

*Covid-19 and its potential stressful effect: how a multidimensional assessment can detect risk factors for stress-related disorders*

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## **Introduction**

The authors fear that there will be a series of consequences due to the pandemic, beginning with a series of psychopathological disorders found in the population who have had to change their life habits and have long been under the negative influence of anxieties, fears, depression, and other distress symptoms.

In this environment, the individual had to process extremely diverse types of messages:

- the continuous information on the pandemic causes stress capable of activating the organism from a psycho-physiological point of view;
- the impossibility of “acting”, of “not being able to do much”, also in the hospital, where people normally feel safer, promotes a sense of helplessness;
- Finally, a further involvement and commitment that risks further frustration with reactions of both physical and psychological fatigue, which is a basis of autonomic over-  
arousal.

Another aspect that emerged during this emergency that most affects the cognitive-verbal level is the loss of predictability of reality and control over events: the ability to have sufficient

knowledge of reality and active control over oneself are aspects of fundamental importance in order to avoid high levels of physical and psychological stress or chronic fatigue [1]. The inability to plan, to anticipate future events, and to exert control, at least partially, over external variables inevitably generates stress and tension. Subsequently, this condition can generate more or less discomfort depending on the subjective evaluation of the individual which is strongly influenced by the individual's stable personality traits. In fact, subjective experiences are never unique: stimuli endowed with the same stressful power do not necessarily cause the same reaction in different individuals, while stressful conditions of varying degrees can induce the same response in different people.

The current health emergency is characterized by multiple factors (distance, difficulty in traveling, decrease or loss of work, loss of a family member or loved one, symptoms related to the disease itself or to the long-covid, etc.) and each person is likely to be more or less sensitive to each of these. It is hypothesized that people affected by one or more of these stressors, and especially if affected by what makes them vulnerable, may show signs of psychological distress.

Generally, we refer to stress conceptualizing it as a response of the organism through which it tries to adapt to different conditions of balance by trying to overcome or endure them [1]. This response is part of the General Adaptation Syndrome [2], that consists in three phases: alarm reaction, resistance, and final exhaustion, with a recovery of the psychophysical balance or, conversely, the development of a psychopathological or physical disorder caused by the loss of coping ability and normal functioning. The stress response is characterized by physiological and hormonal hyper activation that allows the individual to cope with the stressor by mobilizing the body's energy resources. Specifically, the Sympathetic Autonomic Nervous System (SANS) induces the release of neurotransmitters such as Adrenaline and Norepinephrine which promotes the mobilization of glucose, the increase in heart rate, and blood pressure. At the same time, the activation of the Hypothalamic-Pituitary-Adrenal (HPA) axis favors the release of these so-called stress hormones, which enhances physical and cognitive performance. However, all of this has a cost, and if protracted over time, the health of the individual will become endangered because of the consequences on the cardiovascular system and immune system. Specifically, the researchers of the field agree with the fact that psychological stress, through the activation of the HPA axis and the Autonomic Nervous System, would also have an effect on the immune-inflammatory processes. So, the concentration of cytokines in the blood can trigger a series of allergic reactions [3]. Moreover, this aspect is interesting if we consider the adverse effects, which stress can exacerbate, in response to contrast media or vaccine inoculation, for example.

## What is possible to do?

In recent decades, the research have enabled extraordinary advances in investigating the consequences of psychological distress on physical health and the impact of stress-related physical disorders. However, it should also be noted that these aspects have been applied only minimally in the reality of health services. Moreover, this mechanism of functioning has been seen in complex situations such as arduous work and/or jobs that bear huge responsibilities for the lives of other people. Physicians, nurses, and surgeons could need an initial multidimensional to provide a baseline and offer an idea of what their level of stress, and possibility of its management, might be. The same could be useful for all types of workers, regardless of whether their work activity was directly involved in the health emergency [4-6].

## Psycho-physiological evaluation

One more important clinical application of the scientific knowledge is the prevention of stress conditions. Many physical indicators could come from hormonal and neuro-hormonal evaluations. Screening of blood tests could be used to analyze the components such as a dose of thyroid hormone, cortisol, prolactin, GH, etc. [7]. The field of clinical psychophysiology is full of extremely precise molecular tools and methods: for example, it is possible to make registration and storage with specific devices and appropriate software of the physiological functions under the control of the ANS, for example with a Psychophysiological Profile (PPP) that records:

- surface Electromyography of the frontal muscle (sEMG), whose electric potential could be detected using two active electrodes located about 1cm over the eyebrows lining with pupils and one for reference in the middle of the forehead;
- Heart rate (HR) and Inter Beat Interval (IBI), detecting the electric potential of the cardiac muscle with the classical bipolar junction; these indexes are used for electrocardiogram and calculating the existing time between an R wave (ventricular contraction) and the HR and IBI;
- Peripheral temperature (PT), applying a thermistor at the base of the thenar eminence of the dominant hand;
- Skin Conductance Level and Response (SCL/SCR), letting a slight electric current pass between two electrodes located on the last phalanx of the dominant hand fingers [7-13].

PPP is generally divided in three continuative phases: registration at rest, stress presentation, and recovery. While in the first (rest) and last (recovery) phases the basal autonomic activity is detected and recorded, in the halfway phase (stress), the physiological response is elicited through asking to the individual to perform a mental task.

The principal aim of the PPP is to verify how far the psychophysiological balance seems to be maladaptive, basing on the following observations on one or more parameters:

- High level of autonomic nervous activation in the rest phase;
- Slow, unsettled or absent values disposition of one or more parameters during the recovery phase;
- Abnormal width of the activation stress-induced response in one or more parameters during the “stress” phase;
- Slow, unsettled or absent values of one or more of the parameters during the mental task (stress phase);
- Slow, unsettled or absent restoration of the values of one or more parameters in the recovery phase.

Many studies showed the possibility to detect physiological indexes typical of some psychopathological syndromes. In fact, the presence of patterns related with the presence of anxiety and depression was first described in Lader’s research [14] and then confirmed by Stegagno and Palomba [15] as well as more recent studies [7, 10-12, 16, 17].

For instance, while the anxious syndrome is characterized by high levels of heart rate, muscular tone, electro dermal activity (tonic and phasic), and by a decrease in peripheral temperature, the depressive syndrome distinguishes itself by high levels of heart rate, muscular tone, and low level of electro dermal activity (tonic and phasic) [10-15].

Low levels of skin conductance response, at rest, were observed in depressed patients compared to a control group [9-12, 16-21].

It was also found that depressed patients with very high suicidal propensity had higher prevalence of hypo reactivity than those with low suicidal propensity. A recent study confirmed this finding by associating electro dermal hypo reactivity to type and severity of depression in patients with Major, Bipolar and Dysthymic depression [22].

It is important to emphasize that the analysis of SCL/SCR can help in the differential diagnosis in clinical practice not only between anxious syndromes and depressive ones, but also between an episode of major depression and a picture of exhaustion in which the patient can be clinically depressed but psychophysically hyper activated following a period of high stress [10,12].

A recent trend in clinical psychophysiology is examining one parameter known as Heart Rate Variability (HRV). Heart rate variability analysis begins with construction of a series of successive electrocardiographic (ECG) R-wave time intervals (R-R intervals) yielding tachograms,

which are analyzed using techniques in time or frequency domains. Spectral frequency analysis uses Fourier transformations of tachograms yielding spectral power versus frequency functions. This analysis is preferred because it provides frequency bands associated with changes in autonomic activity [23-26]. The analysis reveals 2 main spectral components: (a) low frequency (LF, 0.04–0.15 Hz), reporting both sympathetic and parasympathetic activity, and (b) high frequency (HF, 0.15–0.4 Hz), reflecting primarily parasympathetic activity.

The HF component principally reflects the respiratory sinus arrhythmia (RSA), which is parasympathetically mediated HRV associated with breathing [24,26]. Although some disagreement exists, many researchers view that increased LF power reflects mainly sympathetic activation, reduced HF power indicates parasympathetic deactivation [24-27].

The relationship between LF and HF is called the LF/HF ratio and is an indicator of sympatho-vagal balance as it reflects the dominant ANS branch. In other words, if this ratio is low it reflects that there is dominance of the SNS and that the subject has “tend-and-befriend” behaviors at rest. On the other hand, when the ratio is high, it can indicate dominance of the SNS and that the subject primarily presents fight or flight behaviors.

For this reason, some researchers [28] consider it a good index of resilience and others [29] use it as a parameter for monitoring psychophysical well-being also during invasive medical interventions. In fact, it should not be overlooked that a stressful or traumatic event (such as hospitalization or even the execution of an invasive examination) can activate the person at a psychophysiological level and interfere with the outcome of the intervention. This especially when it comes to the cardiovascular and immune systems. So, HRV is a good indicator of the current state of the patient as it has been shown that in some individuals it remains stable over time despite the presence of stressful events, while others may be more vulnerable and present disturbances in the autonomic balance.

## Conclusion

Therefore, the analysis of psychophysiological parameters is particularly useful for detecting psychophysical distress and making an accurate differential diagnosis if clinically significant signs or symptoms are highlighted and requests only 10-15 minutes.

Having an initial assessment, then a periodic checkup (every two or three months) of the psycho-physiological pattern would be able to detect any deviation from the level of optimal functioning.

Much has already been done, but to be more economical rather than continue preventing physiological and psychological issue would be a huge mistake and is counterproductive. For instance, an error of a surgeon, a pilot, or train conductor can lead to considerable damages

such as serious economic damage as well as loss of human lives. The cost of the multi-disciplinary assessment through using inexpensive apparatus and methodologies would be enormously less than the loss of workdays and sanitary cost for the community in case of full-blown diseases.

## References

1. Pruneti C. Positive Psychology: Old and New Theoretical Requirement for “Living this Moment”. *J Depress Anxiety*, 2016; 5: 242.
2. Selye H. A syndrome produced by diverse nocuous agents. *Nature*, 1936; 138: 30-32.
3. Theoharides TC. The impact of psychological stress on mast cells. *Ann Allergy Asthma Immunol* 2020;125(4):388-392. doi: 10.1016/j.anai.2020.07.007.
4. Young JA. The effects of life-stress on pilot performance. Moffet Field, Calif.: America’s Research Center, USA, 2008.
5. Stokes AF, Kite K. Flight stress: Stress, fatigue and performance in aviation. UK: Routledge, 2017.
6. Pruneti CA. Aircraft Pilots and Psychophysical health and Safety. *J Dep Anxiety*, 2020; 9: 352.
7. Pruneti CA, Cosentino C, Monzani F, Innocenti A., Sgromo D. Depressed But Hyper-activated: The role of psychophysiological assessment in subclinical hypothyroidism. *Int J Behav Med*, 2014; 21: S116-S116.
8. Fuller GD. Biofeedback Methods and Procedures in Clinical Practice. S. Francisco: Biofeedback Press, 1979.
9. Pruneti C, Rossi S, Rota S. Studio preliminare sulle differenze rilevabili a livello psicofisiologico in pazienti con prevalenti sintomi ansiosi e depressivi, con e senza trattamento farmacologico. *Psicoterapia Comportamentale e Cognitiva*, 2000; 6: 3 255-265.
10. Pruneti C, Lento RM, Fante C, Carrozzo E, Fontana F. *Journal of Psychopathology: Autonomic arousal and differential diagnosis in clinical psychology and psychopathology*, 2010; 16:43-52.

11. Pruneti C, Fontana F, Carrozzo E, Fante C. Autonomic Reactivity, Emotions and Stress Response in Psychopathology. *Applied Psychophysiology and Biofeedback*, 2011; 36:217-229.
12. Pruneti C, Saccò M, Cosentino C., Sgromo D. Relevance of Autonomic Arousal in the Stress Response in Psychopathology. *Journal of Basic & Applied Sciences*, 2016; 12: 176-184.
13. Pruneti C, Vanello N, Paterni M, Landini L, Guidotti S, Ferdeghini EM. Combined functional magnetic resonance imaging and skin conductance to detect localized neural response to psychological stress: a pilot study. *Arch Ital Biol* 2021;159(1):21-27. doi: 10.12871/00039829202112.
14. Lader MH. Anxiety and depression. In A. Gale & J. A. Edwards (eds.), *Physiological correlates of human behavior*. Londra: Academic Press, 1983.
15. Stegagno L & Palomba D. Psicofisiologia clinica. In L. Stegagno (eds.) *Psicofisiologia (2): correlati fisiologici dei processi cognitivi e del comportamento*. Torino: Bollati Boringhieri, 1994.
16. Schiweck C, Piette D, Berckmans D, Claes S, Vrieze E. Heart rate and high frequency heart rate variability during stress as biomarker for clinical depression. A systematic review. *Psychological Medicine* 2018; 1–12.
17. Hartmann R, Schmidt FM, Sander C, Hegerl U. Heart Rate Variability as Indicator of Clinical State in Depression. *Front Psychiatry*. 2019; 9:735.
18. Ward NG & Doerr HO. Skin conductance. A potentially sensitive and specific marker for depression. *Nervous Mental Diseases* 1986; 174 (9), 553-9.
19. Thorell LH, Kjellman BF & d’Elia G. Electrodermal activity in relation to diagnostic subgroups and symptoms of depressive patients. *Acta Psychiatrica Scandinavia* 1987; 76 (6), 693-701.
20. Argyle N. Skin Conductance Levels in Panic Disorders and Depression. *Nervous Mental Diseases* 1991; 179 (9), 261-66.
21. Gehricke JG & Shapiro D. Facial and autonomic activity in depression: social context differences during imagery. *International Journal of Psychophysiology*, 2001; 41, 53-64.

22. Thorell LH, Wolfersdorf M, Straub R, Steyer J, Hodgkinson S, Kaschka WP. & Jandl M. Electrodermal hyporeactivity as a trait marker for suicidal propensity in uni- and bipolar depression. *Journal of Psychiatric Research*, 2013; 47, 1925- 1931.
23. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation, and clinical use. *Circulation* 1996; 93(5):1043–1065.
24. Berntson GG, Bigger JT Jr., Eckberg DL, et al. Heart rate variability: origins, methods, and interpretive caveats. *Psychophysiology* 1997; 34(6):623–648.
25. Ernst G. Hidden signals-the history and methods of heart rate variability. *Front Public Health* 2017;5:265.
26. Bhoja R, Guttman OT, Fox AA, Melikman E, Kosemund M, Gingrich KJ. Psychophysiological Stress Indicators of Heart Rate Variability and Electrodermal Activity With Application in Healthcare Simulation Research. *Simul Healthc* 2020; 15 (1): 39-45. doi: 10.1097/SIH.0000000000000402.
27. Kreibig SD. Autonomic nervous system activity in emotion: a review. *Biol Psychol* 2010;84(3):394–421.
28. An E, Noltz AAT, Amano SS, Rizzo AA, Buckwalter JG, Rensberger J. Heart Rate Variability as an Index of Resilience. *Mil Med.* 2020;185 (3-4): 363-369.
29. Baglini R, Sesana M, Capuano C, Gneccchi-Ruscione T, Ugo L, Danzi GB. Effect of hypnotic sedation during percutaneous transluminal coronary angioplasty on myocardial ischemia and cardiac sympathetic drive. *Am J Cardiol* 2004;93(8):1035-8. doi: 10.1016/j.amjcard.2003.12.058.