

Reconditioning the Stress Response Reduces the Inflammatory Cytokine IL6:

A Multiple Case Study

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ABSTRACT

Eleven normally coping and functioning subjects were recruited for a 12-week self-administered CD hypnosis stress reduction intervention designed to recondition and minimize subjects' excessive emotional and physical reactions to perceived work and life stressors. Serum cytokine (IL-6), stress response, coping, social support, psychological well-being and health habits were included as the measures in this multiple case study. After twelve weeks, subjects were observed to have a significantly lower IL-6 serum level from baseline. Further, subjects reported a significant decrease in the use of Negative Appraisal coping (such as, self-deprecating statements, perfectionism, and catastrophic and pessimistic thinking), and an improvement in eating/nutritional habits following the intervention. Baseline eating/nutritional habits and Threat Minimization Coping significantly predicted a change in serum IL-6 over the course of the intervention in stepwise hierarchical regression analyses. Post-treatment IL-6 scores were significantly lower than initial IL-6 scores of a control group, providing limited support that a brief self-administered CD hypnosis stress reduction program can potentially modify a physiological measure of inflammation (IL-6) and self-reporting coping in the face of work and life stress.

Keywords: hypnosis, stress, inflammation, IL-6, cytokines, psychoneuroimmunology, coping

Statement of Confidentiality: The authors are the developers of the hypnosis stress reduction CD and *StressScan* assessment used in this research study.

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It is well established that psychological stress can lead to adverse physical and psychological health changes (Graham, Glaser, Loving, Malarkey, Stowell, and Kiecolt-Glaser, 2009; Schoen, 1993). Chronic stress has been clearly associated with systemic inflammation and an overproduction of pro-inflammatory cytokines (Black, 2009; Kiecolt-Glaser, Preacher, K.J., MacCallum, R.C., Atkinson, Malarkey, and Glaser, 2003; Kiecolt-Glaser, Loving, Stowell, Malarkey, Lemeshow, Dickinson, and Glaser, 2005). Chronic and high levels of inflammation and its cytokine precursors have been linked to long term morbidity and a variety of acute and chronic conditions including heart disease (Paoletti, 2004), autoimmune disorders (Pickup, 2004), cancer (Mantovani, 2005), and depression (Anisman and Merali, 2003). Similarly, inflammation and chronic cytokine production has been shown to be associated with mortality as well in recent studies (Segerstrom and Miller, 2004; Ershler and Keller, 2000).

Only recently, has it become evident that pronounced emotional reactions such as anxiety and fear are directly linked to inflammatory changes in the body as well (Melamed, Shirom, Toker, Berliner and Shapira, 2004; Pitsavos, 2005, Von Kanel, 2007). Additionally, emotions such as anger, hostility, and loneliness are associated with an escalation of inflammatory activity in the body (Steptoe, Owen, Kunz-Ebrecht, and Brydon, 2004).

Research conducted on the inflammation stress connection has focused on several key protein indicators with the inflammatory cytokines most frequently investigated including Interleukin 6 (IL-6) and Tumor Necrosis Factor alpha (TNF-a). A growing number of investigations have evaluated different stress modulating interventions and have observed subsequent decrements in inflammatory cytokines including physical activity/exercise (Starkweather, 2007), music (Conrad, Niess, and Jaunch, 2007), relaxation training (Lutgendorf, Logan, and Kirchner, 2000) meditation (Carlson, Speca, Patel, and Goodey, 2003), and online

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programs (Hasson, Andenberg, Theorell , and Arnetz , 2005; Weber, Arck, Mazurek, and Klapp, 2002).

Several studies have evaluated the effect of hypnosis on modulating inflammatory cytokines. For example, Mawdsley, Jenkins, Macey, Langmead, and Rampton (2008) found that hypnosis treatments with ulcerative colitis subjects led to significant decrease in IL-6. Kiecolt-Glaser and her colleagues (Kiecolt-Glaser, Marucha, Atkinson, and Glaser, 2001) examined immune dysregulation in 33 medical students who were treated with hypnotic relaxation for acute exam stress. They found that frequent hypnotic-relaxation practice was associated with changes in CD3⁺ T and CD4⁺ T-lymphocytes, suggesting that their intervention reduced cytokine production associated with acute exam stress. Wood, Burghi, Morrison, Tanavoli, and Zadeh (2003) also observed changes in the inflammatory response following brief hypnosis sessions, where levels of Interferon-gamma and Interleukin-2 were significantly decreased in the subjects receiving hypnosis. Finally, stress reduction training using self-hypnosis has also been shown to have a significant impact on natural killer (NK) and CD3⁺CD56⁺ in a prospective randomized controlled trial of 48 students designed to help cope with exams (Naito, Laidlaw, Henderson, Frahani, Dwivedi, and Gruzelier, 2003).

Despite the connection between stress, inflammation, and illness, only a small percentage of the population actually make the time to incorporate stress management principles into daily habits and lifestyle practices. Since stress related illnesses constitute a growing segment in healthcare expenditures, it makes intuitive and logical sense to develop stress reduction strategies that would facilitate higher levels of compliance. Therefore, the current pilot study was designed to explore the application of an individualized stress reduction strategy that is predicated on simplicity and brevity.

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An individualized stress management application would have particular value as a preventative measure in healthy populations. In this investigation, healthy subjects were told to simply listen to a brief hypnosis stress reduction CD at bedtime and in the early morning. Relaxation tapes or CDs have proven effective from subjects' subjective reports, but have not been fully evaluated from the perspective of biochemical measures of inflammation (Laidlaw and Willet, 2002; Costello, 1988). This study extends prior research in this area by investigating the impact of hypnosis on inflammatory cytokines using a short-term and self-directed intervention.

The purpose of the current multiple case study is to investigate whether the use of a 12-week self-administered hypnosis stress reduction CD can significantly recondition the emotional and physical stress response and modify self-reported coping and IL-6 in a normally coping and functioning adults. In light of prior research on the effect of stress reduction on physiological and immune outcomes two null hypotheses are summarized below:

H_0 : Subjects listening to the hypnosis stress reduction CD will experience no significant reductions in serum IL-6 from pre-treatment to post treatment.

H_1 : Subjects listening to the hypnosis stress reduction CD will experience significant reductions in serum IL-6 from pre-treatment to post treatment.

H_0 : The hypnosis stress reduction CD will not result in a significantly greater utilization of positive appraisal, threat minimization and problem focused coping, and decreased use of negative appraisal coping strategies from pre-treatment to post-treatment.

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H₁ : The hypnosis stress reduction CD will result in significantly greater utilization of positive appraisal, threat minimization, problem focused coping, and a decreased use of negative appraisal coping strategies from pre-treatment to post-treatment.

METHOD

Participants and Procedure

Subjects:

Thirty individuals responded to an email advertisement and a community presentation about participating in a study related to managing stress. These prospective subjects were screened in two main ways. First, they were evaluated on being able to successfully establish eye closure and the hand lowering task on the Harvard Group Scale of Hypnotic Susceptibility Shor, & Carota Orne, E. (1962) . Secondly, since the study was to focus on healthy individuals (normally coping and functioning subjects), those who were suffering from chronic conditions such as autoimmune disorders, cancer, heart disease, depression, all of which have an inflammatory component, were eliminated. Those taking regular medications that might affect inflammation, such as NSAIDs or statins, were also eliminated. Following the above two screening criteria, twenty individuals began the study. Five of the twenty subjects (after completing their pre blood analysis) were unable to successfully complete the study due to work commitments or other scheduling conflicts. Another subject as a result of the initial blood test was found to have an autoimmune disorder and suffering from gout. As a result, he was excluded from the study. Therefore, 14 normally coping and functioning subjects successfully completed the investigation.

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Three of these 14 subjects had to ultimately be removed from the study's statistical analyses. In one case, the subject had developed a cold and flu at the time of the follow up blood test, another later reported that they had taken the anti-inflammatory over the counter drug (Motrin) for several days prior to the pre-blood test, and the third had experienced acute significant stress immediately prior to the initial blood test (car accident), which resulted in an extreme elevation of her IL-6 level by approximately 3.5 times the average score of all other subjects in this multiple case study.

The five subjects who were initially recruited along with the treatment subjects but could not participate in the study served as a statistical control group. No significant differences were found between these five control subjects and the case study subjects on initial IL-6, stress or coping measures used (all p 's > .05). No post-treatment assessment data was available for this group who were unable to continue in this study.

The majority of case study participants were employed full time (75%) and included 7 women and 4 men with a mean age of 52.4 (S.D. =7.4). All case study subjects signed a document of informed consent explaining the purpose of the study and any associated risks. It is important to note that the current study does have some inherent power limitations from a statistical perspective (O'Keefe, 2007). An a priori power analysis for correlated t-tests or regression using a two-tailed option and an alpha of .05, with a desired statistical power level of .80 and moderate effect size (.15) would suggest a much higher number of participants (60) to detect changes in inflammation and self-reported subjective coping and lifestyle changes.

Design and Measures

Design: A single-case research design with multiple cases as described by Kazdin (1982) was utilized. In this design, baseline measures are collected on multiple subjects prior to the treatment intervention. Since typically there is not a control group in this design, all subjects receive the treatment intervention. Following the treatment intervention, the measures collected during the baseline phase are readministered. According to Kazdin, this type of case study “provides a strong basis for drawing valid inferences about the impact of the treatment, and can rule out specific threats to internal validity in approaching that of true experiments (page 94).” We also had the benefit of comparing the treatment group to the five participants who initially signed up for the study but could not participate and could serve as a control group.

Emotional Well-Being. The measure of emotional well-being in this study was the Psychological Well-being Scale, (StressScan; Nowack, 1994). Psychological Well-Being is measured by a 12-item scale assessing overall life satisfaction and absence of psychological distress during the last three months. High scores suggest low overall distress and emotional negativity (i.e., greater satisfaction with one’s self, ability to enjoy life, and feeling happy with family, work, interpersonal relationships and achievements). This scale shows high internal consistency reliability (alpha) of .93 and test re-test reliability over a two-week period of .86 and is highly associated with measures of depression, distress and anxiety (Nowack, 1999).

Lifestyle Habits. A global measure of health habits and separate scales of eating/nutrition, exercise/physical activity, sleep/rest and preventive practices was measured using StressScan (Nowack, 1994; Nowack, 2008). Descriptions of the development and validation of StressScan and its scales have been described by Nowack (1994). The StressScan has been associated with diverse health and productivity outcomes in both cross sectional and

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longitudinal studies including immune response, job burnout, depression, absenteeism, physical illness, anxiety, job satisfaction, organizational commitment, and performance (Nowack, 2000; Beasley, Thompson, and Davidson 2003; Sharpley, and Yardley, 1999; Sharpley, and Yardley, 1999).

Coping Style. Coping style in this study was assessed by a 20-item scale (StressScan; Nowack,1994) which assesses four trait coping responses to work and life stressors and challenges. Descriptions of the development and validation of these coping scales have been described elsewhere (Nowack, 1994). Respondents are asked how they typically use these four techniques to cope with work, family and personal stressors. The four coping style scales include: 1) Positive Appraisal (realistically emphasizing the positive side of stressful situations through self-talk and cognitively minimizing the importance of the stressor); 2) Negative Appraisal (self-deprecating statements, perfectionism, and catastrophic and pessimistic thinking); 3) Threat Minimization (actively acknowledging and moving ahead without dwelling excessively on the stressor and using humor to put things in the proper perspective); and 4) Problem-Focused Coping (proactive attempts to modify one's behavior or the environment).

High scores on these independent scales suggest frequent use of these coping styles. These coping scales have shown internal consistency reliabilities ranging from .68 to .79 and average test re-test reliabilities over two-weeks of .69 in previous studies. In both cross sectional and prospective studies, each of these coping scales have been associated with diverse outcomes such as physical illness, job burnout, absenteeism, and depression (Giesser, 2005; Nowack, 1989).

Social Support. Social support is measured using an 18-item scale separately assessing the availability, utility, and satisfaction with five separate support groups available to the respondent including co-workers, supervisor/boss, family, friends, and significant others (Nowack, 1999). An

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overall Social Support score is calculated across all five of these groups. This scale has demonstrated an internal consistency reliability (alpha) of .83 and test re-test over two weeks of .94. High scores on this scale suggest that an individual perceives the availability of social resources at work and home, seeks them out when required and reports a level of satisfaction with the type of support they received (e.g., emotional, informational, instructional, etc.).

Stress. Self-reported stress in this study was assessed by a 6-item Stress scale (StressScan; Nowack, 1994) which provides a global index of the appraisal of stress (hassles) over a three-month period. The Stress scale has demonstrated an internal consistency reliability (alpha) of .68 and test re-test reliability over two weeks of .66, and has shown to be associated with immune response (Schwartz, Schwartz, Nowack, and Eichling, (1993), job burnout (Nowack 1987; 1991), absenteeism (Greene and Nowack, 1996; Nowack, 1994a) and physical illness (Nowack, 1990). This scale also seems to be sensitive to changes in specific interventions designed to teach stress management skills to those with a chronic illness (Giesser et al., 2005). This finding has important implications in light of several recent studies indicating the impact of stress management interventions on major chronic conditions and illness (Nowack, 2000).

Pre Testing: All subjects completed the above described self-report measures prior to listening to the hypnosis stress CD. All subjects were scheduled for morning blood tests at Quest Labs, after fasting for twelve hours.

Hypnosis Intervention: The following week all subjects attended an introductory 2-hour meeting. In this meeting they were all given an introduction to hypnosis and the hypnosis stress reduction CD program. The hypnosis stress reduction CD contained two different hypnosis tracks, one to be played prior to sleep at night time and the other to be played in the morning. Each subject was instructed to listen to both tracks once each day for the duration of the 12-week study.

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No other meetings or interactions were scheduled during the 12-week self-administered hypnosis intervention.

The hypnosis stress reduction CD, based on a paradigm for reconditioning the stress response (Schoen, 2001), was designed to minimize subjects' excessive emotional and physical reactions to perceived work and life stressors. The Night CD was 25 minutes in duration, while the Day CD was 7 minutes in length. The Night CD was structured in a relaxation format, with many suggestions given for a quietness, a stillness, an inner peace, and a sense of balance. Additional emotional suggestions were offered for feelings of safety and control. Midway into the CD, these calming sensory sensations and positive emotional feelings were increasingly paired with daily stressors, such as work, commitments, responsibilities, and conflict; for example, "you may notice a feeling of calmness and safety as go through your work day." Direct suggestions were given to the subjects to respond more productively and calmly to unanticipated and anticipated stress. Additional direct suggestions were also given to listeners to help them in reappraising stressful situations in a more positive and productive manner.

To further facilitate reductions in perceived stress, listeners were given direct suggestions for boosting their sense of control, overall feelings of self-efficacy, self esteem, and suggestions for reducing catastrophic thinking. Deepening was accomplished as listeners were taken progressively deeper into a forest setting. The Day CD was a distillation of the suggestions from the Night CD, with suggestions meant to trigger the calming sensory and positive emotional suggestions developed in the Night CD. Unlike the Night CD, there was not a relaxation induction format, nor any deepening suggestions. Also included were a number of the direct suggestions given on the Night CD.

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Post-Testing: At the end of three-months, all subjects completed the same self-report inventories they had taken prior to the study. Additionally, a follow-up morning blood test was drawn at Quest Labs after a 12-hour fast.

RESULTS

Descriptive statistics for pre-treatment time 1 and post-treatment time 2 for the main study variables are presented in Table 1. Consistent with Hypothesis 1, IL-6 significantly decreased (mean difference was .334, $t(10) = .03$) across the intervention from pre-treatment to post-treatment in the paired sample t-test (Table 3). A comparison was also made between the eleven subjects' post treatment IL-6 measures who had completed the study to the IL-6 pre treatment measures of the five subjects who were unable to complete the study due to work commitments. These five subjects served as a convenient quasi-experimental control to the eleven subjects who completed the treatment. Results from a one-way ANOVA were conducted and demonstrated that the mean post-treatment IL-6 scores of the eleven multiple case study participants were lower than the pre treatment mean IL-6 scores of the five controls ($F(1, 15) = 4.50, p = .051$).

To test Hypothesis 2, paired t-tests were run on each of the four unique coping style scales used in this study (Table 3). The experiment-wise error rate for these calculations is .19 which is the probability of making at least one Type I error when performing the whole set of comparisons. Only the change in scores from time 1 to time 2 for IL-6, Eating/Nutrition, and Negative Appraisal coping were significant (all, $p's < .01$).

No significant differences were found in the Overall Health Habits scale which was not surprising in light of the non-significant changes in the majority of its subscales, including physical activity/exercise, rest/sleep, and preventive practices (all $p's > .05$). Additionally, no

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reduction in self-reported work/life stress or increase in overall happiness/psychological well-being was observed (all p 's > .05). So, hypothesis 2 was partially supported with the hypnotherapy intervention leading to less self-reported use of perfectionist, self-blaming, catastrophic thinking, and self-defeating cognitions in the face of work and life stressors consistent with the cognitive hypnotic suggestions that were to be deployed in the face of work and life stress.

A stepwise hierarchical regression analysis was also used to identify the predictors of IL-6 change scores with baseline pre-treatment variables entered from Time 1. Tests of linearity, independence and collinearity were made to assure that assumptions were met in using regression analyses. Linearity was tested by using residual plots which verified an oval shape that ensured this assumption was not violated. Independence of the variables entered in the regression was tested by the Durbin-Watson coefficient which was 1.63 for the overall model summary. The Durbin-Watson statistic should be between 1.5 and 2.5 for independent observations. Step wise hierarchical regression analyses revealed that both Eating Habits ($p < .01$) and Threat Minimization Coping ($p < .01$) proved to be significant in predicting change in IL6 measures (Table 2).

Collinearity diagnostics (SPSS 17.0) were run to analyze unacceptably high level of intercorrelation among the independents in the regression. For the three variables that were entered, the condition index ranged from 1.48 to 3.79. The condition index summarizes the findings, and a common rule of thumb is that a condition index over 15 indicates a possible multicollinearity problem and a condition index over 30 suggests a serious multicollinearity problem (Ho, 2006).

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The hierarchical stepwise regression analysis was completed at two steps, and an overall significant model emerged predicting 88.3% (Adj. R^2) of the variance in the criterion variable of change in IL-6. Overall baseline eating/nutrition significantly contributed in the first step ($F_{\text{change}}(1, 11) = 15.15, p < .05$) followed by baseline threat minimization coping which significantly increased the predicted variable by 15.3.% ($F_{\text{change}}(1, 11) = 5.54, p < .01$).

DISCUSSION

This multiple case study suggests that listening to a self-administered hypnosis stress reduction CD program for three months may be associated with self-reported coping style changes (Negative Appraisal), self reported improvements in eating and nutritional habits, as well as a significant decrease in proinflammatory cytokine production (IL-6) in normal subjects. These multiple case study findings suggest that a self-administered hypnosis stress reduction program and cognitive suggestions may help reduce the use of self-critical, self-blaming, catastrophic, and perfectionist thinking as evidenced by the significant reduction in the use of *Negative Appraisal Coping* as well as facilitate healthy lifestyle practices as evidenced by the significant change in eating/nutrition habits. Individuals who perceive work and life stress with greater use of Negative Appraisal Coping tend to report greater stress, job burnout, anxiety and depression (Nowack, 1994; Geisser et al., 2008).

Prior research has shown that hypnosis can successfully change the use of cognitive coping strategies and appraisal processes (Ter Kuike, Sinhoven, Linseen, and Van Houwelingen, 1996). Hypnosis can also lead to a decrease in anxious thoughts and pessimism, and improvements in self-esteem (Lioffi and White, 2001). In light of the stress reduction hypnotic intervention used in this study, the finding of a significant change in cognitive coping (negative

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appraisal) and the finding that baseline Threat Minimization Coping is predictive of IL-6 change in the regression is not surprising. Subjects who cognitively react more modestly to stress are more likely to reveal a lowered physiological reactivity and concomitant systemic inflammation. Self-reported changes in health habits may be reflective of hypnotic suggestions aimed at coping skills, self-esteem, and self-efficacy, which in turn were facilitative of enhanced health behaviors such as eating and nutrition. This is consistent with a previous investigation which found self-efficacy leading to improvements in adults' lifestyle practices and health behaviors (Grembowski, Patrick, Durham, Beresford, Kay, and Hecht, 1993).

It is possible that subjects' hypnotically induced sense of self-efficacy led to a greater sense of empowerment and conscientiousness about adopting healthy stress coping behaviors. Prior research has shown that conscientious-related traits are typically negatively correlated to all risky health related behaviors while positively related to all health enhanced behaviors (Bogg and Roberts, 2004).

Self-reported changes in health habits may be reflective of hypnotic suggestions aimed at coping skills, self esteem, and self efficacy, which in turn were facilitative of enhanced health behaviors such as eating and nutrition. This is consistent with a previous investigation which found self-efficacy leading to improvements in adults' lifestyle practices and health behaviors (Grembowski, Patrick, Durham, Beresford, Kay, and Hecht, 1993).

This multiple case study provides some preliminary suggestions for how a physiological outcome of stress (IL-6) may in fact be mediated by alterations in cognitive appraisal of work and life events. In the present multiple case study a reduced inflammatory response was associated with a reduction in negative appraisal over the 12-week period, while there was no relationship with other aspects of self-reported cognitive coping (e.g., positive self-talk or

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problem focused coping strategies). This finding suggests that lower systemic inflammation may be a direct result of reductions in self-blaming, and negative, catastrophic, and perfectionistic thinking all of which are characteristic of individuals who score lower on the Negative Appraisal coping scale (Nowack, 1990).

A growing body of evidence has established the involvement of inflammation in a variety of illnesses and diseases. This multiple case study focused on the proinflammatory cytokine interleukin-6 (IL-6) which is involved in arthritis, osteoporosis, Alzheimer's disease, Type II diabetes, some cancers, cardiovascular disease, and cognitive decline (Kiecolt-Glaser, 2009). Of great importance is that anxiety, depression, and negative affect have been found to be significant factors in contributing to the production of pro-inflammatory cytokines (Kiecolt-Glaser et al., 2005). Self-directed stress management interventions like the one used in this study may be a strategy to help moderate the impact of acute and chronic stressors on pro-inflammatory processes that are associated with physical health and well-being.

Self-directed and Internet based interventions have shown utility for a variety of health conditions and behaviors (Tate, Finkelstein, Khavjou, and Gustafson, 2009). For example, effect sizes reported in meta-analytic studies of Internet interventions are consistently larger than those found in the control groups, and typically range from -0.01 to 0.75 (Tate et al., 2009). These findings add support for the cost effectiveness and efficacy of self-directed interventions for facilitating changes in physical and psychological health. Even if self-directed programs are found to be slightly less effective than traditional intervention modalities, the cost effectiveness and simplicity of this type of intervention can still play an important role in facilitating health changes. Ultimately, additional research will be needed to determine the cost effectiveness of such self-directed and web-based interventions compared to traditional therapy modalities.

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As Kiecolt-Glaser argues, the possible intersection of stress, depression, diet and immune function opens the door for considering diverse interventions aimed at influencing overall lifestyle practices and stress management (Kiecolt-Glaser, 2009). Future research will be required to validate our finding of enhanced health habits and determine whether these types of hypnotic suggestions are also correlated with other preventive lifestyle practices and behaviors.

Limitations

Despite finding preliminary support for the two hypotheses detailed within this study, there are several inherent limitations to this multiple case study. Without randomized control groups (e.g., non-hypnosis stress management CD and non-intervention CD) and post-treatment measures, generalization of results beyond the scope of the current multiple case study are limited.

Interestingly, there was not a significant difference between multiple subjects' pre-test and post-test self-reported overall work/life stress scores although self-reported stress did decrease for study participants. Since decrements in IL-6 are correlated with reduced stress levels in prior research (e.g., Kiecolt-Glaser et al., 2005), it is somewhat unclear as to the exact mechanism in which the intervention led to changes in these serum levels beyond changes in cognitive coping strategies. It is possible that the self-reported stress measures employed in this study were not sensitive enough to detect changes in a normal and healthy population. Additionally, it is not possible to determine whether the reductions in inflammation, although statistically significant, are clinically meaningful and confer some increased resistance to actual illness and disease over time. Future longitudinal research, using both physical and

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psychological health measures, should be planned to explore the clinical significance of IL-6 reductions with diverse physical and psychological health outcomes.

Another limitation was the small sample size available in this study. The study size may have also lowered the probability of finding differences in perceived stress levels, in that the effect size might have been too small to be significant. With a larger sample size, the difference in perceived stress levels might have been more obvious given the brief measure used in this study has been shown to be a reliable measure of work/life stress (Nowack, 1990). Yet despite the small sample size, the effect sizes for the other self-reported measures and serum IL-6 levels were much more evident (Table 1)

Although screening on underlying medical conditions was used, it was entirely self-report so it is possible that more clinical conditions, infections or other diseases unknown to the subjects might have affected both baseline and follow-up serum IL-6. Unfortunately, no other existing medical information other than self-report was available for the subjects of this pilot study. In summary, since no formal randomized control group was available for this multiple case study, it is not possible to conclusively suggest that the hypnosis intervention alone resulted in the changes observed in the dependent variables despite post IL-6 scores of the participating subjects being significantly lower than the initial cytokine scores of the 5 subjects unable to continue with the study.

Implications and future directions

Despite the obvious research limitations afore mentioned, Kazdin (1982), as discussed previously, asserts that multiple case studies make it possible to draw valid inferences with respect to the impact of the study's treatment intervention., Therefore, the results of the present

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multiple case study may be suggestive of some possible short-term beneficial effects from just a 12-week self-administered hypnosis intervention.

Future studies may want to evaluate when is the best time to listen to a stress reduction CD. In this multiple case study, subjects were instructed to listen to the CD at bedtime and in the morning. It is possible, that there may be differences between these listening times, with one being superior to the other (e.g., before bed at night). It would also be useful to compare the benefits derived from subjects experiencing hypnosis directly from an experienced practitioner to those delivered on a CD program like the current study. Since the CD hypnosis is more expedient and inexpensive, it would be very edifying to learn that CD hypnosis is comparable to a therapist administered hypnotic intervention. Furthermore, verification of usage patterns of the hypnosis CD may contribute with knowledge about how self-administered interventions could be improved.

CONCLUSIONS

The results of this multiple case study with normally coping and functioning adults provide some limited support for a self-administered stress reduction hypnosis program's potential for reconditioning the stress response. In this multiple case study, subjects' objective measures revealed a decrement in IL-6, and improvements in subjective measures of cognitive appraisal coping and health behaviors in the face of work and life stress. Despite some design limitations, this multiple case study provides some promising suggestive evidence that a self-administered stress reduction program that is simplistic and time efficient may be a clinically effective tool for modifying the stress response. This multiple case study also corroborates the observation found in the clinical setting where patients can report little or no improvements in

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their stress levels, yet experience significant improvements in other areas of their lives, such as physical symptoms and improved life choices. Since there is such a low adherence to stress management strategies, a self-administered stress reduction program such as this may offer a solution to those who are reluctant to devote time to stress reduction methods. Finally, this multiple case study provides a useful model to replicate for future research using a randomized control group to extend and expand upon these findings

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Table 1

Means, standard deviations, and intercorrelations between variables Time 1 Versus Time 2

	Time 1		Time 2		Effect Size
	Mean	SD	Mean	SD	
1. IL-6	1.01	.55	.68	.21	.61
2. Stress	17.67	4.09	15.33	1.94	.57
3. Health Habits	93.67	10.97	98.44	10.69	.44
4. Exercise	12.11	3.02	11.55	3.47	.19
5. Eating/Nutrition	29.0	3.04	31.89	4.04	.94
6. Positive Appraisal	15.44	1.74	16.44	2.29	.57
7. Negative Appraisal	14.00	3.00	12.10	2.08	.63
8. Threat Minimization	14.56	1.74	15.33	1.08	.45
9. Problem Focused Coping	16.89	2.02	17.11	1.83	.48
10. Social Support	50.33	4.92	51.44	6.44	.23
11. Psychological Well-Being	41.0	5.83	42.22	4.89	.21

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Table 2

Summary of Step-Wise Hierarchical Regression Analysis for Time 1 Variables Predicting Change in IL-6 (N=11)

		IL-6			
Variable	<i>B</i>	SE	B	R ² Change	
Eating Habits	-.08	.02	-.79*	.63	
Threat Minimization	-.11	.18	-.66*	.15	

* $p < .01$. *

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Table 3

Paired Sample Tests

Variable	Mean Difference	df	<i>t</i>
IL6	0.33	10	2.48*
Stress	2.33	8	1.61
Health Habits	4.78	8	1.88
Eating	2.89	8	3.93**
Social Support	1.11	8	1.61
Positive Appraisal	1.00	8	1.50
Negative Appraisal	1.89	8	3.09**
Threat Minimization	0.78	8	1.36
Problem Focused Coping	0.38	8	0.38
Psychological Well Being	0.22	8	0.75

* $p < .05$; ** $p < .01$