

Management of stress and stress-related diseases: Emerging computer-based technologies and the rationale for clinical laboratory assessment

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Citation: Nwose EU, Richards RS. Management of stress and stress-related diseases: Emerging computer-based technologies and the rationale for clinical laboratory assessment. *North Am J Med Sci* 2009; 1: 288-294.

Availability: www.najms.org

ISSN: 1947 – 2714

Abstract

Background: Over the years, the issue of stress management in mental health has been discussed without reference to the clinical laboratory perspectives. Translational research and the vast array of emerging diagnostic technologies in alternative medical practice are now bridging the gap. While it would be scientific arrogance for the clinical practitioner and scientist to ignore the trend, the new technologies seeking clinical acceptability necessarily require expatiation of the scientific aspects of their products. **Aims:** This commentary builds on a comparative critical review to further our hypothesis that oxidative stress is the biochemical basis of the emerging computer-based diagnostic technologies. **Materials & Method:** The available information on Computer Meridian Diagnostics, Neuropattern and Virtual Scanning technologies were critically reviewed. The differences and similarities were articulated. **Results:** The technologies seem different, but have similarities that have not been articulated before. The seemingly different theories are traceable to Russian scientists and are based upon stress-induced adrenal secretions and the associated effect on glucose metabolism. The therapeutic effects of antioxidant nutrition, exercise or relaxation that are inherent in the technologies are highlighted. **Conclusion:** This commentary furthers explanation of the alterations in antioxidant activities as a result of biofeedback, oxidative stress and/or physiological effects as the biochemical basis of the technologies. The place for antioxidant indices and whole blood viscosity are also highlighted. This provides a rationale for the evaluation of available clinical diagnostic tests both to validate the technologies and as clinical laboratory correlates in stress management.

Keywords: Clinical laboratory evaluation, complementary medicine, mental stress, oxidative stress, whole blood viscosity.

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Introduction

The concept of stress in mental health is related to the complexity of the interactions between the cells, organs and systems of the body. The body wishes 'constancy of the internal environment' (homeostasis). This concept was first described by a 19th century physiologist, Claude Bernard [1]. Homeostasis requires that any tendency

towards change is automatically resisted by a feedback or feedforward response [2, 3].

Two of the adrenal hormones involved in the neuro-endocrine response to stress are catecholamines and glucocorticoids. The latter mainly potentiates the former. The catecholamines decrease production of insulin whilst increasing the release of glucagons. The cumulative effect

is increased availability of glucose in the blood for energy production [1, 4].

Over the years, the issue of stress management in mental health has been discussed with exclusion of the clinical laboratory perspectives. Currently, a vast array of diagnostic technologies in alternative medical practice is emerging. Each technology is purporting to be unique and seeking acceptance and integration into clinical conventional practice, however a hypothesis for validation and integration into diagnostic pathology services has not been proposed. Therefore, this article reviews the available online information on three emerging technologies with a view to generate a rationale for laboratory indices in stress management in mental health.

The emerging technologies for stress management: three examples

Among the emerging array of technologies, all of which hold promise for the management of stress in alternative medicine practice, are computer meridian diagnostics (CMD), Neuropattern and Virtual Scanning.

I: Computer Meridian Diagnostics technology

The CMD is proposed as a health-check system that detects imbalances in the body as a diagnostic means to prevent health problems. The system was developed by a team of Russian scientists.

The principle: It is based on signals in illness, which could be traced to an imbalance in the body's energy systems. CMD can detect the warning signals using a computer, internet connection and a sensor. CMD translates these signals into easy-to-understand charts and text that can reveal underlying imbalances at an early stage.

Diagnostic procedure: The subject's measurements of his or her body's energy levels are taken using the CMD-Sensor. The measurements are then sent, via the Internet, to the central CMD-Server in Germany, where the readings are compared with known data collected from people of the same age and gender in various states of health. The results are sent back via the Internet in a few seconds to the subject's computer screen. The entire health check procedure can be done in less than three minutes, and has been credited to be a boon to therapeutic practitioners [5].

A typical report presents wellness in ten grades ranging from super (as maximum) down through normal, subnormal and unfavorable to pathological. Each bar represents the measure for two systems. For instance, the first bar indicates the state of immune system as well as oxygenation while the second bar indicates the state of digestive and lymphatic systems. Fig. 1 shows a typical report presenting the state of wellness of a 48yo male.

Limitation: What has yet to be explained is the biochemical basis of the technology. Some points are

noteworthy about CMD, which form the basis of developing the biochemical premise of the technology.

- CMD does not detect cancer, and is not a substitute for a clinical consulting physician
- The technology recognizes that any immune reaction means an increased activity and elevated energy levels
- Treatment options such as acupuncture and exercise programs, as well as massage with a soft laser pointer on the acupuncture points are recommended in the CMD program.
- Short and light exercise leads to a state of energy activation and results in negative CMD readings as an indication of better health.

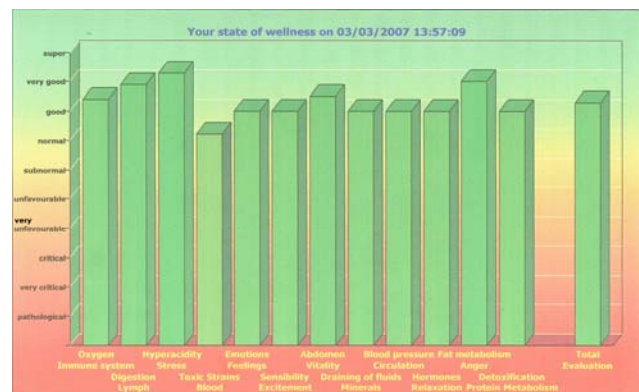


Fig. 1 Typical CMD report (de-identified, unformatted)

Central to this hypothesis is the proposal that energy activation is (i) triggered by exercise in the form of increased physiologic energy demand; (ii) responded to by increased glucose metabolism to generate energy; (iii) a biochemical process associated with ATP, which in turn is associated with antioxidant activities and electron transfers. The latter is synonymous with photon or ultra weak light emission, which translates to chemiluminescence and electrophysiological signals [6].

II: Neuropattern

This is a technology that focuses on the gap between basic research and the clinical application of knowledge of stress-related biological, psychological and symptomatological relationships. That is, bedside-to-bench and bench-to-bedside systematic translational strategies for clinical management of stress-related diseases. It is based on the argument in neurobehavioural medicine that manipulation of the brain by photostimulation technologies can be applied in clinical management [7].

Principle: Every Neuropattern is composed of a concomitant manifestation of specific and previously defined biological, psychological and symptom variables. This is a sort of endophenotyping of neuroendocrine systems. It takes cognizance of issues of complexity and heterogeneity of mechanisms of stress, missing covariance in biological and psychological measures, and practitioner accessibility amongst others. The concepts of glandotropy, ergotropy and trophotropy are translated to explain the

involvement of the hypothalamic-pituitary-adrenal axis (HPAA), the sympathetic nervous system and the parasympathetic nervous system respectively. A diagnostic system of questionnaires as well as laboratory and physiological measurements (bedside-to-bench and vice versa) constitute the clinical routine procedure [7].

Diagnostic procedure: This involves some questionnaires and laboratory test as well as consideration of clinical and demographic data. Four sets of questionnaires are involved as listed below

- One. Amnestic data to be completed by the physician
- Two. Personal perspectives information to be completed by the patient
- Additional, for women only is a pre-, peri-, and/or postnatal questionnaire.

Salivary cortisol is determined on three consecutive days. Ambulatory autonomic measures are extrapolated from heart rate. In addition to psychopathological conditions, all data are analyzed and assigned to a neuropattern. The report will include the diagnosis and possible treatment [7].

Limitation: Cortisol is an indirect HPAA biomarker of psychological stress [8]. Its measurement is proposed in Neuropattern technology, but subject to establishment of cost-effectiveness [7]. How cortisol and the HPAA form part of the biochemical basis of stress, or influence the biochemical alterations during stress requires explanation. In view of ongoing research for cost-effectiveness and therapeutic advantages, such explanation will be useful for developing alternative methods for measuring cortisol. Most diagnostic laboratories do not test for cortisol but may easily employ other valid alternatives.

It is known that cortisol level, oxidative damage and antioxidant status are related in motor neuron functions. Anti-stress agents counteract neuroendocrine and oxidative stress including increasing erythrocyte malondialdehyde and plasma cortisol levels [9]. It is also known that cortisol as an anti-inflammatory corticoid has the capacity to modulate oxidative stress [10]. Thus, a component of this hypothesis is that oxidative damage indices could be potential diagnostic alternative biomarkers in the neuropattern method.

III: Virtual Scanning

Virtual Scanning is a unique medical concept with a role in the diagnosis of diseases. It purports to be able to provide a full diagnosis of almost every physiological system and organ. The condition of each organ is reported in precise medical terms including subclinical conditions that may not be satisfactorily diagnosed by conventional procedures [11-13].

Principle: Claude Bernard had conceptualized that the internal environment of an organism *vis-à-vis* its physiological state is constant with the existence of control

processes to achieve such constancy, and further envisaged possible mathematical modeling applications [4]. Progress on the mathematical modelling has been achieved by Grakov [11, 12]. Virtual Scanning is a further progression on the mathematical model and is based upon the body's inherent biochemical processes as a source of light emission and color defects associated with pathologies. The level of ultra weak light emission is determined mathematically by computer system and reported in medical terms.

Diagnostic procedures: The practical diagnostic methodology includes interviewing the patient, followed by the patient using the computer system to solve a standard task that involves color matrices. The computer then processes the patient's response and shows the results on the screen [12]. Each condition comprises a pairing of blue and red signals [11, 13]. The red signals report the extent of the pathology whilst the blue signal reports the extent of the body's natural compensatory response. The scale and balance of pathology and compensation enables the practitioner or researcher to distinguish between acute and chronic conditions [13].

The diagnostic procedure ends with a recommendation of patient treatment strategy. The standard therapy involves three basic steps [13].

1. First, the area (organ, system), where correction is necessary, and features that are subject to correction are identified.
2. The course or dose and sessions of *flashing light* are determined. One session of treatment takes average of 30 minutes and one course comprises average of 15 sessions.
3. The healing signals are sensed, as the patient's system responds, via the monitor.

Limitation: Available literature shows that the mechanism of Virtual Scanning technology involves detection of neural regulatory problems by presentation of stimuli and measuring the body's perceptive reactions to those stimuli. The concept of ultra weak light emission by biochemical processes is not acknowledged. Much is yet to be elucidated regarding this technology, particularly the biochemical basis of the signals.

Depletion of reduced glutathione (GSH) leads to a cascade of exponential oxidative activities with other co-antioxidants, including mitochondrial ubiquinone [14, 15]. Studies have shown that injured cells will emit a higher energy (or in this context, biophotons) rate than normal cells, and organisms with illnesses will likewise emit a brighter light *vis-à-vis* bioluminescence [16]. This has been interpreted as implying a sort of distress signal being given off [17]. The proposition in this hypothesis is that oxidative stress, which would not be exactly of equal intensity for all diseases, may be determined as a characteristic of different disease conditions according to colour and intensity; as well as attenuated by chromotherapy (using Virtual Scanning technology. This

proposition is based on the fact that antioxidant activity is associated with light emission and antioxidant quenchers decrease such emissions [18-20].

Furthermore, it is worth considering that neurons (i) communicate by electrical signals; (ii) are influenced by antioxidants such as superoxide dismutase (SOD); and (iii) impairment of SOD in a neuron cell line leads to biochemical abnormalities with decreases in the mitochondrial electron transfer chain. This can be likened to when the cell line is experimentally subjected to oxidative stress [21]. Thus, our hypothesis is hinged on oxidative stress as a biochemical basis of Virtual Scanning.

Antioxidant activities as biochemical basis of the technologies: basis for hypothesis

Differences and similarities in the technologies: A face look at the diagnostic procedures presents the technologies as entirely different. However, a critical comparison of the three technologies, based on available information, would indicate some similarities.

The CMD and Virtual Scanning protocols do not yet involve any laboratory assessment of biochemical or hematological indices. The two methods give computer generated results in form of histograms where normality is determined by deviation from a certain column height. The ATP associated with energy activation implicated in CMD is also associated with luminescence implicated in Virtual Scanning. Looking at the CMD and neuropattern, there is no flash light treatment option as there is in Virtual Scanning. Meanwhile, the neuroendocrine system's involvement has been implied in both neuropattern and Virtual Scanning, but not yet in CMD (Table 1).

In particular and relevant to our hypothesis is one striking feature that can be gleaned from Neuropattern and Virtual Scanning. It is known that light therapy affects cortisol rhythm [22]. While the Neuropattern technology acknowledges cortisol rhythm without recourse to light therapy, Virtual Scanning uses light therapy without recourse to laboratory assessment of cortisol. Therefore, central to this hypothesis is the premise that, except for reason of availability and cost effectiveness, the proposed unique laboratory diagnostic protocol in Neuropattern can be employed to determine as well as monitor therapeutic outcome in Virtual Scanning.

In addition, there are the following similarities in all three methods

- All techniques evaluate stress using computer and/or integrative data analysis
- The theories involve brain-body or neuroendocrine communication, but lack an articulated biochemical basis
- Exercise, nutrition and relaxation are treatment options common to all technologies.

Treatment options attenuate oxidative stress: In our opinion, one way to explain antioxidant activities as the biochemical basis of the technologies is to have an overview of the mechanism of action of the treatment options. All three methods suggest appropriate treatment to accompany results. The common treatment options (exercise, nutrition and relaxation) as well as flash light therapy in Virtual Scanning are known to potentiate antioxidant activities thereby attenuating oxidative stress.

Exercise: Although immoderate exercise could trigger stress, there is overwhelming evidence of the benefit of exercise in the management of cardiovascular diseases. One of the known effects of exercise is regulation of antioxidant activities and oxidative metabolism [23]. For instance, it is known cigarette smoking is a health risk by its oxidative stress effects and that exercise minimizes this effect [24]. Oxidative stress is implicated in neurodegenerative diseases and associated with this is the potential therapeutic effects of exercise on immune factors and stress to promote brain health [25]. Further associated with mental stress and neurodegeneration is aging, which is strongly linked to oxidative stress wherein regular exercise is of known therapeutic benefit [26].

Flash light: Low level (infrared) light is known to be a therapeutic agent that attenuates hyperglycemia-induced oxidative stress and enhances the antioxidant protection system [27]. The technique of chromotherapy dates from ancient Egypt to the contemporary treatment of seasonal affective disorder. It is one of the concepts of irradiation of acupuncture points in complementary medicine (28). The concept of selective photothermolysis is applicable in vascular lesions management. For instance, flash light is a therapeutic agent for atherothrombosis [29], pain relief during venous cannulation [30, 31], and Raynaud's syndrome [32]. Efficacy in this range of conditions is an indication of applicability to stress-related conditions.

Nutrition: For more than 50 years, it has been known that many diseases including cardiovascular, diabetes and neurodegenerative conditions amongst others have been linked to damage by oxidative stress. For this reason, antioxidant therapy has been lauded in alternative and complementary medicine [33]. The significance of micronutrients in mental health has recently been re-emphasized [34]. Thus, there are medical nutritional counseling programs and guidelines aimed at improving blood levels of antioxidants [35-37].

Relaxation: There is no dispute regarding meditation or relaxation therapy in alternative and complementary medicine. Relaxation is a common therapy for anxiety [38]. Perhaps, what needs emphasis is the potential effect of long-term meditation in the control of antioxidant activity. It is known that persistent relaxation attenuates the spontaneous ultraweak photon emission that arises from antioxidant activities [39]. For instance, migraine is a systemic disorder that involves the vascular and nervous systems as well as [40, 41]. Associated with this is relaxation therapy on the basis of cognition and

mind-body interaction [42-44], which is known to attenuate oxidative stress [45, 46].

Table 1 Differences and similarities in the technologies

	CMD	Neuropattern	Virtual scanning
Diagnostic focus	Energy systems	Psychopathologies	Organs & systems
Diagnostic marker	Energy signals	Multi-test data	Perception signals
Result presentation	Histogram [†]		Histogram [†]
Clinical lab assessment	Nil	√	Nil
ATP implicated in principle	√	No	√
Flash light therapy option	No		√

Keys: CMD = computer meridian diagnostic; ATP = adenosine triphosphate; [†]different terminologies are used in CMD and Virtual scanning

The hypothesis: the implication for antioxidant indices and whole blood viscosity in mental health

Normal human physiological processes are strongly dependent on glucose metabolism, which is increased during stress. Increase in glucose metabolism leads to alterations in energy state (acknowledged in CMD technique), and is due to the HPA axis effect on cortisol level (acknowledged in Neuropattern). The feedforward effect can include antioxidant imbalance and alterations in antioxidant activities, which would affect biophoton emission (acknowledged in Virtual Scanning). Thus, measurement of cortisol is suggested and may prove to be cost effective [7, 8]. Here, we hypothesize that *GSH as well as tests for vitamins C and E levels have a role as alternative laboratory indices in mental health management.*

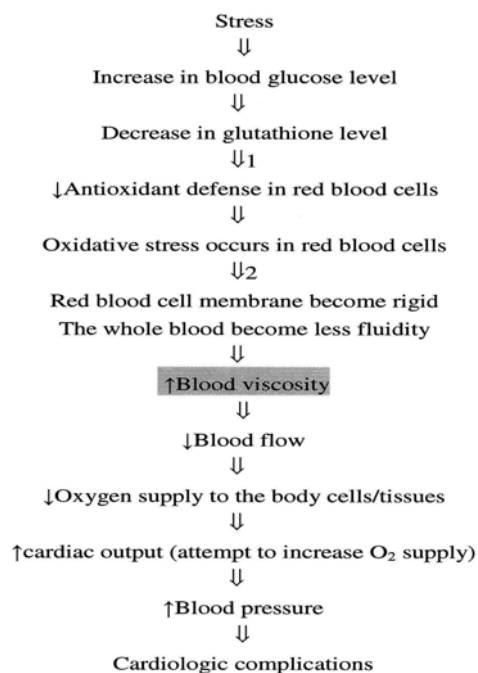


Fig. 2 Sequence of how stress can cause cardiovascular complications (Keys: 1 = GSH supplementation; 2 = vitamins C and E).

When stress leads to a persistent more-than-normal level of production of oxidants, the likely effect is that

antioxidants become overwhelmed and depleted in level and oxidative stress ensues. When the oxidative stress involves the red blood cells, cardiovascular complication begins with increased whole blood viscosity (WBV) as illustrated in the flow diagram (Fig. 2).

Thus, we further hypothesize that *WBV is a laboratory index in stress management.* Especially, WBV has recently been shown to exhibit rhythmic patterns [48]. This property buoys its potential as an alternative to salivary cortisol, which has daily rhythmic changes in level. The flow diagram in Fig 2 illustrates how chronic stress can cause hypertension. Heart rate increases as part of the physiologic effort to increase cardiac output and normalize blood/oxygen supply.

Clinical significance of the hypotheses: advantages of the alternative laboratory indices

Currently, laboratory evaluations in mental health care involve full blood count (FBC), blood sugar, liver function tests, and fluid/electrolyte balance (urea, electrolyte and creatinine). Other tests such as erythrocyte sedimentation rate, lipid profile and red cell folate are done but rarely. Salivary cortisol is not evaluated, because there is no evidence-based recommendation [personal communication].

Based on the Australian scenario, a salivary cortisol test costs more compared to measurement of antioxidant vitamins or WBV. Furthermore, salivary cortisol is not available in most laboratories. A major advantage is that WBV can be determined for patients that have FBC and plasma protein results, and at no extra cost to the health care provider or laboratory.

Oxidative damage to the liver also raises plasma protein level [49]. It is known that chronic alcoholism and dehydration raise haematocrit. Thus, beside oxidative stress as the biochemical basis, causes of high WBV including dehydration, haematocrit and plasma protein

level are already being assessed in mental healthcare. We suggest that WBV can be used as alternative to salivary cortisol. In order to test and validate this hypothesis, the timing of rhythmic changes needs to be ascertained together with determination of the reference values for the different periods of the day.

Conclusion

Stress-induced alteration in cortisol level leads to alterations in metabolic processes especially glucose metabolism, which in turn leads to alterations in antioxidant levels, energy levels and antioxidant-based electrophysiological signals. This is our interpretation of the summary biochemical basis of the emerging computer-based technologies for stress management described herein. The feedback and feedforward responses to antioxidant imbalance leads to erythrocyte oxidative stress through to increase in WBV and forms the rationale of this hypothesis that antioxidants and WBV are potential laboratory indices that could be useful in stress management.

Acknowledgement

The intellectual and professional advice of Dr Simon Tawasu, Psychiatrist, Nolan House; Albury Base Hospital is appreciated. Fig. 1 is one of a set of de-identified reports, courtesy Olive Health Foods, Albury NSW Australia. There is no financial or other contractual agreement and no conflicts of interest to declare.

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