

HEALTH AND STRESS

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DIAGNOSING AND TREATING STRESS VIA NEUROIMAGING

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Stress is not a very useful term for scientists because it is a highly personalized phenomenon that is difficult to define. In addition, like beauty, stress is often in the eye of the beholder. As the Greek stoic philosopher Epictetus emphasized to his pupils some 2,000 years ago, **"We are disturbed not by things, but by the views we take of things . . . It's not what happens to you but how you react to it that matters."** Eleanor Roosevelt similarly said, "Nobody can make you feel inferior without your consent." And some individuals can create their own stress by constantly worrying about the worst possible scenario for a future event.

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Things like a steep roller coaster ride that proves very distressful for many passengers, can be an exhilarating delight for others, or seemingly have little significance either way. We can all also respond to stress quite differently. Some people blush, while others grow pale, or have varied gastrointestinal, cardiovascular, skin, neurological or emotional complaints

Hans Selye, who coined the term stress as it is currently used, initially defined it as "The nonspecific response of the body to any demand for change." He was primarily addressing an audience of basic science researchers with a special interest in endocrinology and his experiments in rats using what amounted to various forms of acute and severe torture did not appear to have any clinical relevance. What was different about Selye's concept of stress was his observation that many very different things could

cause the same pathologic picture. This was in sharp contrast to the prevailing view that each disease had its own specific cause. Bacterial infections like tuberculosis and anthrax were due to the tubercle and anthrax bacilli, and scurvy and rickets to deficiencies of vitamin C and D. On the other hand, as Selye pointed out, many different diseases do have the same symptoms of low grade fever, malaise, and generalized aching during their initial 24 -48 hours, and perhaps stress was an analogous phenomenon. Selye's subsequent studies on the effects of sustained stress led to the development of his "Diseases of Adaptation" hypothesis, and attempts to extrapolate the results of his animal research to humans. In trying to explain what he meant by stress to a lay audience, he redefined it as "The rate of wear and tear on the body." That's a good definition of biological aging, but it isn't very helpful in explaining exactly what stress is to scientists. Selye struggled all his life, as have others, to develop a satisfactory definition of stress, without success. When asked about this, he could only tell reporters, **"Everyone knows what stress is — but nobody really knows."**

What's The Distinction Between Stress, Strain, Tension, Stressor And Eustress?

Selye's initial description of this nonspecific response he called "biologic stress" was published as a 74-line letter to the editor of *Nature* in 1936 entitled "A Syndrome Produced by Diverse Nocuous Agents". But the editor insisted that the word "stress" had to be deleted since it was commonly used to mean nervous strain, especially in women. As a result, the word stress never appeared and "Alarm Reaction" was substituted to describe this response, which was viewed as a coordinated mobilization of the body's defensive mechanisms. Other problems surfaced, as stress rapidly became a popular buzzword that seemed to be a synonym for distress. Selye was fluent in nine or ten languages, including the Latin and Greek roots from which many English words were derived. But he was not aware that stress had been used for centuries in physics to describe an external force that caused deformation or strain. As expressed in Hooke's Law of 1658, the magnitude of an **external force, or stress, produces a proportional amount of deformation, or strain**, in a malleable metal. The maximum amount of stress a material can tolerate before becoming permanently deformed is known as its elastic limit. This ratio of stress to strain is a characteristic property of each material, and its value is high for rigid materials like steel, and much lower for flexible metals like tin. Selye often complained to me that, had his knowledge of English been more precise, he would have gone down in history as the father of the "strain" concept.

Stress had evolved from the Latin *strictus* (tight, narrow) and *stringere* (to draw tight). This became *strece* (narrowness, oppression) in Old French, and *stresse* (hardship, oppression) in Middle English. In vernacular speech, stress represented a contraction or variant of distress, a condition

characterized by tension. Tension, from the Latin *tensio* to stretch or strain, usually referred to mental or emotional strain, whereas distress could mean either mental or physical suffering. These nuances also created considerable confusion when Selye's English publications had to be translated into foreign languages. There was no suitable word or phrase that could convey what he meant by stress, since he was really describing strain. When he was invited to give the Keynote Address at the prestigious *Collège de France*, the academicians responsible for maintaining the purity of the French language struggled with this problem for several days, and eventually decided that a new word would have to be created. Thus, *le stress* was born, quickly followed by *el stress*, *il stress*, *lo stress*, *der stress* in other European languages, and similar neologisms in Russian, Japanese, Chinese and Arabic. Stress is one of the very few words you will see preserved in English in these latter languages that do not use the Roman alphabet.

This same confusion over cause and effect was also a problem in colloquial communication, since stress was used interchangeably to describe both physical and emotional challenges, the body's response to such stimuli, as well as any resultant illness or pathology. Thus, an unreasonable, over demanding boss might give you heartburn or stomach pain due to a duodenal ulcer. For some, stress was the bad boss while others used it to describe either their "*agita*", or the peptic ulcer. Even Selye had difficulties in making these distinctions, and when assisting him to prepare his *First Annual Report On Stress* in 1951, I included the comments of one critic that had appeared in the *British Medical Journal*. Using verbatim citations from Selye's own writings, he complained **"Stress, in addition to being itself, was also the cause of itself, and the result of itself."**

To distinguish between cause and effect, Selye had to create a new word, "stressor", to describe a bad boss or other unpleasant stimuli that caused what he had called stress. Based on his animal studies, stress was always harmful, or bad, so it is not surprising that Selye viewed stress as a synonym for distress. Yet, it was clear that this was not always true for humans. In some situations, increased stress improved productivity or performance. Winning a race or an election could be just as stressful, or more so than losing, but would not likely have the same health consequences. A few passionate kisses and contemplating what might follow is stressful, but quite different than waiting to learn whether a biopsy report will reveal cancer. Weddings, births, graduation from college, a major promotion at work or winning the lottery can be very stressful, but these are usually happy and enjoyable events that are shared with others. Selye referred to these as "eustress" (good stress), to differentiate it from distress.

If You Can't Define Stress, How Can You Possibly Measure It?

Lord Kelvin, the 19th century mathematician-physicist who developed the absolute or Kelvin temperature scale wrote, "To measure is to know", and **"If you cannot measure it, you cannot improve it."** But if you can't define something, how can you possibly measure it? Nevertheless, there are numerous devices that claim to measure stress by evaluating changes in various biophysical activities associated with distress, including:

- Stress dots, squares, cards etc. containing heat sensitive substances that vary in color depending on skin temperature. During stress, increased tension in the large muscles of the extremities and the shunting of blood to vital organs reduces its flow to the extremities resulting in a reduction of temperature that can be as much as 10 degrees F. in the fingers and toes, as measured by small specially calibrated thermometers that can adhere to the hand. The stress dots etc. change color ranging from purple (very relaxed) 94.6°F., to black (very tense) 87.0°F., with blue, green, brown and gray reflecting stress levels in ascending order in between.
- Temperature dependent mood rings, bracelets, pendants and earrings containing thermotropic liquid crystals whose molecules twist or change position depending on the amount of heat they are exposed to. These changes affect the wavelengths of light that are absorbed by the crystals, which produce an apparent change in the stone's color. As the temperature increases, the resultant twist causes more absorption of the red and green portions of the visible light spectrum and more of the blue part is reflected, so that the stone now appears to be dark blue. As the temperature falls, the molecules start to twist in the opposite direction and a different portion of the spectrum is reflected. The inside of a mood ring conducts heat from the finger to the liquid crystals which are calibrated, so that green, which signifies average, is approximately 82°F. An increase in temperature indicating relaxation causes the color to aquamarine, light blue, whereas increased stress is reflected by yellow, gray and black, depending on how low the temperature falls. There are also mood lipsticks that can change color but these operate on an entirely different principle that has relatively little to do with the wearer's mood. They contain weak acid pigments of one color conjugated with a base of a strikingly different color, and the prevailing hue depends on the acidity or pH of your skin. However, in addition to stress, the pH of skin can depend on numerous factors, including diet, amount of physical activity and even the menstrual cycle. In addition all of these devices are influenced by room temperature, how recently you ate or drank, smoking, etc., so their primary value is entertainment.
- Galvanic skin resistance, electrodermal conductivity and devices that indicate various skin electrical activities that can be influenced by

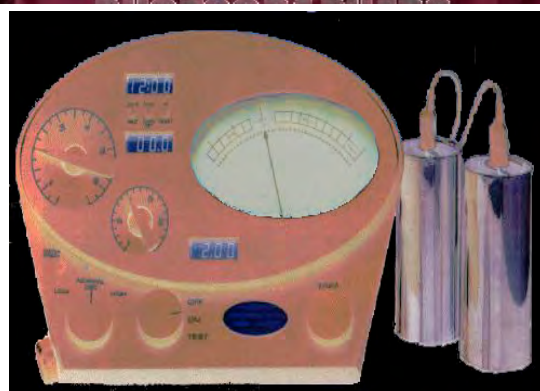
stress. In addition to cold hands, emotional stress may also cause sweaty palms and increased perspiration elsewhere in the body that can be detected by measuring the electrical activity of the skin. There are several methods, including skin resistance (SR), skin conductance (SC) and skin potential (SP). SR and SC are monitored by the external application of a weak voltage across the skin and measuring its resistance to the flow of electricity. SP is measured by recording the internal electrical activity of the skin in the absence of any external influence by using silver/silver chloride electrodes that are particularly sensitive to such changes. Electrodes are usually placed on the palms of the hand or soles of the feet because these have the most sweat glands per surface area in the body and also respond more to emotional stress than to increased heat compared to sweat glands elsewhere. Other terms used to describe electrodermal activities include galvanic skin resistance (GSR) and psychogalvanic skin response (PSR). The most popular devices measure galvanic skin resistance, which reflects sweat gland activity and pore size, both of which are controlled by the sympathetic nervous system.



One popular instrument is the GSR II shown to the left. Instead of a visual cue or meter, the GSR level is relayed by a tone or sound signal generated when you rest two fingers on the sensing plates. This is frequently used as a biofeedback device, since the tone rises and falls depending on your "stress level". With practice, you can quickly learn ways to relax that will make the tone fall, thus confirming the success of this biofeedback approach.

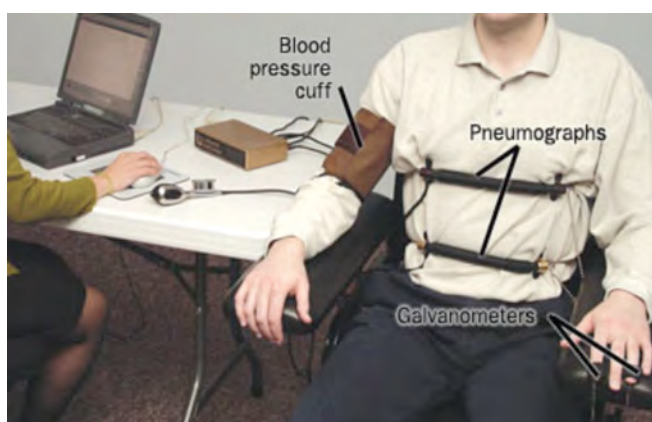
There are various enhancements, including a meter that responds in a similar fashion, as well as software connections to a PC that provide more elaborate color displays to improve biofeedback capabilities. The Micronta Biofeedback monitor utilizes sensors contained in Velcro wrapped around two fingers connected to an oscillometer. When you are tense and GSR falls, it emits a high-pitched buzz that progressively changes to a slow popping sound as you become more calm and relaxed. Like the GSR II, this device is also used to lower stress levels and assist with such things as reducing the urge to smoke by using supportive audiocassettes.

Probably the most widely publicized device based on GSR effects is the E-Meter promoted by the Church of Scientology to recruit new members and to sell copies of *Dianetics*, a book authored by its founder, L. Ron Hubbard. E-Meter is short for electro-encephaloneuromentimograph, and although the 1966 patent application was made by Hubbard, the device had been invented years before by a chiropractor named Volney Mathison and was known as the Mathison electropsychometer as shown in the illustrations below to the left. It was designed to be an aid in psychotherapy, which was anathema to Hubbard. Nonetheless, he still used the device to attract members until 1954, when he quarreled with Mathison and abandoned it. In 1958, Scientologists modified the device by changing its shape and composition and using smaller batteries. It was christened the Hubbard E-meter, came in different colors and was aggressively advertised as being able to provide an accurate and free stress test, as shown below to the right.



Although the Quantum Super VII E-meter model shown above sold for over \$4,000 it is no different than the original Mathison device Hubbard rejected. Both consist of a galvanometer that is attached to two metal cylinders that are grasped in each hand. During psychological stress, sympathetic nervous system stimulation causes sweaty palms, and the resultant salt solution facilitates the conduction of electricity by reducing skin resistance. The problem is that some people perspire more than others, and alcohol, caffeine and spicy foods as well as common drugs like aspirin and Tylenol can influence sweating. How much of the metal cylinder is in contact with your hands and how tightly it is held can also affect the readings.

How Accurate Are Devices And Methods To Measure The Stress Of Lying?



The polygraph shown to the left is designed to detect and assess the stress of lying by measuring changes in heart rate, blood pressure, respiration patterns and galvanic skin resistance. A trained investigator is required to administer the test and interpret the results. Costs can range from \$400 to \$1,600 or more/test depending on who is doing it and where and why it is being conducted.

Although it has been used as a lie detector by law enforcement agencies, state governments and the private sector for decades, most scientists doubt its accuracy. People can be taught to fake their responses, innocent but psychotic individuals who actually believe they committed a crime, will also have false results. Individuals cannot be coerced to take a lie detector test, and in New York and a few other states, the results of polygraph tests are inadmissible as evidence in courts of law. In other states, both parties must agree and/or a judge will decide. The reason so many private sector, law enforcement and government employers seek to use polygraphs is that they think the test will discourage liars and cheats who are seeking jobs, or it will frighten confessions out of those accused of wrongdoing. As **Richard Nixon said, "I don't know anything about lie detectors other than they scare the hell out of people."** Essentially, the users of the machine don't really believe it can detect lies, but they know that subjects they test *think* the machine can catch them in a lie. So, the result is the same as if the test actually worked and they don't hire the liar or cheat and they can often catch dishonest employees.

Numerous attempts have been made to develop more accurate lie detectors that Courts would accept as valid evidence. In Brainfingerprinting, relevant

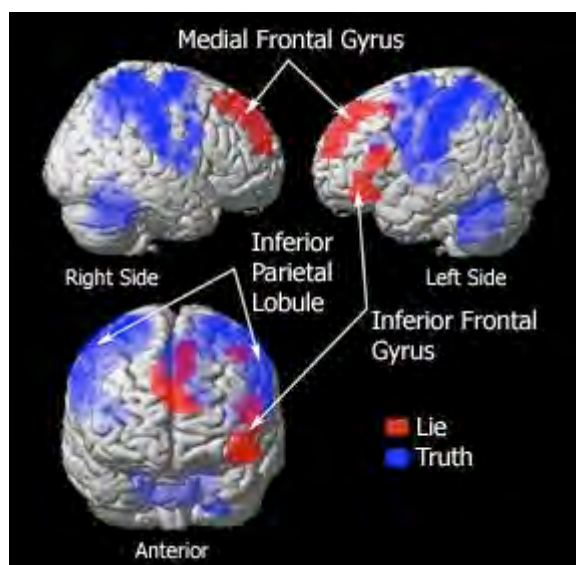
words, pictures or sounds intermixed with irrelevant and neutral stimuli are presented to a subject whose brain waves are monitored on a computer. A specific EEG spike known as P300 is emitted by anyone who has the pertinent information stored in their brain, but not by individuals with no memory of the same stimulus. This P300 spike occurs between 300 to 600 milliseconds after the appropriate stimulus is presented, long before the subject would be able to control any response, and is strongest in electrodes over the parietal lobe. In one Iowa case of a man serving a life sentence for murder, Brainfingerprinting showed that the record **stored in his brain did not match the crime scene but did match his alibi**. Confronted with this evidence, the only alleged witness to the crime recanted and confessed that he had lied in the original trial to avoid being prosecuted for the crime. Brainfingerprinting of a suspect in a 15-year old unsolved Missouri murder case showed that the record stored in his brain matched critical details of the crime that only the perpetrator would have known. Faced with almost certain conviction and a probable death sentence, he pled guilty in exchange for life imprisonment without the possibility of parole and then also confessed to the previously unsolved murders of three other women.

A computer screen embedded with infrared light sensors can also track eye movement in a way that can elicit the truth without anything being said, when pertinent pictures are flashed on the screen. This has proven useful in child abduction cases when suspicious individuals are shown a picture of the missing person or the probable crime scene. The technology is based on the principle that people's eye movements will betray if the person or place they're staring at is familiar to them. Lying is also often associated with an increase in blood flow to the face that can be detected by thermal cameras sensitive to minute changes in facial temperature. Laser Doppler vibrometry testing involves pointing a laser at the skin over the carotid artery to obtain a baseline pattern of how the vessel expands and contracts normally and during a conversation in which neutral questions are answered. When loaded questions are interspersed, a detectable minute change in vibrations due to stress can indicate if the subject is lying. Vocal muscle vibrations are also the basis for the Computer Voice Stress Analyzer used by thousands of law enforcement agencies that is explained below.



A computer attached to a sensitive microphone can analyze each voice pattern response to any question. It can detect certain tell-tale inaudible vibrations in frequency modulated sound waves that cause microtremors, which are seen during the stress of lying or deliberate deception, as graphically illustrated to the left.

So called "truth specs" or voice analysis glasses utilize an invisible chip inside the glass that can measure 129 aspects of speech. These are analyzed and the results are displayed on the inside of the frame as a red, yellow or green light to indicate a lie, possible lie, or the truth, with an alleged 95% accuracy. It has been used in Israeli and Russian airports to screen for terrorists. Also available is a PC program that can analyze telephone or TV voices to detect whether witnesses during trials or candidates in presidential debates are telling the truth. fMRI (Functional Magnetic Resonance Imaging) is a form of magnetic resonance imaging that registers blood flow to functioning areas of the brain and is often used to detect brain tumors. Researchers have also discovered that blood flow to certain parts of the brain are altered when a lie is being told since people who intend to lie use certain sites more than others, as noted below.



In one study, six of eleven volunteers were asked to fire a toy gun and then lie about whether they had pulled the trigger. The other five were asked to tell the truth. fMRI scans during the questioning correctly identified all of those who were telling the truth, as well as those who lied. In contrast, polygraphs that were administered at the same time had errors of omission and commission. fMRI scans have also shown that some vegetative patients are actually conscious.

All of the above techniques may be useful to detect and possibly even assess the degree of distress associated with lying. However, they bring us no closer to defining stress, much less the ability to measure it.

Heart Rate Variability, Neuroimaging Biomarkers, Depression And PTSD

It's unlikely that there will ever be a method to accurately measure stress simply because scientists cannot agree on verifiable criteria to define it. One possible exception is HRV (heart rate variability), which many believe is the most objective and sensitive barometer of "stress". As will be demonstrated in a subsequent Newsletter, low heart rate variability is seen in almost all stress related disorders and is a powerful predictor of coronary morbidity and mortality. Conversely, exercise, meditation and other agencies that reduce stress and have cardioprotective effects are associated with an increase in HRV. Although diminished HRV tells you something is awry, it is not diagnostic for any specific disorder. Spectral analysis of power components reveals very low, low and high frequency oscillations that reflect

different parasympathetic and sympathetic influences. It is conceivable that further investigations may reveal specific HRV patterns that will have more diagnostic significance when combined with other stress biomarkers.

In that regard, acute and severe stress is associated with an outpouring of catecholamines followed by a rise in glucocorticoids, and chronic stress is characterized by increased cortisol levels. While these and other stress related hormones can be measured in blood, saliva and urine, their values vary depending on so many factors that they are not useful in demonstrating their relationship to different diseases or distinguishing between cause and effect. As a result, efforts have concentrated on assessing the contribution of stress to specific disorders such as depression, hostility, anger, anxiety, PTSD, and Type A behavior, whose severity can be quantified using specific questionnaires. These can be administered to large numbers of subjects with the responses scored by computer at very little expense. In some instances, the responses to selected groups of the over 500 items of the MMPI (Minnesota Multiphasic Personality Inventory) are used to rate everything from depression and paranoia to hostility and PTSD. The MMPI has been administered to hundreds of thousands of individuals seeking employment, entry into the armed forces and for medical reasons since it was made available over seventy years ago. All that is necessary is to compare the results of specific responses to death certificates, hospital records and other databases that are readily available to demonstrate some correlation that has statistical significance. However, such self-report instruments are notoriously unreliable, especially for Type A traits such as hostility and aggression, which are best measured by observers who are trained to elicit and quantify certain characteristic traits and responses. While this can markedly improve the accuracy of diagnosis and rating severity, it is very expensive, time consuming and not cost effective for large studies.

Depression is a leading cause of disability in the United States and a growing health problem. The World Health Organization predicts that **depression will be the second leading cause of death by the end of this decade**, exceeded only by heart disease, which it also contributes to. What causes depression is not clear, which explains why there are so many very varied therapies, ranging from psychiatric interventions, ultraviolet light, sleep deprivation, acupuncture, and exercise to vitamins and other supplements, hormones, vagal and other types of electrical stimulation treatments and at least four different classes of antidepressant drugs. However, there is no way to predict which of these will work best in any given patient, which is why the vast majority fail to improve. Most patients are treated by drugs designed to boost serotonin, despite clinical trials demonstrating that they are hardly more effective than placebos, have serious side effects, and serotonin levels are usually normal. In some European countries, certain

antidepressants are banned for anyone under the age of 18 because of increased risk of suicide. Another drawback is the difficulty in trying to stop antidepressant therapy because of severe withdrawal symptoms.

The major problem has been the lack of any objective way to confirm the diagnosis of depression, but this may no longer be true as illustrated below.



PET (Positron Emission Tomography) studies have revealed that depressed patients have markedly diminished electrical activity, as shown by the lack of yellow-red areas in certain brain sites (far left). Noninvasive electrical stimulation of these areas in patients resistant to antidepressants results in a restoration to the normal pattern that correlates with the patient's progressive improvement.

The diagnosis and treatment of Post Traumatic Stress Disorder is also a disaster because of the lack of any objective biomarker, but this has now changed with the demonstration **that magnetoencephalography can diagnose PTSD with 95 percent accuracy, even in patients who are asymptomatic**. It is not surprising that "energy therapy" relieves depression, since ECT "shock" treatment has long been acknowledged as the preferred treatment for severe cases. Nobody knows why ECT works, and less drastic types of cranioelectrical stimulation may provide similar rewards. This has already been demonstrated for certain repetitive transcranial and cranioelectrical stimulation devices. As will be explained in a subsequent Newsletter, these modalities may also benefit PTSD patients— so stay tuned!

Paul J. Rosch, MD, FACP
Editor-in-Chief

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