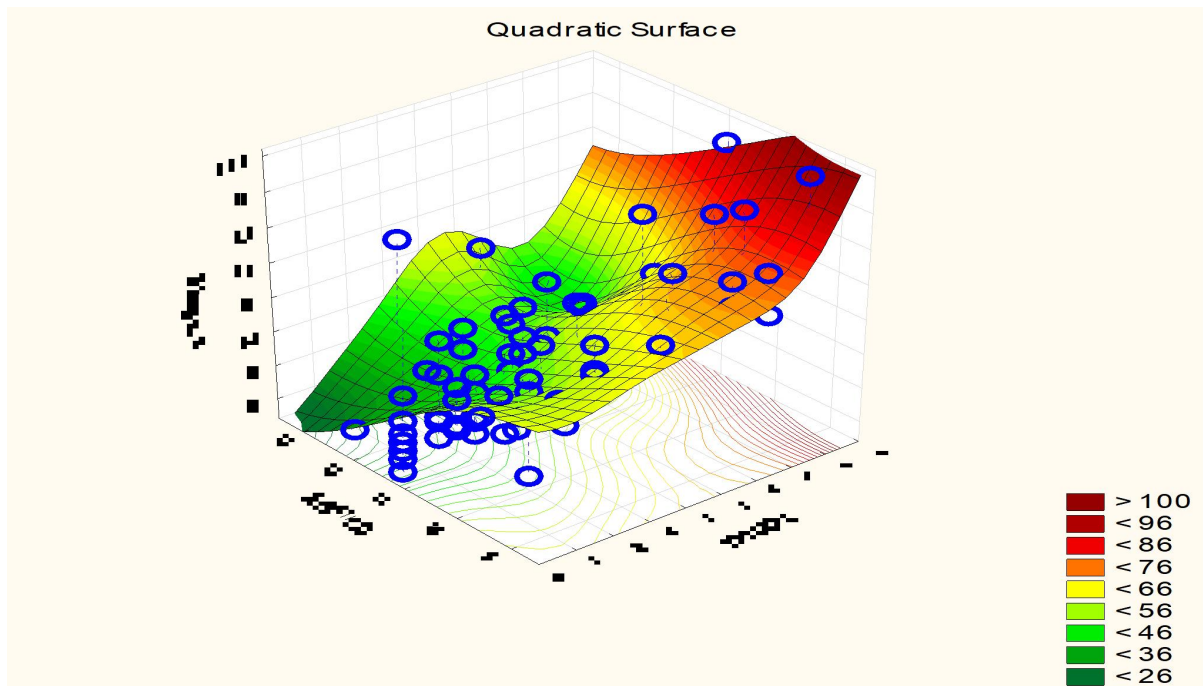


Fig. 6. Scatterplot of correlation between α -rhythm frequency (X-line) and Stange's test (Y-line)



$$\text{Stange (sec)} = 124 \pm 20 + 3.30 \pm 0.62 \cdot \text{BARSII (units)} - 7.51 \pm 1.84 \cdot \text{ARF (Hz)}$$

$R = 0.668$; $R^2 = 0.446$; Adjusted $R^2 = 0.433$; $F(2,8) = 33.8$; $p < 10^{-5}$; $SE = 12 \text{ sec}$

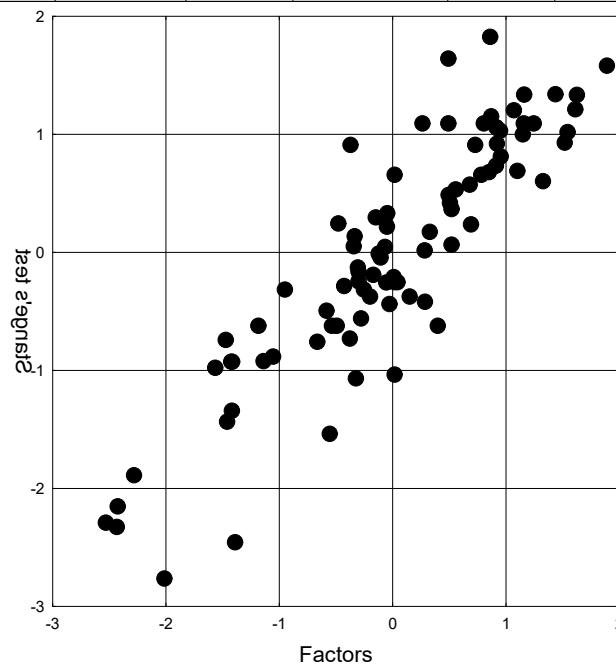
Fig. 7. Dependency of Stange's test (Z-line) on Baevskiy's ARSI (X-line) and frequency of α -rhythm (Y-line)

Table 5. Regression summary for Stange test vs. neuro-metabolic variables

$R = 0.911$; $R^2 = 0.830$; Adjusted $R^2 = 0.806$; $F(11,8) = 33.8$; $p < 10^{-6}$; $SE = 7.3 \text{ sec}$

N = 2·44	r	Beta	St. Err. of Beta	B	St. Err. of B	t(76)	p-level
Intercept				128.9	14.0	9.22	10^{-6}
Baevskiy's ARS Index, units	0.592	0.276	0.054	1.896	0.372	5.10	10^{-5}
pNN₅₀ HRV, %	0.457	0.368	0.058	0.489	0.077	6.352	10^{-6}
Electrokinetic Index, %	0.368	0.195	0.053	0.266	0.073	3.65	10^{-3}
SPD C4-θ, %	0.367	0.359	0.071	1.217	0.243	5.02	10^{-5}
Calcium Excretion, mM/24 h	0.273	0.086	0.051	0.460	0.273	1.68	0.097
Creatinineuria, mM/24 h	0.270	0.112	0.051	0.500	0.225	2.22	0.029

SPD C3- θ , $\mu\text{V}^2/\text{Hz}$	0.269	-0.349	0.113	-0.106	0.034	-3.10	0.003
SPD Fp2- α , $\mu\text{V}^2/\text{Hz}$	0.254	0.348	0.122	0.054	0.019	2.85	0.006
SPD O2- θ , $\mu\text{V}^2/\text{Hz}$	0.235	0.174	0.066	0.056	0.021	2.64	0.010
SPD P4- α , $\mu\text{V}^2/\text{Hz}$	0.228	-0.183	0.094	-0.011	0.006	-1.94	0.056
Frequency- α , Hz	-0.489	-0.507	0.056	-10.90	1.21	-8.99	10^{-6}



$$R = 0.911; R^2 = 0.830; \chi^2(10) = 127; p < 10^{-6}; \Lambda\text{-prime} = 0.204$$

Fig. 8. Scatterplot of canonical correlation between some factors (X-line) and Stange test (Y-line)

Discussion

Three findings of the present study deserve emphasis. First, the durations of the two classical voluntary-apnoea tests are uncorrelated. Second, neither test is predicted by the variables that the textbook tradition treats as their physiological substrate — cardiac output, ejection fraction, peripheral resistance, blood pressure or ergometric working capacity. Third, both tests are predicted, although by largely non-overlapping sets, by parameters of central-nervous and autonomic regulation.

Independence of Stange and Guenchi. The lack of any correlation between the two tests ($r = -0.02$; Fig. 1) is by itself a powerful argument against a common pulmonary or cardiovascular substrate. If both tests measured the same reservoir of oxygen, the same compliance of the lungs or the same circulatory reserve, their durations should be strongly correlated. The fact that they are not, even in 88 paired observations, suggests that the two

manoeuvres tap different neural circuits. Stange's test is preceded by a maximal inspiration, which strongly activates pulmonary stretch receptors and the Hering–Breuer reflex, providing tonic inhibition of the inspiratory generator (Trembach & Zabolotskikh, 2019). Guenchi's test starts from a passive end-expiration, in which lung volume is at functional residual capacity and stretch-receptor input is minimal; the duration of apnoea therefore depends on the tolerance to rising CO₂ and on descending cortical inhibition alone. The two tests have a common end-point (the breaking point) but different starting conditions and different afferent inputs.

Failure of the cardiorespiratory hypothesis. The textbook claim that breath-holding duration reflects the state of the lungs and heart (Belotserkovskiy, 1986; Mishchenko, 1990) is not supported by our data. None of the 17 cardiovascular variables (Table 1) reaches the critical $|r|$ for Stange, and only PWC₁₅₀ — a global, integrated measure — does so for Guenchi (negative direction). Importantly, the negative sign of this correlation is the opposite of what the cardiorespiratory hypothesis predicts. A higher PWC₁₅₀ is associated with a shorter, not longer, post-expiratory apnoea. The most parsimonious explanation is that PWC₁₅₀ in our sample is a marker not of generic fitness but of sympathetic drive — patients with higher PWC₁₅₀ also have higher Baevskiy's ARSI and lower α -rhythm power, conditions that reduce cortical inhibition of the inspiratory generator. A similar paradox has been reported in elite endurance athletes, who often show shorter expiratory apnoea than sedentary controls (Schagatay, 2010; Bain et al., 2018).

Neural substrate of Stange's test. The regression model for Stange (Table 5; Figs 5–8) explains 83 % of variance, and is dominated by autonomic and EEG variables: Baevskiy's ARSI (a global index of autonomic regulation), pNN₅₀ (a marker of parasympathetic tone), θ -power in central loci (C3, C4) and the frequency of the α -rhythm. The positive coefficient of BARSII and the negative coefficient of α -frequency are notable: a longer Stange duration is associated with stronger central regulation and slower α -rhythm — both pointing to a state of focused, internally directed attention with relative cortical inhibition. The α -rhythm has long been recognised as a marker of cortical idling and inhibitory control (Klimesch, 2012); its slowing during voluntary apnoea is consistent with active suppression of the inspiratory drive. The contribution of θ -rhythm in fronto-central loci further supports an interpretation in terms of executive control: fronto-midline θ is generated in the anterior cingulate cortex and is enhanced during effortful inhibition (Cavanagh & Frank, 2014).

Neural substrate of Guenchi's test. The regression model for Guenchi (Table 3) is different. It is dominated by serum urea, %CD22 B-lymphocytes, frontal δ -power, occipito-temporal α -

power, HF-band of HRV and β -index. The presence of serum urea and B-lymphocytes in the predictive set is at first sight surprising, but it is consistent with the concept of a unified neuro-endocrine-immune complex (Popovych et al., 2022; Korda et al., 2024) and with the well-documented influence of hyperammonaemia on central neurotransmission (Felipo, 2013). Frontal δ -power is generated in deep prefrontal structures and has been linked to motivational/reward processing (Knyazev, 2012); occipito-temporal α -power reflects visual cortical idling. The negative β -index is again consistent with a state of reduced cortical arousal during the apnoea. Together these variables sketch a picture in which post-expiratory breath-holding is mediated by a slower, more limbic and metabolic loop than post-inspiratory breath-holding.

Implications for the use of the tests. Our results do not imply that Stange's and Guenchi's tests are useless — they imply that they should be re-interpreted. As markers of cardio-respiratory reserve they are unreliable; as windows on the central capacity for volitional inhibition of inspiratory neurons they may be uniquely valuable, because they are simple, cheap and require no equipment. The independence of the two tests means that they should not be used interchangeably: a comprehensive assessment should include both, and the difference between Stange and Guenchi durations may itself carry information about the balance between vagal-mediated (Hering–Breuer) and cortical-mediated inhibition.

Relation to previous work. The notion that voluntary apnoea is essentially a central-nervous phenomenon is not new (Mithoefer, 1965; Parkes, 2006; Faull et al., 2022), but it has rarely been tested against simultaneously measured haemodynamic, autonomic, EEG, metabolic and immune variables in the same persons. The Truskavets' Spa series (Popovych et al., 2003; 2022; Żukow et al., 2022; 2024) and the recent Ukrainian–Polish–Romanian collaborations on higher nervous activity and physical education (Berezhna et al., 2024; Kozina et al., 2024) provide the necessary framework. Our results extend that framework by showing that the same neuro-endocrine-immune block that explains balneotropic effects on PWC, microbiota and immunity also explains the duration of voluntary apnoea.

Conclusions

In a sample of 44 patients with chronic pyelonephritis and cholecystitis examined twice ($n = 88$) the durations of the post-inspiratory (Stange) and post-expiratory (Guenchi) breath-holding tests proved to be independent of each other and largely independent of classical cardiorespiratory parameters. Both tests were tightly linked to variables of central-nervous and autonomic regulation: Stange to Baevskiy's ARSI, pNN_{50} , central θ -power and α -rhythm

frequency ($R^2 = 0.83$), Guenchi to serum urea, CD22 B-lymphocytes, frontal δ -power, occipital α -power, HF-band of HRV and β -index ($R^2 = 0.52$).

We therefore conclude that the good old breath-holding test does not reflect the state of the cardiorespiratory system; it reflects the central nervous capacity for volitional inhibition of the inspiratory generator. Stange's and Guenchi's tests tap two different inhibitory circuits and should not be used interchangeably. Their value as simple, cheap and equipment-free markers of central inhibitory control deserve to be re-evaluated in a wider range of populations, including healthy adults, athletes and patients with neurological or psychiatric disorders.

Conflicts of interest

The authors declare that they have no conflicts of interest related to this study.

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