Committee 2
Holistic Medicine in Modern Health Care

Draft – January 1, 2000
For Conference Distribution Only

Successful Holistic Treatment of Chronic Depression

Paul Thomlinson
Vice President
Research and Quality Assurance
Burrell Behavioral Health
Springfield, Missouri
and
C. Norman Shealy
Holos Institutes of Health

The Twenty-second International Conference on the Unity of the Sciences
Seoul, Korea February 9-13, 2000

SUCCESSFUL HOLISTIC TREATMENT OF CHRONIC DEPRESSION

The use of electrical current in the treatment of illness and disease has been considered since antiquity (Jarzembski, 1985), and has appeared in the psychiatric literature since at least the early 1960s (Heath, 1963). However, it is only since the 1970s that appropriate devices for provision of stimulation currents have been available to clinical scientists for application and evaluation. Since that time, such devices have been used fairly extensively, with recent research demonstrating their safety and efficacy in improvement of attention and concentration (Southworth, 1999), short-term smoking cessation (Pickworth, Fant, Butschky, Goffman, et al., 1997), anxiety and other stress-related disorders (De Felice, 1997), headache, insomnia, and brain dysfunction (Klawansky, Yeung, Berkey, Shah, et al., 1995), and substance abuse (Jarzembski, 1985), among other clinical problems.

For 28 years our work has focused primarily on individuals with chronic pain, virtually all of whom are also suffering from chronic depression. Over the last 11 years, we have evaluated more thoroughly the treatment of depression focusing upon that rather than upon the pain itself. In 1975, we were introduced to a specific transcutaneous electrical nerve stimulator, at that time called the Pain Suppressor^{R}. It later evolved into the Liss cranial electrical stimulator (CES). Our earliest work with this device indicated that it had a striking ability to normalize total serotonin

production (Shealy, Kwako, and Hughes, 1979).

This finding, of course, has major implications for the application of CES to the treatment of a broad array of disorders, given the fact that "serotonin metabolism is disordered in a variety of clinical states, including both medical and mental disorders," and the very tenable hypothesis "that potentially treatable low serotonin states are the final common pathway in many medical disorders" (Nash, 1996, p. 35). Indeed, it is not too strong to suggest that "an individual's genetically determined stable set point for serotonin may be disordered by environmentally induced events, leading to altered sleep, dysthymia, and depression. This imbalanced neurochemistry cascades into an autonomic nervous system hyperactivity causing symptoms" (Nash, 1996, p. 35). This "serotonin connection," coupled with our early work showing serotonin normalization from the CES, gave rise to a long line of clinical studies, some of which will be reviewed in this paper.

In the initial studies on this device, 40% of the patients were found to produce an excess of serotonin as measured by 24 hour output of 5-hydroxyindolacetic acid (5HIAA) and 40% had a deficiency in the production of serotonin (Shealy, Kwako, and Hughes, 1979). In both cases, application of the Liss stimulator transcranially normalized total serotonin production. Interestingly, those patients who had a normal 24-hour 5HIAA, did not change their serotonin production and did not improve from

any of the treatment modalities employed. Thus, it has been our experience for the last 24 years that the Liss stimulator applied transcranially is of particular value in normalizing serotonin production, and later studies have shown it to be effective when no other modality is used in at least 50% of people with chronic depression (e.g., Shealy, Cady, Wilkie, Cox, Liss, and Closson, 1989). Its ideal use seems to be primarily to treat depression itself. The great advantage of this particular therapy is that with the exception of patients with cardiac pacemakers, there is no contraindication to its use and, indeed, this is purely a theoretical contraindication. We have, on a number of occasions, checked patients with cardiac pacemakers while they were hooked up to their EKG and no adverse effects were found. Nevertheless, we do not recommend that one ordinarily use this type of stimulator in patients with pacemakers. A similar, but equally theoretical, caveat might be extended to patients with implantable cardioverter defibrillators.

RESEARCH

Of considerable importance in looking at the broad field of chronic pain associated with depression, is the recent international study on the relation between somatic symptoms and depression (Simon, VonKorff, Piccinelli, Fullerton, and Ormel, 1999). It appears that in virtually all countries, depression is often either denied by the patient or masked when the patient presents with somatic symptoms

rather than primarily with depression. Implications of this will be further explored in this paper.

According to Munoz, et al. (1994), "the majority of cases of clinical depression go unrecognized and untreated, despite the fact that depression is an eminently treatable disorder..." (p. 42). These authors go on to note that the recently published clinical practice guidelines from The Agency for Health Care Policy and Research (AHCPR), which focused on depression in primary care settings, "should enhance the detection of depression and the quality of pharmacotherapy for depression...however, the guidelines encourage primary care physicians to provide pharmacotherapy to their depressed patients as the first line of treatment" (p. 42). At the very least, as Munoz, et al. point out, "patients should be informed of the broad array of treatment options available and provided with a more balanced presentation of the potential benefits of psychotherapy for depression" (p. 42). Unfortunately, it appears that the AHCPR guidelines, data based though they are, and their critics (e.g, Munoz, and others), well-intentioned though they are, both ignore a vast array of safe, efficacious alternative treatments that might loosely be grouped together as "holistic treatments for depression," including those described in this paper. The remainder of this work will focus on CES as one element of holistic treatment.

Our clinical studies have involved some 15,000 patients with chronic pain

and/or depression. Specific research studies purely on the neurochemistry and/or clinical effectiveness of the Liss stimulator applied transcranially have been done in over 1,000 patients. The next study done after that mentioned in the introduction (Shealy, Kwako, and Hughes, 1979) has not been previously reported. It was considered a pilot study at the time, and in 24 patients with chronic depression as measured by the Zung Test for Depression, patients were instructed in the use of the transcranial stimulator to use at home, with instructions to return two weeks later for a follow-up Zung Test and clinical evaluation. Twelve of these patients were out of depression with no treatment other than the Liss stimulator transcranially. When compared with the average antidepressant drug, this is a remarkably important observation, however, we have done considerable further testing.

One of our earliest neurochemical studies was that of plasma catecholamines (Shealy, 1988a). Fifty-five percent of 44 patients with chronic pain and depression had norepinephrine levels elevated above the upper limit of normal; one patient having some 500% of the upper limit of normal. Dopamine was elevated in only 12% of these patients and standing norepinephrine levels were elevated above the upper limit of normal in 80% of these patients.

In another early neurochemical study (Shealy, 1988b), 42 of 80 patients had pre-treatment plasma beta-endorphin levels well below the lower limit of normal (2.2

picograms/ml). Normal levels for the standards are 4 to 10 picograms/ml. Nine control individuals without chronic pain and depression had normal plasma beta-endorphins. Six of the 80 patients had pre-treatment plasma beta-endorphin levels above the normal level, their average being 14.4 picograms/ml, and 30 more of the 80 patients had plasma beta-endorphin levels within the normal range. Following two weeks of intense therapy, the central component of which was the Liss cranial stimulator, the 6 patients with elevated plasma beta-endorphins remained elevated. All but one of those, however, with a low beta-endorphin level evidenced increases to normal levels. Other studies have included measurements of plasma fasting levels of serotonin, beta-endorphin, norepinephrine, cholinesterase, as well as the ratios of norepinephrine to serotonin, norepinephrine to beta endorphin, norepinephrine to cholinesterase, serotonin to beta endorphin, and norepinephrine to the serotonin and beta endorphin ratio. Striking abnormalities were found in one or more of these tests in 92% of 14 chronically depressed patients who also had chronic pain (Shealy, Cady, Wilkie, Cox, Liss, and Clossen, 1989).

This research revealed that after two weeks of daily 20-minute applications of CES, 67% of the depressed patients showed improvements in their basic neurochemical profiles and 60% had improved on the Zung Test by 9 points or more, with 50% of the depressed patients at that point having Zung Test scores below 50,

indicating no depression. These findings are consistent with our previously noted research, which had shown a 50% improvement with cranial electrical stimulation.

Later research with 104 depressed patients indicated the same type of findings (Shealy, Cady, Veehoff, Houston, Burnetti, Cox, and Closson, 1992). Ninety-two percent of the depressed patients had one to seven neurochemical abnormalities such as those listed earlier. In addition, in another 200 patients with depression, 80% were found to be deficient in magnesium. All of 60 other depressed patients were found to be deficient in one or more essential amino acids, most commonly taurine. Another of our studies (Shealy, Cady, Cox, and Murrell, 1996) showed that, in 29 patients with chronic depression, 6 were clearly deficient (below the lab's range of "normal") and all of the others had DHEA levels below the average, except one patient with bipolar depression. Only two of these patients had levels of DHEA above the first quartile. Thus, 93% of these patients were in the lowest quartile of DHEA levels, or were clearly deficient.

In addition to these neurochemical studies, we have also looked at total symptomatology in relation to the Total Life Stress Score (Shealy, 1984). The average patient we see has 49 chronic symptoms. Such elevated levels of emotional, chemical, and physical stress can be construed as either causes or consequences of significant dysfunction of the autonomic nervous system, and/or significant precursors of

disease or illness. This symptomatic picture becomes extremely important in the assessment and treatment of depression, particularly in light of Simon, et al.'s (1999) international study of the relationship between somatic symptoms and depression. Particularly, depressed patients from a multiplicity of world cultures tend to report "somatic symptoms, such as headache, constipation, weakness, or back pain" (p. 1329), and varying degrees of somatization. Of particular interest to the present work is that many of these so-called somatization symptoms are well-suited for treatment with transcutateous electrical stimulation.

In our recent study of 351 patients with specific depression, 275 females and 76 males who had failed to respond to one or more antidepressant drugs, were treated with a combination of 10 hours of educational lectures, daily CES with the Liss stimulator, vibratory music on the music bed with built-in speakers, and photostimulation at an average rate of 10 Hz (Shealy, Cady, and Cox, 1995). At the end of therapy over a two-week period with treatments only Monday through Friday, 85% of the patients were considerably less depressed and three months later 70% remained improved without further intervention. Neurochemical abnormalities found in 90% of the patients pre-treatment were present in only 29% of those patients at three-month follow-up, and only 4% of the improved patients continued to have neurochemical abnormalities.

In a later study that has not yet been published, in 36 patients who were treated only with photostimulation, vibratory music, and an educational program, 58% improved on the Zung Test, falling to below clinical significance levels. This study highlights some of the other promising holistic modalities under investigation in our clinical research programs.

Thus, by way of summary of our clinical research findings, we can say that cranial electrical stimulation by itself appears to be effective in at least 50% of patients with chronic depression, relieving both their depression and markedly improving and normalizing their neurochemical profiles. If we use photostimulation, education and vibratory music for two weeks, we get 58% of patients out of their depression within two weeks. When we combine the photostimulation, education, and music with the Liss stimulator, 85% of the patients improve initially and 70% remain improved at three months without any further intervention. Obviously, much further and longer-term research needs to be done. However, it is our impression that the vast majority of our patients who have improved at three months remain improved up to two years later. Clearly, though the focus of this paper is electrical stimulation, it is the integration of this modality with the other methods mentioned above, in addition to psychotherapy, nutritional therapy, exercise, and other therapies, that yields a truly holistic approach to the treatment of depression.

STANDARDS

In our experience of using cranial electrical stimulation in well over 15,000 patients over the last 24 years, there have been no complications. An occasional patient has a very transient complaint of headache, dizziness or slight confusion. All of these cleared within an hour, and we are not aware of a single patient who has had any prolonged or serious complications or side effects of CES. In general, we use one to two milliamps of current, and the output of the Liss stimulator is 15,000 Hz modulated 15 times per second and 500 times per second. Although our work has been only bitemporal or nasion inion, there are many other transcranial possibilities that could be tried. Obviously, other frequencies might also be used, but we have no experience with those. Federal law in the United States requires that the Liss cranial electrical stimulator be used only by or on prescription from a physician. Certainly as long as that requirement is in place, and considering not only our experience with 15,000 patients but many thousands by other practitioners, we know of no risk in the use of this modality. It is unfortunate that at the present time a psychologist or other health care practitioner cannot prescribe it.

It is important to emphasize that the Liss stimulator or the cranial electrical stimulator is very different from regular TENS devices used for treatment of pain. In general, TENS devices use a maximum output of 100 Hz and up to 80 milliamps of

current, whereas the Liss stimulator uses a maximum of 4 milliamps and usually only one or two milliamps at 15,000 Hz, as was mentioned above.

MEDICAL EDUCATION

Since psychologists and many other mental health practitioners are capable of working with patients with chronic depression, it certainly seems desirable that ways be found for them to use this most effective and simple therapeutic approach as part of their treatment repertoire. This is particularly true given the safety record of the devices in our and others' clinical research, and the two merely theoretical contraindications enumerated earlier (i.e., pacemakers and implantable defibrillators). Indeed it is our position that a one-day training session for any licensed mental health professional should be quite adequate for them to become proficient in the use of this particular modality.

PUBLIC AWARENESS

At the present time, cranial electrical stimulation is wildly underutilized in the entire field of mental health care, and most mental health professionals know only about the use of drugs or psychotherapy in the treatment of depression. It is critically important that patients in the public be made aware that cranial electrical stimulation is not in any way related to electroshock therapy or electroconvulsive therapy (ECT). Although some studies suggest that these much more drastic therapies may help 80%

of severely impaired patients (Valente, 1991), the risk profile and potential adverse consequences of ECT put it in a completely different category of possible harmfulness than the cranial electrical stimulation advocated here. The stimulator is so safe that one can drive one's car while wearing it. Indeed, the second author has personally used it when traveling to and from Europe or the Orient, as its stabilizing effect upon serotonin is a tremendous adjunct in avoiding and minimizing jet lag. In our opinion, cranial electrical stimulation is the modality of choice for treatment of chronic depression, although when it is combined with photostimulation, education and vibratory music, it shows even more impressive outcomes.

COST EFFECTIVENESS

The commercial retail cost of a cranial electrical stimulator is $980.00. We have stimulators that have been in use for over 15 years without any defect. In fact, the only major problem that we have seen is when one of the stimulators was_ inadvertently dropped into a tub of water. Then it has to be sent back to the factory.

Considering the fact that modern antidepressant drugs have a complication rate of 25% or greater and a cost that often is $100 or more per month, the cost of the cranial electrical stimulator is clearly an advantage because it is a once-in-a- lifetime purchase and can be used for many years, if necessary. Unfortunately, at the present time in the United States, third party carriers generally recognize this type of

stimulation only for treatment of pain, and although it is approved for the treatment of anxiety and depression and insomnia, it is not generally covered by medical insurance. Nevertheless, its safety and efficacy make it a first choice in our treatment of depression.

References

De Felice, E.A. (1997). Cranial electrotherapy stimulation (CES) in the treatment of anxiety and other stress-related disorders: A review of controlled clinical trials. Stress Medicine, 13(1), 31-42.

Heath, R.G. (1963). Electrical self-stimulation of the brain in man. American Journal of Psychiatry, 120(6), 571-577.

Jarzembski, W.B. (1985). Electrical stimulation and substance abuse treatment. Neurobehavioral Toxicology & Teratology, 7(2), 119-123.

Klawansky, S., Yeung, A., Berkey, C., Shah, N., et al. (1995). Meta-analysis of randomized controlled trials of cranial electrostimulation: Efficacy in treating selected psychological and physiological conditions. Journal of Nervous & Mental Disease, 183(7), 478-484.

Munoz, R.F., Hollon, S.D., McGrath, E., Rehm, L.P., et al. (1994). On the AHCPR Depression in Primary Care guidelines: Further considerations for practitioners. American Psychologist, 49(1), 42-61.

Nash, R.A. (1996). The serotonin connection. The Journal of Orthomolecular Medicine, 11(1), 35-44.

Pickworth, W.B., Fant, R.V., Butschky, M.F., Goffman, A.L., et al. (1997). Evaluation of cranial electrostimulation therapy on short-term smoking cessation.

Biological Psychiatry, 42(2), 116-121.

Shealy, C.N. (1984). Total life stress and symptomatology. Journal of Holistic Medicine, 6(2), 112-129.

Shealy, C.N. (1988a). Hyperadrenergia in chronic pain. The Journal of Neurological & Orthodaedic Medicine & Surgery, 9(2), 105-106.

Shealy, C.N. (1988b). Plasma beta-endorphin levels in chronic pain patients at a comprehensive pain treatment center. The Journal of Neurological & Orthodaedic Medicine & Surgery, 9(3), 264-265.

Shealy, C.N., Cady, R.K., and Cox, R.H. (1995). Pain, stress and depression: Psychoneurophysiology and therapy. Stress Medicine, 11, 75-77.

Shealy, C.N., Cady, R.K., Cox, R.H.., and Murrell, M. (1996). DHEA deficiency in patients with chronic pain and depression. The Journal of Neurological & Orthodaedic Medicine & Surgery, 17, 6.

Shealy, C.N., Cady, R.K., Veehoff, D., Houston, R., Burnetti, M., Cox, R.H., and Closson, W. (1992). The neurochemistry of depression. American Journal of Pain Management, 2(1), 13-16.

Shealy, C.N., Cady, R.K., Wilkie, R.G., Cox, R.H., Liss, S., and Closson, W. (1989). Depression: A diagnostic, neurochemical profile & therapy with cranial electrical stimulation (CES). The Journal of Neurological & Orthodaedic Medicine &

Surgery, 10(4), 319-321.

Shealy, C.N., Kwako, J.L., and Hughes, S. (1979). Effects of transcranial neurostimulation upon mood and serotonin production: A preliminary report. Il Dolore, 1(1), 13-16.

Simon, G.E., VonKorff, M., Piccinelli, M., Fullerton, C., and Ormel, J. (1999). An international study of the relation between somatic symptoms and depression. The New England Journal of Medicine, 341(18), 1329-1335.

Southworth, S. (1999). A study of the effects of cranial electrical stimulation on attention and concentration. Integrative Physiological & Behavioral Science, 34(1), 43-53.

Valente, S.M. (1991). Electroconvulsive therapy. Archives of Psychiatric Nursing, 5(4), 223-228.