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Effects of Chin-Don Therapy on Blood Levels of Cortisol, Beta-Endorphins, and Natural Killer Cell Activity: Relationships with Emotion, Behavior and Immunodefense System of the Elderly

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Full Article

Effects of Chin-Don Therapy on Blood Levels of Cortisol, Beta-Endorphins, and Natural Killer Cell Activity: Relationships with Emotion, Behavior and Immunodefense System of the Elderly

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Abstract

We employed an objective method in assessing changes in blood levels of cortisol (CT), beta-endorphin (BE), and natural killer (NK) cell activity in relation to emotional and physical behaviors. Elderly subjects (n=30) were divided into 2 groups: 18 (age range: 70 - 89 yr; male: 1, female: 17) were subjected to CDT (CDT group), while 12 (age range: 60-89 yr; male: 3, female 9) served as controls. On the day of investigation, patients were administered either with CDT (CDT group; n=18) or without CDT (non-CDT group; n=12). Thirty minutes before and after CDT was administered to patients, blood was sampled from each participant in a serially ordered manner. Blood levels of CT and BE in the CDT, but not the non-CDT, group were significantly elevated after CDT. As for NK cell activity levels, an increased tendency was observed in CDT (but not in non-CDT) group when administered with CDT of similar visual stimuli and time intervals. Patients were jubilant and joyful, and appeared to be positive in participating in the dance with rhythmic steps and laughter. CDT improved emotional and physical performance of elderly patients: the favorable outcomes synchronized well with changes in blood levels of CT, BE, and NK cell activity. Significantly increased blood CT and BE levels coincided with smiles/laughter and elevated physical activity shown by participants during and after CDT. Although immunodefense system-related parameters were not monitored, an increased level (without statistical significance) of blood NK cell activity levels was noted.

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1. Introduction

Increased longevity has imposed multifaceted and heavy demands on the quality-of-life (QoL) for the elderly and for health authorities. Apart from

oral intake of chemical and natural compounds, recent approaches¹⁻¹¹ - including Chin-Don therapy (CDT) or a kind of traditional Japanese music - have been found to improve QoL of in a multiple-case study.^{8,9,11} In our previous study, we focused on neurotransmitters adrenalin (AD), noradrenalin (NA), and dopamine (DP).⁹ The stress-related hormone cortisol has also found to be significantly associated with CDT in experiments measuring the hormonal content in subjects.¹¹ As humor/laughter, music, and certain forms of alternative medicine are known to favorably relieve depression and dementia/Alzheimer's disease,^{1,3,5,8,9} elevate emotion⁹⁻¹² and strengthen the immunodefense system^{7,13,14} while attenuating stress,^{6,11,12} in the present objective study we investigated endogenous indexes: i.e. blood variation levels of β -endorphins (BE), natural killer (NK) cell activity, and cortisol (CT), closely associated in the elderly with the aforesaid perspectives.

In this study, we employed an objective method which assessed certain blood indexes to assess changes in blood levels of the stress-/emotion- and immunodefense-related neurotransmitters/hormones (such as BE, NK cell activity, and CT) before and after CDT. The indexes, which have previously documented to associate with emotional⁹⁻¹² and immunodefense systems^{7,13,14} affecting QoL of humans, especially the elderly, were selected to complement previous study of blood level variations of AD, NA, and DP in order to gain a more complete understanding of the roles of these transmitters/hormones in improving elderly human QoL. Of 3 monitored indexes, CDT induced significant CT and BE increases in blood level changes in the CDT but not the non-CT group.

2. Methods and Subjects

2.1 Subjects

The subjects and methods were basically those of a previous study.⁹ Briefly, of a total of 30 elderly subjects commuting to a Daycare Community Service Center (DCSC) in Prefecture A participated in the study: 18 (age range: 70 - 89 yr; male: 1, female: 17) were subjected to CDT, while 12 (age range: 60-89 yr; male: 3, female 9) served as controls. Physical states of subjects (CDT Subjects vs *controls*) were as follows: independent (n=1 vs 1); needed nursing support degree 1 (n=12 vs 7), degree 2 (n=2 vs 1); nursing care degree 1 (n=1 vs 2); and nursing care degree 2 (n=0 vs 1). Subjects with (n=15 vs 10) and without (n=3 vs 2) pre-existing diseases were physically independent or slightly dependent and psychologically functional/normal, and only 3 vs 2 were on sleeping pills. Based on the Tombaugh report, the Mini Mental State Examination (<http://www.dementiatoday.com/wp-content/uploads/2012/06/MiniMentalStateExamination>) or MMSE subjects (CDT Subjects vs *controls*) showed that they exhibited slight dementia (n=2 vs 3) or were otherwise normal (n=16 vs 9), and those with MMSE scores of <17 were omitted from the study. Subjects and their next-of-kin (whenever necessary) were briefed orally and in written form on the purpose, methods and outcome of the study. Written consent was obtained from those (or their next-of-kin) who decided to participate in the study. Additionally, those with MMSE scores of <17, or disagreed to participate in the study were omitted from the present investigation. Based on their mean Barthel index (BI) of 92.5±9.43 (CDT subjects) to 95.83±5.97 (controls), (<http://www.strokecenter.org/wp-content/uploads/2011/08/barthel>) they were both categorized as physically independent. The moral and ethical codes in the treatment of participants were approved by the Ethics Committee of the Faculty of Medicine, Shiga University, Japan.

2.2 Methods

2.2.1 Timing and use of CDT

Elderly non-residential subjects participated in our study, which lasted from June 20 to September 28, 2008. Subjects arrived at about 09:00 am on every visit, and engaged in daily chores and activities designated for the day at the DCSC. On the day of investigation, subjects were divided into 2 groups: 18 patients were administered with CDT (CDT group) and 12 were without CDT (non-CDT group). Thirty minutes before CDT was administered to patients (10:00–10:30 hr), blood was sampled from each of 18 patients in a serially ordered manner. Blood sampling for controls were conducted in a similar manner. While the CDT group was given CDT, controls were allowed to spend a similar time-interval leisurely/comfortably doing nothing, and with free access to the washroom and non-alcoholic beverages (without CDT) in a room layered with Japanese mattresses (tatamis) at a site away from CDT-treated participants, and where rhythmic sounds from CDT were not audible. After 30-min CDT, blood sampling of each patient in the

CDT group were repeated in the serially similar order duplicating pre-CDT administration. As for the non-CDT group, blood sampling was similarly repeated in the same serial order and manner to pre-control procedures. The rhythm and dance incorporated in the CDT used were similar to that used in a previous study.⁹ Patients complained of occasional pain sensation or discomfort in physical movement, and showed emotionless or unhappy faces before CDT. Briefly, the ‘chin’ and ‘don’ are sounded respectively by beating a gong-like instrument and a drum with a stick to produce a rhythmic musical flow of 3 (don x 3) + 7 (chin x 7) beats by colorfully dressed performers who move and dance in circles.⁸ In this study, we measured the blood levels of BE, CT, and NK cell activity before and after CDT administration and compared the differences between the CDT and non-CDT groups.

2.2.2 Statistical analysis

Mean scores of both methods for CDT subjects and controls were compared before and after CDT using the Wilcoxon rank-sum test. Differences where $p < 0.05$ were considered significant. All calculations were done using statistical analysis software Windows SPSS-15.0.

3. Results

3.1 Personal particulars, physical data, and health status

The personal particulars, physical data, and health status of subjects were similar to those in a previous study.⁹ Briefly, the percentage (tested/total number) of participants required nursing care level 1, 2 and 1+2 were 66.6% (12/18), 11.1% (2/18), and 5.6% (1/18) in the CDT group as well as 58.4% (7/12), 8.3% (1/12), and 25.0% (3/12) in controls, respectively. Moreover, the BI and MMSE values of Group IN registered 92.50 ± 9.43 and 27.06 ± 2.94 , while those of controls were 95.83 ± 5.97 and 24.92 ± 2.74 , respectively. Except for the gender factor, there were no significant differences in personal particulars and relevant items between the two groups.

Based on facial scores reported in the previous study, the CDT group was in a significantly happier mood with smiles/laughter during and after CDT (i.e. 1.78 ± 0.65 versus 2.89 ± 1.20). No significant changes were observed in the non-CDT group. Physical movements were improved and elevated during CDT with no complaints of pain or discomfort.

3.2 Changes in CT, BE, and NK cell activity levels in the blood

Blood levels of CT ($p < 0.004$) and BE ($p < 0.005$) in the CDT group were significantly elevated after CDT, while the non-CDT group did not show any marked changes in blood CT (Fig. 1) or BE (Fig. 2) levels. As for NK cell activity levels, marked changes in either the CDT or non-CDT group were noted when administered with CDT of similar visual stimuli and time intervals (Fig. 3). Patients were jubilant and joyful, and appeared to be positive in participating in the dance with rhythmic steps and laughter. Their pupils were dilated, they were breathing heavily, sweating, and physically exhausted, but they were otherwise in a joyful mood (happy and satisfied with smiles/laughter).

4. Discussion

Previous findings have demonstrated that humor and laughter can improve depression and dementia^{1,3,5,12} and therefore QoL as well as attenuating stress^{1,4,6,7,9,12} in psychologically affected patients. Accordingly, humor can be seen as a specific defense mechanism where positive emotions can overcome the undesirable negative emotions involved in a stressful situation.¹⁶

In previous studies,^{8,11,15} we showed that Chin-Don therapy (CDT) can evoke smiles/laughter and improve mood to yield useful effects with positive psychological and neurological outcomes via re-

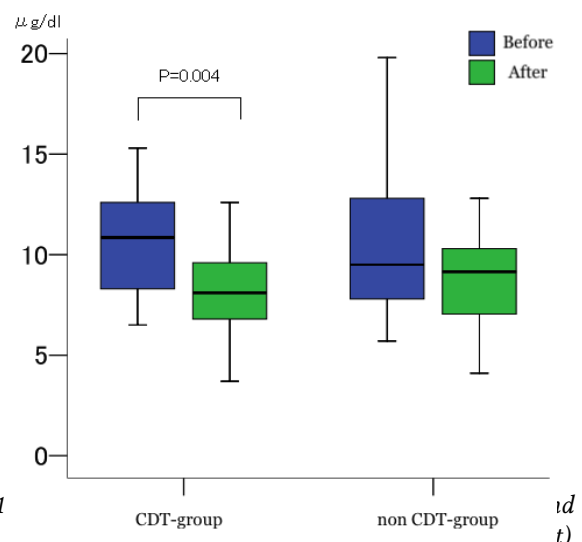


Fig. 1
after
CDT

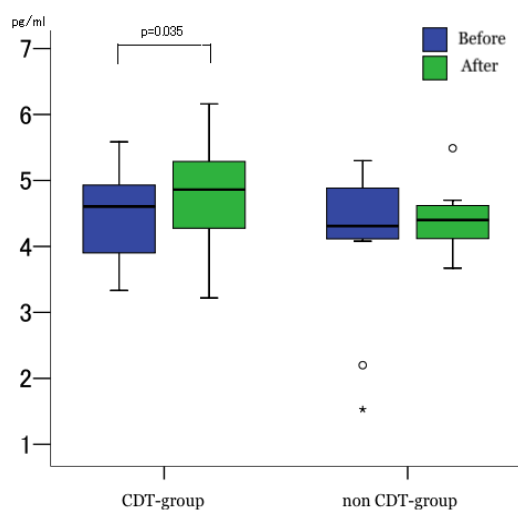


Fig. 2: Change in blood beta-endorphins (BE) levels before (blue) and after (green) CDT in subjects with (left) and without (right) CDT

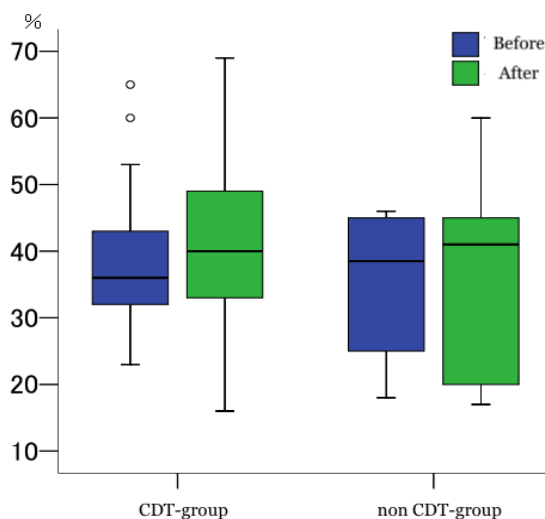


Fig. 3: Change in natural killer (NK) cell activity in blood before (blue) and after (green) CDT in subjects with (left) and without (right) CDT

retrieval of fond memories of past events and experiences in the case of three elderly Japanese patients.¹¹ In another investigation,⁹ we verified the blood levels of adrenalin (AD), noradrenalin (NA), and dopamine (DP) in patients of the present study, thus confirming the above mentioned findings.⁹ The changes in blood AD, NA, and DP levels were accounted for accordingly in terms of relevant physiological and psychological responses.⁹ This therefore reconfirmed that CDT therapy works effectively in improving mood (emotional and psychological states) for the CDT group. Although it might appear that CDT may only work in the elderly (age range: 70-89 yr) that have previously been exposed to CD performance/music (participants in this study) when young or during their childhood, a recent study¹⁵ using young subjects (<60 yr) has proven otherwise.

Of the 3 indexes we investigated here, we first focused on CT, which is closely associated with stress. Stress is closely associated with endogenous releases of steroid hormones, such as CT, in the living system. Therefore, the significant ($p < 0.004$) blood CT level decreases in CDT patients may have been due to less stress during CDT exposure, as elevated CT release is closely associated with elevated stress input. We did not measure the effect of immunity by CT decrease, as the effect would be transient and short-lived.

Physiologically, stress is defined as a situation where the living system is disturbed by threat to the stability or functioning of the body.¹⁷ Stress consistently influences the body system as follows: 1) the hypothalamus-pituitary-adrenal system, and 2) the NA-associated - including sympathetic nervous (SNS) and the locus coeruleus - systems.^{17,18} In a previous study,⁹ we found significant increases in AD and NA levels in blood of participants exposed to CDT, with typical physiological responses manifesting in the above systems 1) and 2). In this study, we further confirmed the stress-relieving effect of CDT by observing significant ($p < 0.004$) decreases in Blood CT levels. In other words, patients were actively engaging in dancing with the CDT rhythmic beats with the 'fright-fight-flight' response (heavy breathing, sweating, dilated pupils, etc.) while forgetting unhappy or depressive emotions (i.e. resulting in joyful mood).^{8,9,15} The effects of AD- and ND-induced responses with apparent happy expressions⁹ most likely persisted from during CDT to, at least, 30 min after CDT (time when blood was sampled for analysis). In the previous⁹ and present studies, under certain stressful conditions (e.g. CD music, aggressive behavior of other patients, etc.), the bodies of patients produces larger quantities of AD, DA, and DP in response to these stressors. These triggered an increased heart rate, heightened muscle preparedness, sweating, and alertness that we observed in the CDT group. All these factors improve the ability to respond to a challenging situation such as in the case we witnessed in this study.

An endogenous opioid neuropeptide and peptide hormone, β -endorphin (BE),²¹ is associated with hunger, thrill, pain, maternal care, sexual behavior, and reward recognition. From the broadest perspective, β -endorphin is primarily used in living systems to attenuate stress and maintain homeostasis (<https://en.wikipedia.org/wiki/Beta-Endorphin>). Of the two main (local vs global) categories of functioning,

the global function is more relevant in the present study in decreasing body stress and maintaining homeostasis (e.g. in pain management, reward effects, and behavioral stability), providing enthusiastic participation and positive post-event emotions/behavior in the CD dancing.

CD-induced dancing is a form of exercise: it could generate much joy in some. BE release in response to exercises was documented in the 1980s,¹⁹ and induces a euphoric feeling or “runners’ high”.²⁰ With regard to significant ($p < 0.005$) BE increases, patients could have felt a certain degree of euphoria in joining the dancing with nostalgic rhythmic CD beats in the background. Despite slight physical difficulty and pain/discomfort in some participants, they participated in the dancing willingly, and they totally forgot pre-CDT depressive emotion and pain/discomfort during and after the dancing. This is probably due to the significant release of BE, because this opioid neuropeptide has a high affinity for and elicits a persistent effect on μ -opioid receptors (a receptor that morphine binds selectively to produce analgesia),²² yielding euphoria and analgesic effects in the CDT patients in the present and previous^{9,15} investigations, although we did not monitor pain/discomfort indexes and emotional scores in patients. It is intriguing to note that BE has 18- to 33-fold the analgesic potency of morphine²³ (albeit species-dependent²⁴). The analgesic mechanism most probably involves BE binding to opioid receptors in the dorsal root of the spinal cord to inhibit onsite release of substance P, thus reducing pain impulses relayed to the brain.^{25,26} The hypothalamus responds to the pain impulse by releasing BE through the periaqueductal grey network, which acts to release γ -aminobutyric acid (GABA), a neurotransmitter that inhibits dopamine release.^{25,27} This GABA-suppressing effect on DP might have prevented significant release of DP despite elevated physical activity performed by participants.⁹

Natural killer (NK) cells are a type of cytotoxic lymphocyte crucial to the innate immune system. The role of NK cells is analogous to that of cytotoxic T-cells in the vertebrate adaptive immune response. Upon viral infection, NK cells respond within 3 days. They respond to tumor formation as well. Typically, immune cells detect major histocompatibility complex (MHC) attached on infected cell surfaces, triggering cytokine release to induce lysis and apoptosis. Additionally, NK cells have the ability to recognize stressed cells in the absence of antibodies and MHC, triggering facilitation of immune reaction. They were named NK cells because of the original conception that they did not require activation to kill cells that are missing ‘self’ markers of MHC class 1.²⁸ The roles of NK cells in both the innate and adaptive immunoresponses are important because they can be used for potential cancer therapies by exploiting their NK cell activity *per se*.

Approaches to influence the psychological and physiological perspectives of the body system have been adopted according to limitations of acoustic, visual, and cognitive abilities of the elderly. The effect of laughter on recovery of a patient suffering from connective tissue disease was documented in 1976.²⁹ Subsequently in 1994, Itami et al.¹³ reported that two Japanese breast-cancer patients showed elevated NK cell activity after enjoying stand-up comedies and comedy shows. Moreover, rheumatism-arthritis patients show attenuated interleukin-6 levels with significant decrease in pain scores after listening to comic stories told by professional storytellers,¹⁰ Furthermore, patients suffering from atopic dermatitis indicate significantly lower wheal and erythema reactions when they are exposed to laughter comic-videos.³⁰ Therefore, certain cell activities (such as that of NK cells)^{13,31} induced by laughter and joyful feelings of stand-up comedy shows, comic-videos, and CDT attenuate unwanted chemical/peptide release in the human body to yield useful immunity-related outcomes. Although the elderly patients in this study were in a joyful mood with transient favorable emotional and physical improvements, the level of NK cell activity did not reach statistical significance, albeit an increased tendency in NK cell activity level was registered (Fig 3).

Although we attempted to complement previously monitored previous endogenous indexes (AD, NA, DP) with additional parameters (CT, BE, NK cell activity) in this study, there were other important indexes that we could not measure in this investigation. With emotional behaviors and physical responses in tandem to CDT administrations, changes in blood levels of AD, NA, DP in the previous and CT, BE, and NK cell activity in the present study were monitored. As far as scientific literature has been able to document, the previous and present studies are the first to account for the various blood indexes in relation to CDT-induced emotional and physical activity. In the present study, CDT induced favorable lowering of stress, euphoric relief, reduction in pain/discomfort and/or slight physical handicaps experienced by the elderly participants. Intriguingly, these favorable psychological and physiological responses were quantifiable by the relevant blood indexes, advocating thus for the useful benefit of CDT.

5. Conclusion

CDT improved emotional and physical performance of elderly patients: the favorable outcomes synchronized well with changes in blood levels of CT, BE, and NK cell activity. Significant ($p < 0.004$) increases in blood CT levels were registered with smiles/laughter shown by participants, while markedly ($p < 0.005$) increased blood BE levels coincided well with elevated physical activity of slightly physically handicapped patients, who did not complain of pain or discomfort during and after CDT. Although immunodefense system-related parameters were not monitored, an increased tendency in blood NK cell activity levels was noted.

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