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Research Article

Neurotest: A New Paradigm for Monitoring Biphasic Trend of Organic Pathologies

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Abstract

Sympathetic and parasympathetic systems innervate various organs and cause different responses in the body. Sympathetic system has stimulating, exciting and contracting functions and prepare the organism to face the danger. From an anatomical point of view, the nerves of the sympathetic system are distributed to blood vessels, sweat glands, salivary glands, heart, lungs, intestines and numerous other organs. Parasympathetic system has functions opposite to the sympathetic one, predisposing the organism to a resting situation. The nerves of the parasympathetic nervous system are distributed to blood vessels, salivary glands, heart, lungs, intestines, genital organs, eyes, tear glands and numerous other organs and tissues. Both sympathetic and parasympathetic systems cause different signs in all the diseases. The variation of the sympathetic and parasympathetic systems is shown by different clinical signs that can be taken as a reference to assess a pathological condition in humans. From this perspective, the aim of this article is to provide a first message to the scientific community to help them understand how the monitoring of patients' clinical symptoms could be useful to better evaluate the therapeutic act in response to pathologies. The latest events related to Covid-19 infections have brought even more evidence to the need to monitor this clinical picture. Monitoring these aspects can be helpful in making decisions, taking into strong consideration the pharmacological role on the sympathetic and parasympathetic system.

Keywords: *Neurotest; Sympathetic; Parasympathetic; SARS-CoV2; Monitoring*

Abbreviations

GABA: γ-Aminobutyric Acid; Ach: Acetylcholine

Introduction and Methodology

In all types of pathologies, a sequence of alternating symptoms of sympathicotonic and vagotonic phases has been observed. The accentuation of sympathetic and parasympathetic aspects provides elements for monitoring the course of the disease and ensures a more appropriate approach to the therapeutic act.

Sympathicotonia indicates a condition in which the sympathetic system prevails and is characterized by: (i) narrowing of peripheral blood vessels (cold hands and feet), (ii) increased blood pressure with a decrease in vessel content and (iii) poor appetite and limited functioning of the digestive tract and metabolism. The sympathetic system has a stimulating, exciting and contracting function. It responds to fight or flight mechanisms and its activation causes obvious clinical signs (Table 1).

On central nervous system, sympathetic activation stimulates brain activity and influences emotional behavior, inducing a state of attention and stress useful to the individual to deal with emergency situations.

NEUROTEST				
Stimulus	**Sympathetic**	**N°**	**Vagal**	**N°**
Hunger	↓	3	↑	3
Eye	dryness	2	teary eyes	1
Stomach	Meteorism	2	stomach acid	2
Cholecyst			contraction	1
Intestine perstalsis	↓	2	↑	2
Anal sphincter	contraction	2	relaxation	2
Nose itch	present	2	absent	
Hands	cold	3	hot	3
Sleepiness	<	2	>	2
Saliva	dryness	1	sialorrhea	2
Breathing	relaxation	2	contraction	1
Blood pressure	↑	2	↓	2
Heartbeat	↑	2	↓	2
Bladder sphincter	contraction	2	relaxation	2
Sexual organs	premature	3	frigidity	2

GABAergic NEUROTEST				
Stimulus	**Normal**	**↓ GABA**	**↑GABA**	**N°**
Hunger	normal	Absent	Present	2
Sleep	normal	Absent	Present	3
Libido	normal	Absent	Present	3

Table 1: *Correlation between sympathetic and parasympathetic stimulus.*

Vagotonia indicates a condition in which the parasympathetic system prevails. Vagotonia follows sympathicotonia and is characterized by what is listed below, with manifestations opposite to those of the sympathicotonic phase: (i) dilation of peripheral blood vessels (warm hands and feet), (ii) lowering of blood pressure with an increase in the content in the vessels and (iii) great appetite and good functioning of the digestive tract and metabolism. The hormone that regulates the activation of these mechanisms is Acetylcholine (Ach).

Regarding the heartbeat, unlike vascular tone, heart rate at rest depends on vagal tone and circulating humoral substances [1], while if subjected to stressful stimuli it is sympathetic control that takes over (Figure 1).

γ-aminobutyric acid (GABA) participates in central cardiovascular control and has an influence on heart rate and blood pressure. GABA plays key roles in the control of the autonomic nervous system, for example in reproduction, energy and fluid balance [2] and activates part of parasympathetic and sympathetic modulation. The GABAergic system controls various functions, such as hunger, sleep and desire/apathy [3,5].

Emotional stress cause clinically important effects on cardiovascular function through the Autonomic Nervous System. Cardiovascular changes characteristic of emotional stress affect sympathetically mediated increases in blood pressure and heart rate, as well as inhibition of vagal heart rhythm activation.

GABAergic system controls different functions, such as hunger, sleep and desire/apathy. Several lines of study have suggested that GABA plays a role in promoting food intake in the hypothalamic feeding center. Recent studies have revealed that GABA acts as an orexigenic [3]. Reduced levels of GABA can promote difficulty falling asleep and early awakening. It is well known that the activation of GABAA receptors promotes sleep. It has also been shown that GABAB receptors increase brain-activated behavioral states (wakefulness and REM sleep) [4]. The GABAergic system is also involved in hedonistic processes. The subcortical GABA signals engage the hedonic sphere at nucleus accumbens level and amplify the emotional reactions of pleasure [5].

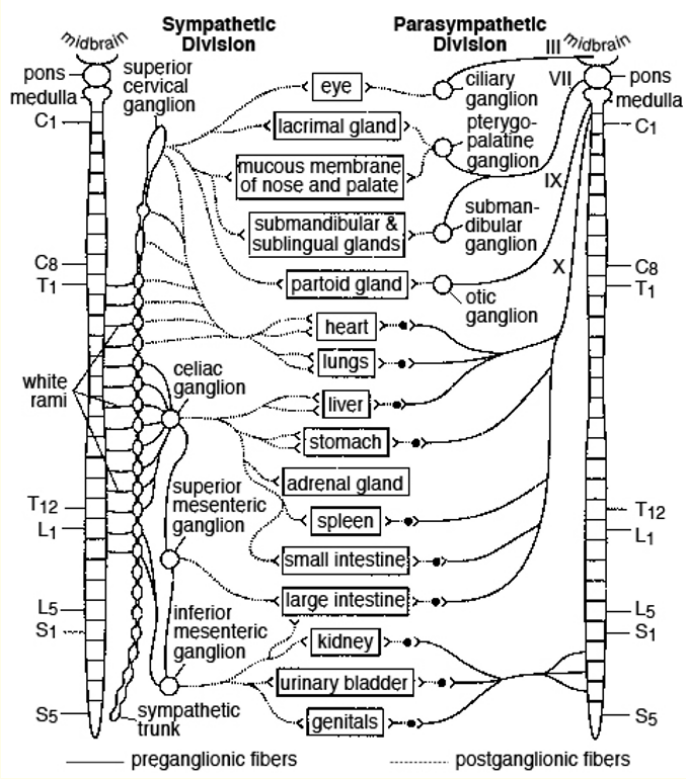

Figure 1: *Organs innerved by sympathetic or parasympathetic system.*

Peci., *et al*. have developed Neurotest, a self-assessment questionnaire that investigates sympathico-vagal symptomatology combined with the contemporary evaluation of the expression of the GABAergic system that manifests itself with specific clinical signs such as: sleep, hunger, desire [6].

The main sympathico-vagal and GABAergic symptoms investigated are reported in table 1. A variable score from 1 to 3 to each symptom associated with the sympathetic and parasympathetic system has been assigned, in relation to the weak, mean or strong presence of the single symptom, perceived by the patient. This score is the result of our clinical experience: the values have been assigned according to the weighting of the symptom and its importance in the clinical setting, but it still needs to be critically reviewed in order to assign a more appropriate value to the individual symptom. GABAergic symptomatology, on the other hand, is measured as present or absent.

The results obtained from a study carried out in 2016 by our team [6] are interesting and worthy of speculation. Neurotest allows to keep sympathetic and parasympathetic system under control, and to verify its progress and even minimal variations at each therapeutic change, both in pharmacological and rehabilitative nature, including all those manifestations that can influence normotonia, thus being

able to verify any changes and modify the effects. In addition, it was possible to combine the simultaneous evaluation of the GABAdrenergic expression which manifests itself with specific clinical signs such as sleep, hunger, desire.

When the values take on clearly unbalanced connotations in favor of the first or the second system (sympathetic or parasympathetic), both physical and pharmacological methods can be used to promote or dampen the effects. On the other hand, if the score rises and we have the simultaneous and clear presence of symptoms both of the one or the other system, we are faced with an alarm reaction and we can warn the patient to keep the medical team informed about the symptomatologic evolution, preventing any excess of autonomous response, both in a sympathetic and vagal sense. At any stage, monitoring represents a way of keeping the "neuro" functions under control, which are now decisive for the success of a therapeutic act, to prevent Nocebo phenomenon [7].

Results and Discussion

All diseases have 2 phases: the first is the sympathetic one, in which there is an absence of symptoms, the second is the vagotonic phase in which the symptoms are accentuated.

When the normotonic curve changes, the whole organism enters a state that involves a neurovegetative alteration of the sympathicotonia. The phase of the curve, which follows a traumatic event or considered dangerous by the organism, can be viewed in the upper part of the graph (Figure 2): the organism is in a permanent stress condition, a state of alert that serves to find a rapid solution to a problem. In this phase there is vasoconstriction and high blood pressure. In most cases, there are no symptoms that make us think of a disease, which is why this phase is characterized by the absence of symptoms.

The next phase is the resolution or repair phase. It is characterized by vasodilation and lowering of blood pressure. The tissues begin to be repaired. At this phase, symptoms such as fever, pain, inflammation begin to appear; we are entering the vagotonic phase in which the biology of the body asks for rest to allow the functional recovery of the tissues that have remained under stress throughout the active phase.

The more intense the sympathetic phase is, the more the vagotonic phase will be. To get out of the conflict situation, the body must react. We visualize this reaction with a peak in sympathotonia, a phase called epileptoid crisis, as a manifestation of the patient's recovery of functions, and the consequent vagotonic response. At this point, normotonia normally returns (Figure 2).

In some cases, the patient's neurovegetative rhythm can persist at a sympathetic or vagotonic level, not following the subsequent epileptoid crisis that leads the body towards normotonia. In the first case, the body experiences a phase of constant alertness, due to the maintenance of the autonomic rhythm in sympathetic tone. In the second case, with the prolongation of the autonomic rhythm in the vagotonic phase, we are witnessing the onset of chronic pathologies.

However, it may happen that, in case of diseases or serious traumatic events, an epileptoid crisis occurs, characterized by an overall improvement in the patient's clinical picture. During this phase, there is a final lash that the body makes to get out of an emergency situation that is characterized by a generalized well-being perceived by the patient. At this particular moment, the patient does not feel any kind of pain or symptoms and seems "miraculously" cured. This sympathetic peak is followed by a second very intense vagotonic peak; in this case the organism cannot tolerate the subsequent neurovegetative phase and precipitates towards a fatal outcome (Figure 3).

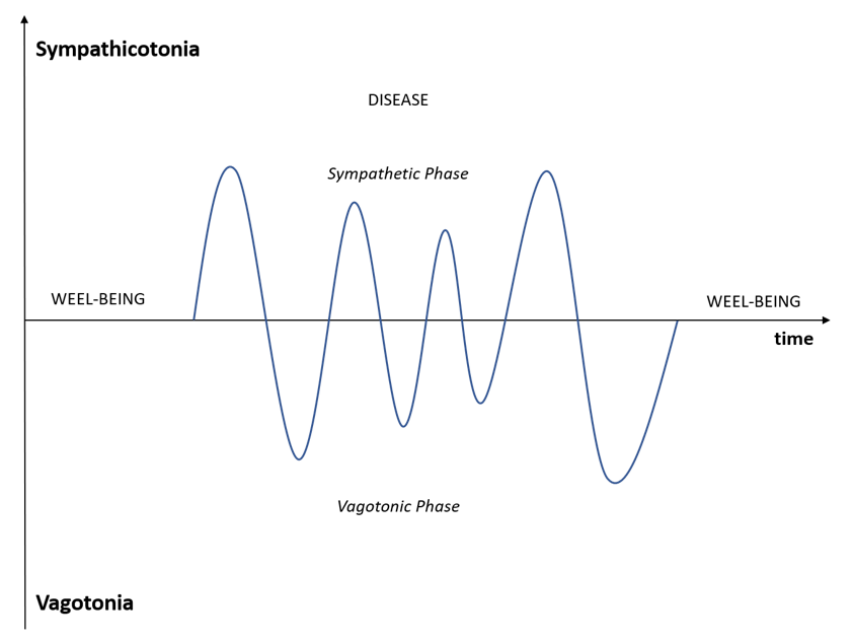

Figure 2: *The graph shows the alternation of the normotonic curve followed by the appearance of the sympathetic phase and subsequent parasympathetic phase during the manifestation of a pathology.*

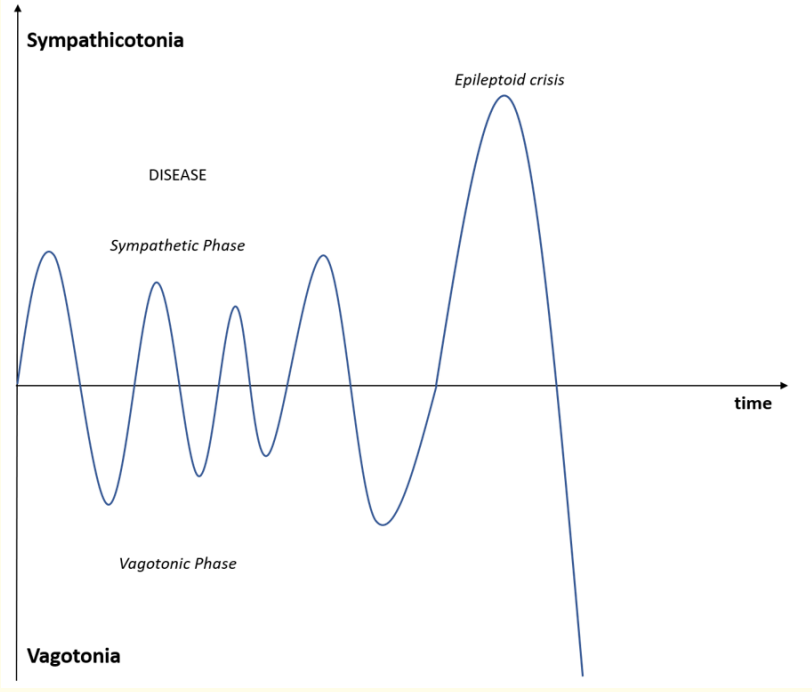

Figure 3: *The peak of the epileptoid crisis in sympathetic phase is followed by a peak in the vagotonic phase, so strong that the organism cannot react.*

Death occurs by brain expansion, since the sympathetic and parasympathetic systems also regulate body fluids. At the cerebral level, in vagotonia the cerebral fluids expand; the meninges try to contain the cerebral expansion and force themselves to hold back the expansion, so the intracranial pressure increases due to a greater leakage of expanding liquids and the interstitial pressure rises due to the recall of fluids that interpose themselves in the interstitial intracellular spaces. During the epileptoid crisis there is a constriction of the brain, due to the re-entry of interstitial fluids and consequent lowering of the intracranial interstitial pressure. This phase is followed by a precipitation in the vagotonic phase so intense that it causes the interruption of communication of the autonomic nervous system and the heart, with a consequent fatal outcome (Figure 3).

This acute process is not easy to handle and it is important to avoid the extreme fall of the peak into vagotonia.

Knowing the alternation of phases and anticipating the symptoms could be the key to stop the process.

Conclusion

Understanding the modulation of brain activity during anticipation, contextual learning and pain perception is an important step, with theoretical and practical implications, to explain how even externally reinforced stimuli interact with individual traits to induce analgesic responses through the Nocebo effect [7]. In clinical practice, the Nocebo effect creates negative expectations on symptoms and can have effects that affect the patient's recovery and must be considered during symptom assessment. Furthermore, the various therapies taken by patients can also cause alterations in the perception of symptoms.

To give importance to the symptoms experienced by patients, in order to make a correct evaluation of the therapeutic act, Peci., *et al*. used the Neurotest [6].

The use of Neurotest allows us to detect the symptoms felt by the patient and associate them with clinical signs as a manifestation of a sympathicotonic or vagotonic phase. Analyzing the symptomatology to be treated as a sign of an event that is about to happen, would allow the medical staff to intervene on the patient. In this way they would not intervene in view of the sympathicotonic or vagotonic phase that the patient manifests, causing an exacerbation of the condition to which the organism is subjected and against which it is fighting. The focal point concerns the anticipation of the next phase, in order to act on it. Therefore, Neurotest could be extremely useful in association with laboratory values or with neurosystemic measurement, to predict the subject's disease phase and intervene in an early stage.

The monitoring of patients clinical symptoms of patients through Neurotest opens new horizons for the treatment of pathologies, directing doctors and healthcare professionals towards a more appropriate treatment in full compliance with the patient.

The use of the Neurotest can be contextualized in the clinic of the current Covid-19 pandemic. Observing hospitalized patients suffering from SARS-CoV2, it is possible to note the alternation of the sympathetic and vagal phases. By working in such way as to anticipate the next phase, it may be possible to understand how to intervene correctly on the patient's state and in some cases, this can save their life.

Conflict of Interest

Authors declare there is no conflict of interest.

Bibliography

1. VM Smirnov. "Tone of sympathetic nerves and regulation of heart activity". *Bulletin of Experimental Biology and Medicine* 130.10 (2000): 930-933.

2. Henderson LP., *et al.* "Anabolic Androgenic Steroids and Forebrain GABAergic Transmission". *Neuroscience* 138.3 (2006): 793-799.

3. Suyama S and Yada T. "New insight into GABAergic neurons in the hypothalamic feeding regulation". *The Journal of Physiological Sciences* 68.6 (2018): 717-722.

4. Gottesmann C. "GABA mechanisms and sleep". *Neuroscience* 111.2 (2002): 231-239.

5. Faure A., *et al.* "Desire and dread from the nucleus accumbens: cortical glutamate and subcortical GABA differentially generate motivation and hedonic impact in the rat". *PLoS One* 5.6 (2010): e11223.

6. Peci S., *et al.* "The symptomatology of the sympathetic and vagal system as monitoring model of the therapeutic act (Neurotest)". Abstract, 2016; Poster in XXIV National Congress of the Italian Society of Psychophysiology (2016).

7. Peci S and Peci F. "Nocebo phenomenon". *Neuropsychological Trends* (2016).

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