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SELF-HYPNOSIS AND EXAM STRESS: COMPARING IMMUNE AND RELAXATION-RELATED IMAGERY FOR INFLUENCES ON IMMUNITY, HEALTH AND MOOD

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Abstract

The effects of self-hypnosis training on immune function, mood and health at exam time in medical schools were examined, comparing instructions of enhanced immune function with relaxation, whereas instructions of increased energy, alterness, concentration and happiness were common to both procedures. Training consisted of three weekly group sessions, with unrestricted home practice with an audiocassette. Immune assays involved CD3, CD4, CD8, CD19 lymphocytes, CD56 natural killer (NK) cells and blood cortisol. Students receiving immune-related imagery reported fewer viral illnesses, such as colds and influenza, during the exam period. Immune-related imagery was also more successful than relaxation imagery in buffering decline in total lymphocytes and subsets. Independent of instructions, hypnosis buffered the decline in CD8 cytotoxic T-cells observed in control subjects, an effect associated with hypnotic susceptibility (Harvard group scale). Evidence of a buffering effect on NK cells could not be replicated, which may have been confounded by generalized stressors. As found previously, dissociations between negative mood and raised cortisol followed hypnosis training. These findings along with a contemporaneous one with patients with herpes — preliminary due to the small scale of the study — demonstrate for the first time that there are benefits for reported illness as a result of a psychological intervention shown to strengthen the immune system and improve well-being. The benefits of self-hypnosis encourage investment in large-scale illness prevention studies and controlled clinical applications.

Key words: health, imagery, immunity, mood, self-hypnosis, stress

Introduction

The aim of this work was to replicate a study where self-hypnosis training before medical school examinations buffered the effects of stress on cellular immune parameters, including NK cells and CD8 T-cells and the CD8/4 ratio, when compared with a non-intervention control group (Gruzelier, Clow, Evans, Lazar and Walker, 1998; Gruzelier, Smith, Nagy and Henderson, 2001). Energy levels monitored by self-ratings were also preferentially raised by self-hypnosis training, and increases in calmness following hypnosis training correlated with increases in CD4 T-lymphocytes. After hypnosis, an unexpected result was a dissociation between negative

aspects of affect, such as tension and tiredness, and cortisol, commonly regarded as a stress hormone (Evans, Hucklebridge and Clow, 2000). Attempts to validate the implications of the immune findings by monitoring the health of students at examination time were thwarted by the generally excellent health of the students. This necessary validating step has so far been lacking in the developing field of psychoneuro-immunology.

Following the delineation of pathways between the central nervous system and the immune system allowing mutual influences (Ader, Felten and Cohen, 1991; Leonard and Miller, 1995; Evans et al., 2000), there have been many demonstrations of immune compromise in association with disease, stress and negative affect (O'Leary, 1990; Ader et al., 1991; Bennett Herbert and Cohen, 1993; Leonard and Miller, 19995; Evans et al., 2000). Alleviation of stress and improvement in health by psychological therapies have been reported, as well as up-regulation of immune function coincident with psychological intervention. Thus far, the essential step combining all these aspects has not been demonstrated; in other words, a psychological therapy that strengthens immune competence and which coincides with improvements in health. This final validating step is essential. As the immune system is a complex, tightly integrated system full of checks and balances, measures of immune parameters in the absence of measures of health remain ambiguous markers.

Another aim of the present study was to compare two different types of suggested hypnotic imagery. There is provocative evidence that beneficial influences on the immune system have more often followed training evoking active imagery about the immune system rather than following conventional relaxation imagery. In the majority of reports, relaxation has been induced through mixed intervention packages aiming to induce a relaxed and passive attitude in the participant (Kiecolt-Glaser, Garner, Speicher, Penn, Holliday and Glaser, 1985; McGrady, Conran, Dickey, Garman, Farris and Schurmann-Brzezinski, 1992; Johnson, Walker, Heys, Whiting and Eremin, 1996). Although there is extensive and important evidence from uncontrolled studies (Simonton, Matthews-Simonten and Creighton, 1997), fewer controlled studies have examined training that targets imagery of the immune system. This requires an active and alert cognitive attitude of the participant who, at the same time, maintains a state of physical relaxation (Olness, Culbert and Den, 1989; Rider, Achterberg, Lawlis, Govern, Toledo and Butler, 1990; Gregerson, Roberts and Amiri, 1996; Richardson, Post-White, Grimm, Moye, Singletary and Justice, 1997). Superior health and immune function was predicted in those students receiving training in immune-related imagery compared with students receiving relaxation imagery, and in those students receiving hypnosis compared with a non-intervention control group.

Method

Subjects

Thirty-one volunteer pre-clinical medical students (19 males, 12 females; mean age 19.1 years) gave written consent to participate in a study approved by the hospital ethics committee. None suffered from any chronic illness or took medication known to influence immunity. They were all nïave to hypnosis. Hypnotic susceptibility was assessed with the *Harvard Group Scale of Hypnotic Susceptibility*, Form A (Shor and Orne, 1962). A potentially confounding factor is that the effects of exam stress, although representing an ecologically valid stressor compared with the artificiality of

laboratory stressors, may be masked by other less well-recognized stressors such as adaptation to university life (Baker, Irani, Byrom, Nagvekar, Wood, Hobbs and Brewerton, 1985; Kiecolt-Glaser, Glaser, Strain, Stout, Tarr, Holliday and Speicher, 1986; Whitehouse, Dinges, Orne, Keller, Bates, Bauer, Morahan, Haupt, Carlin, Bloom, Zaugg and Orne, 1996). Although the majority of subjects recruited were second-year students (n=21), sufficient first-year students (n =10) were accepted to allow stratification of year of admission to medical school for some aspects of the study design.

Subjects were assigned to a control group (n =9), immune imagery group (n =11) or relaxation imagery group (n =11), balanced for hypnotic susceptibility, sex and year of admission to medical school. First-year students were distributed as follows:

- Control subjects, 3.
- Immune imagery group, 3.
- Relaxation imagery group, 4.

There were three females in each group. The groups did not differ in hypnotic susceptibility scores; mean hypnotic susceptibility scores were 7.33, 6.9 and 8.3, respectively.

Immune assays

Three vacutaner tubes of blood were taken from each subject, between 12.30 pm and 2.00 pm, to control for diurnal effects on cortisol. Flow cytometry analysis: total white blood cell and lymphocyte counts were assessed by use of a Coulter model T-540 haematology analyser. The lymphocytes included:

- CD3, which is a protein involved in adhesion between lymphoid cells, in particular T-cells and natural killer (NK) cells, and is up-regulated when T-cells are activated.
- CD4 T-helper cells.
- CD8 T-cytotoxic and T-suppressor cells.
- CD19 a B-lymphocyte which produces antibodies.
- CD56 NK cells.

Monoclonoal antibodies against the lymphocyte markers were obtained from Coulter Electronics (Beford). Ten µl of appropriate antibody was added to 100 µl EDTA whole blood. Samples were then left for 15 minutes before being lysed, buffered and fixed using the Coulter Q-prep system. Samples were then analysed on a Coulter EPICS profile II flow cytometer. Results were expressed as cells/µl. Blood cortisol was also assayed with the ELISA procedure. The lymphocyte measures were assayed as one batch (both conditions) by the same experimentally blind assistant under the supervision of one of the researchers (DH). Analyses of three control subjects and all functional NK cell cytotoxicity data (methods not described) were abandoned due to an outbreak of mycoplasma infection in the laboratory.

Self-report questionnaire

The number of hours' weekly exercise was surveyed in view of the influence of exercise on some immune parameters in the previous investigation. Here, statistical analysis indicated that exercise was not a moderating factor and it is not considered

further. A health checklist, including physical illnesses such as coughs/colds/'flu, increased allergies, increased incidence of asthma attacks, psoriasis, etc., covered the training period, the examination period and the subsequent three weeks' vacation. Emotional state at the time of the blood draw (a mild stress) was assessed by scales of tension, calmness, energy and tiredness (Thayer, 1976) administered before each blood draw.

Study design and analysis

The first session consisted of the assessment of hypnotic susceptibility, followed by a group assignment. Those in the two hypnosis groups all attended three weekly group sessions of hypnosis with one of the researchers (JW), one session per week for each group. After the first of these, subjects were given audiocassettes with which to practise hypnosis at home for a minimum of three sessions per week, giving a minimum of 10 sessions of hypnosis in all. Subjects were also instructed to keep practice diaries. The groups did not differ in the frequency of practice sessions: immne group mean 9.5 sessions; relaxation group mean 9.0 sessions. All subjects attended for a blood draw and completion of the mood scale at baseline and during the examination period, which was held in the last week of term. All blood draws were taken at the same time of day by an experienced phlebotomist (JL).

The hypnotic induction began with standard instructions involving visual fixation and eye closure followed by relaxation and deepening suggestions. In the immune imagery group instructions followed which aimed at improving immune function. This involved envisaging increases in NK cells and lymphocytes and surveillance by white blood cells in the form of sharks or dolphins devouring germ cells. In the relaxation group these dynamics were replaced by instructions of peace, happiness and tranquility. After this, both groups received hypnosis instructions to mobilize resources by increasing alertness, energy and concentration. A transcription of the instructions (which lasted 20 minutes) is available from the authors.

Statistics

The groups were compared with repeated-measures analysis of variance (ANOVA) combined with planned comparisons with Student's *t*-tests (paired and unpaired, as appropriate) to compare differences between pairs of means on immune and mood parameters. A chi-squared test was used for examining the consistency of effects for individuals within groups and to compare groups for health status. The main predictions were, first, should students succumb to illness around the examination period this was less likely to occur in those with training in immune-related hypnotic imagery. Second, there would be preferential effects in buffering the effects of stress on immune function with the hypnotic immune imagery. Similarly, there would be beneficial effects of hypnosis on mood, in particular energy, in the case of the immune imagery. Correlations were examined with the Pearson's *r* method, notably to replicate the previous evidence of a dissociation of the negative effects of cortisol following hypnosis training.

Results

Effect of hypnosis on health

Thirteen students succumbed to illness around the examination period. Their group membership is shown in Figure 1. Importantly, only 2/11 (18%) of subjects in the

immune imagery group fell ill (exact probability, $p<0.065$) compared with 6/9 (67%) of control subjects and 5/10 (50%) of the relaxation imagery group. The difference between the immune imagery and control groups was highly significant (chi-square test (19)= 12.7; $p<0.001$).

Effect of hypnosis on immune function

Means and standard deviations (SDs) for the various immune parameters at baseline and post-treatment are shown in Table 1 for the three experimental groups, with a combined hypnosis group (active imagery plus relaxation). There was clear evidence of immune compromise in lymphocyte numbers at examination time in the group as a whole.

Effect of hypnosis independent of imagery on immune function

Decline in lymphocyte numbers with examination stress was confirmed in repeated-measures ANOVAs with two groups (hypnosis and control subjects) and two sessions (baseline and examinations). There was a main effect of session, indicative of a highly significant decline for the group as a whole, in the analysis of total lymphocytes ($F(1,25) = 271.84$; $p<0.0001$), whereas many reductions in lymphocyte subsets were also highly significant, such as those in CD8 cells ($F(1,25) = 19.43$; $p<0.0001$) and CD3 cells ($F(1,25) = 11.78$; $p<0.002$), to a lesser extent in CD4 cells ($F(1,25) = 5.52$; $p<0.027$) and approaching significance for CD19 cells ($F(1,25) = 2.89$; $p<0.10$). There was a mean decline in NK cells which did not reach significance ($p<0.133$), and there was no consistent change in cortisol with 12 subjects showing a reduction with examination stress.

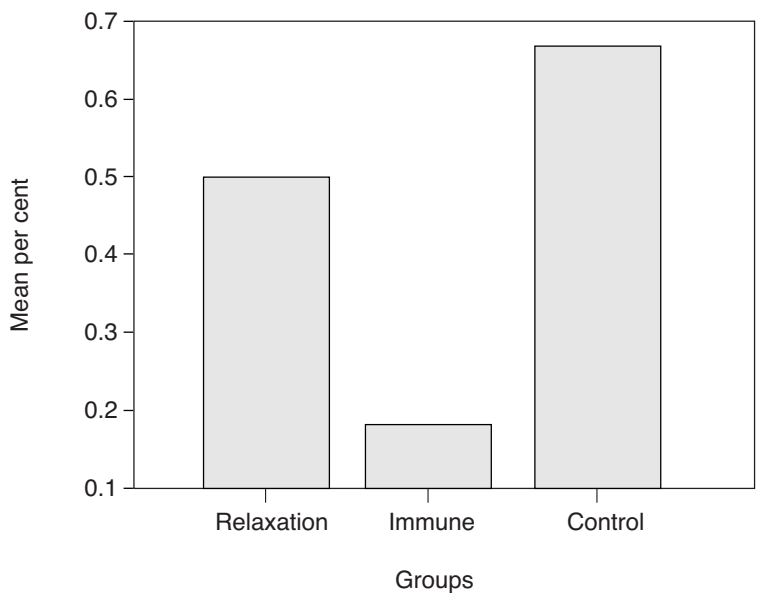

Figure 1. Percentages of students falling ill during the examination and post-examination periods in the three experimental groups. The difference between the immune and control groups was highly significant ($p<0.001$).

Table 1. Mean (SD) baseline and examination levels of immune parameters for the three groups and the combined hypnosis group

		Control		Immune		Relaxation		Combined hypnosis	
		Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
CD8 cells µl	Baseline	56.00	(155.0)	423.3	(183.2)	505.9	(126.4)	463.0	(161.0)
	Exam	450.0	(93.0)	389.6	(117.7)	422.2	(100.2)	415.0	(110.0)
CD8% cells µl	Baseline	29.5	(5.9)	23.9	(7.3)	24.9	(4.2)	4.4	(5.9)
	Exam	27.4	(4.0)	23.5	(6.3)	26.5	(2.7)	24.9	(5.1)
CD4 cells µl	Baseline	682.3	(265.9)	685.6	(152.4)	757.7	(189.9)	719.9	(170.9)
	Exam	628.8	(181.5)	654.4	(160.5)	641.4	(169.3)	648.2	(160.7)
NK cells µl	Baseline	285.0	(137.2)	223.4	(94.5)	264.2	(163.2)	242.8	(129.9)
	Exam	230.8	(109.1)	215.7	(72.3)	232.7	(125.9)	223.8	(99.1)
CD3 cells µl	Baseline	1374.7	(382.1)	1226.9	(305.8)	1419.8	(298.3)	1318.8	(306.8)
	Exam	1189.7	(264.4)	1164.7	(231.8)	1221.5	(258.8)	1191.8	(240.6)
CD19 cells µl	Baseline	272.5	(88.8)	308.9	(157.8)	330.2	(158.7)	319.1	(154.6)
	Exam	234.3	(64.2)	286.9	(103.1)	206.3	(73.2)	248.5	(97.1)
Total cells µl	Baseline	1951.5	(553.8)	1771.2	(449.8)	2029.2	(400.9)	1894.2	(436.9)
	Exam	1688.7	(672.5)	1687.5	(332.0)	1663.8	(329.8)	1676.2	(322.8)
Cortisol (nmol/l)	Baseline	284.4	(97.3)	252.1	(92.0)	208.6	(39.6)	231.4	(73.7)
	Exam	288.6	(86.5)	232.4	(123.8)	239.6	(59.2)	235.8	(96.2)

SD = Standard deviation.

Considering the influence of hypnosis independent of hypnotic imagery, the decline in CD8 cytotoxic T-cells was buffered with hypnosis, as may be seen from the mean results in Table 1. A group × session effect approached significance for CD8 numbers ($F(1,25) = 3.21$; $p<0.08$) and reached significance when expressed as a percentage of total lymphocytes (group × session, $F(1,25) = 4.50$; $p<0.044$), shown in Figure 2. The group difference was consistent across individuals (chi-square test (3) = 13.15; $p<0.004$), despite wide individual variation in baseline and examination values. There were no group main effects, and consistent with this, no systematic differences between the groups at baseline. Only in the case of CD8% did an effect approach significance (Student's *t*-test (25), $p<0.07$); as this was in a direction which disadvantaged the hypnosis group it did not detract from the buffering effect of hypnosis.

Effect of hypnotic imagery on immune function

In Figure 3, baseline hypnosis lymphocyte change scores are shown for the two types of hypnotic imagery. There were noteworthy differences, in line with hypotheses, in their efficacy in maintaining lymphocyte levels in the face of examination stress, as shown by group × session interactions ($F(19) >2.56$; $p<0.03–0.06$). There was an exception in the case of CD8 counts ($F = 0.68$, NS) which had shown in the analysis above an advantage of hypnosis *per se*. All differential effects advantaged immune-related imagery as confirmed by paired Student's *t*-tests within groups between the baseline and examination counts. Thus, relaxation imagery failed to halt the stress-induced decline in total lymphocytes and in the lymphocyte subsets (DFs all = 9):

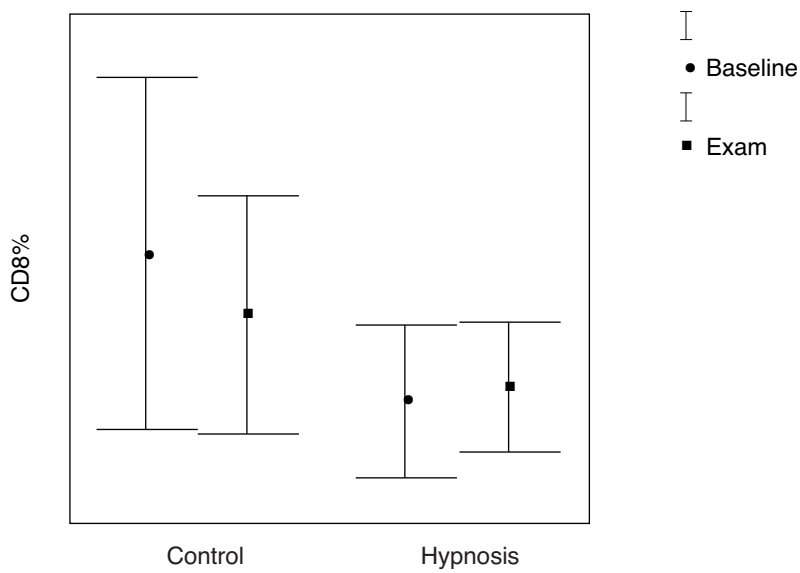

Figure 2. Baseline and examination means and standard errors (SEs) of CD8 cells showing a decline in control subjects and the buffering of hypnosis (group × session; p<0.04; chi-square test, $p<0.004$). Baseline levels advantaged the control group at a level approaching significance ($p<0.07$).

- Total lymphocytes, Student's *t*-test = 3.41; $p<0.008$.
- CD3, Student's *t*-test = 3.43; $p<0.007$.
- CD4, Student's *t*-test = 3.40; $p<0.008$.
- CD8, Student's *t*-test = 2.69; $p<0.025$.
- CD19, Student's *t*-test = 2.36; $p<0.042$.

Immune imagery buffered decline in all lymphocytes (Student's *t*-test (10) <1.24). There were no significant changes in NK cells or cortisol (TS<0.94).

In all those who fell ill there was a greater decline in CD4 counts (baseline mean 706.2, SD 231.3; examination mean 586.9, SD 161.3; Student's *t*-test (12) = 3.03; $p<0.01$), whereas in students remaining well the decline was not significant (baseline mean 720.5, SD 177.4; examination mean 679.6, SD 160.7; Student's *t*-test (17) = 1.53; $p<0.15$). The group × session effect approached significance ($F(1,28) = 2.83$; $p<0.08$). There were no other distinguishing features of immune function.

Effect of hypnosis on mood

Of the four Thayer (1967) activation mood scales — calmness, tension, tiredness, energy — repeated-measures ANOVAs disclosed only one examination main effect. Subjects rated themselves less calm at examination time (baseline mean 13.3; examination mean 10.38; $F(1,29) = 17.25$; $p<0.001$), irrespective of hypnotic instructions ($F = 0.253$). The only impact hypnosis had on mood was found in energy ratings. There was an increase in energy ratings following hypnosis (baseline mean 10.61; examination mean 12.11) and a decrease in control subjects (baseline mean 10.40; examination mean 7.40), although the differential group effects were not representative of all subjects

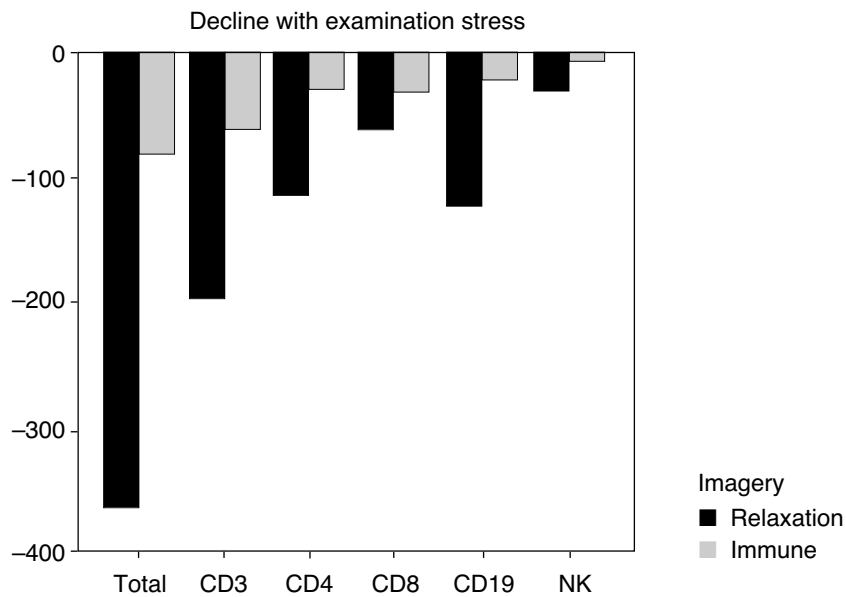

Figure 3. Mean declines with examination stress in the various lymphocytes, total lymphocytes and cortisol for the two hypnosis groups showing the greater compromise in the relaxation imagery group (Student's *t*-test >2.36; $p<0.008$–0.04) compared with the immune imagery group (Student's *t*-test <0.94, NS).

(group × session; $p<0.13$). Energy at examination time was negatively correlated with both tiredness (Pearson's $r = -0.499$; $p<0.035$) and calmness (Pearson's $r = 0.495$; $p<0.037$).

Effect of hypnotic susceptibility on immune function

A small differential effect in buffering the decline in CD8 cells was disclosed when comparing subjects with high and low hypnotic susceptibility ($F(1,19) = 4.53$; $p<0.05$). This was in keeping with the results showing beneficial effects of hypnosis training on this parameter that were independent of imagery. Hypnosis subjects were subdivided according to susceptibility scores (high score >7). CD8% tended to increase in highly susceptible subjects (baseline mean 24.2; examination mean 25.5; Student's *t*-test (13) = 1.99; $p<0.07$), whereas low-susceptible subjects showed a non-significant decrease (baseline mean 24.7; examination mean 23.9; Student's *t*-test = 1.2; NS). In order of magnitude, this was a small effect, but it was supported by a correlation between change in CD8% and hypnotic susceptibility which approached significance (Pearson's $r = 0.395$; $p<0.08$). Further correlations were made for exploratory purposes but no relations with changes in immune parameters were disclosed.

Individual variations in cortisol

Correlations between cortisol and the two scales of negative affect — tension and tiredness — were examined before and after hypnosis training in the combined hypnosis group. Whereas tiredness correlated with baseline cortisol (Pearson's $r = 0.40$; $p<0.049$, one-tailed), there was a negative correlation between the changes in cortisol and tiredness following hypnosis (Pearson's $r = -0.44$; $p<0.07$). In other words, here, the relation following hypnosis training between cortisol and negative affect went beyond dissociation to an actual reversal. Consistent with this, increases in tiredness following hypnosis training were associated with decreases not increases in cortisol.

In order to elucidate the individual variation in the effect of examination stress on cortisol, the 10 subjects in the hypnosis group who showed a decline in cortisol were compared with the eight subjects who showed an increase in cortisol for relations to the mood scales. In support of stress raising cortisol, those students characterized by the increase in cortisol had higher levels of tension at baseline (mean tension 9.38, SD 2.9) compared with those with a decline in cortisol (mean tension 6.7, SD 1.50; Student's *t*-test (16) = 2.56; $p<0.02$).

Adaptation to medical school

In view of implications that differences in adaptation to medical school life, according to year of admission, may mask the impact of examinations, comparisons were made between first-year ($n=8$) and second-year ($n=19$) students, who incidentally did not differ in hypnotic susceptibility, frequency of practice or mood ratings at baseline or examination assessments. When examining mood ratings a tendency was found for tension to increase with examinations in first-year students (mean 3.5, SD 4.4), but to remain unchanged in second-year students (mean 0.33, SD 3.6; Student's *t*-test (21) = 1.86; $p<0.08$).

Regarding NK cell changes, the results provided support for the implied immunosuppression in first-year students in the reports of others. Here, first-year students showed evidence of immune suppression ($F(1.25) = 4.93$; $p<0.036$), which was accentuated at the baseline which was closer to the beginning of the academic year (Student's *t*-test (25) = 4.02; $p<0.0005$). Differential changes with examinations were

seen between first- and second-year students ($F(25) = 7.68$; $p<0.01$). In first-year students NK cell numbers rose non-significantly (baseline mean 731.7, SD 190.2; examination mean 648.3, SD 147.7; Student's *t*-test = 1.20), whereas in second-year students they declined (baseline mean 714.0, SD 167.7; examination mean 648.14, SD 172.2; Student's *t*-test (18) = 3.15; $p<0.005$).

Discussion

The demonstrable immunosuppression that accompanied the stress of examinations in students has been widely documented before (Kiecolt-Glaser et al., 1985; Glaser, Rice, Sheridan, Fertel, Stout, Speicher, Pinsky, Koyur, Post and Beck, 1987; Halvorsen and Vassend, 1987; Deinzer and Schuller, 1998). As a corollary, the health of 13 students was found to suffer during the examination and post-examination period. Only two students (18%) in the immune imagery group became ill around the examination period compared with six of the control subjects (67%) and five (50%) of the relaxation imagery group. The advantage to the immune imagery group when compared with the control subjects was highly significant ($p<0.001$). Furthermore, the incidence of ill health in those having relaxation imagery was more than double the incidence in those with immune imagery. Evidence for advantageous influences on health, as distinct from immune function and/or mood, has been lacking in the field. This finding has now been supported by a contemporaneous study using the same hypnotic induction protocol where patients with chronic and virulent herpes simplex virus-2 saw a 48% improvement in rate of recurrence as a result of six weeks' self-hypnosis training (Fox, Henderson, Barton, Champion, Rollin, Catalan, McCormack and Gruzelier, 1999).

In corroboration with the advantage to student health from the hypnotic immune imagery was the evidence that the buffering of lymphocyte compromise was specific to immune imagery. This extended to the full range of lymphocyte subsets assayed, including CD4 counts whose decline was found to be associated with health status. Advantages for immune function of immune imagery confirmed earlier reports (Gregerson et al., 1996; Richardson et al., 1997). Among the earliest, Olness et al. (1989) had reported that immune up-regulation measured by salivary IgA only occurred in children given specific immune-related imagery, in contrast to those given non-specific relaxation imagery whose immunity was no different from a no-intervention control group.

The CD4 helper T-cell lymphocyte that distinguished the students who avoided illness compared with those who succumbed to illness is involved in cytokine production, at the heart of immunoregulation. CD4 lymphocytes are less influenced by acute stress-mediated sympathetic activity, and tend to be depleted more as a result of chronic stess (Evans et al., 2000). Compared with other lymphocyte subsets they are particularly depleted with HIV infection (Catalan, Burges and Klimes, 1995). Their depletion has been associated with prolonged negative affect (O'Leary, 1990), and conversely, their elevation may be associated with positive affect.

Hypnosis training with students also provided some benefits independent of type of imagery. This was disclosed by an absence of stress-induced compromise in those receiving hypnosis when compared with the non-intervention control group in CD8 cytotoxic T-cells. These cells play a role in immunosurveillance. CD8 cells are released into the peripheral circulation at times of stress through sympathetic innervation of lymphoid organs (Evans et al., 2000). This advantage to hypnosis in general

was validated by comparison between subjects with high and low hypnotic susceptibility which showed differential effects solely on CD8 cells in the form of increases in highly susceptible subjects and decreases in subjects with low hypnotic susceptibility. The importance of CD8 lymphocytes was also seen in the original study where, among lymphocytes, only the decline in CD8 cells was buffered by self-hypnosis training along with NK cell counts, though on that occasion there was no relation with hypnotic susceptibility. In order of magnitude, these effects were small.

However, in comparison with the original study, among lymphocytes, only CD8 T-cell counts held up, the stress-buffering influence of hypnotic immune imagery was more extensive in terms of the impact on the lymphocyte subsets, which encompassed the full range of T-cell (CD3, CD4 and CD8) and B-cell (CD19) lymphocytes assayed. Aside from CD4 and CD8 cells already mentioned, this included CD3 cells which activate NK cells and macrophages, and a B-cell surface marker (CD19), B-cells being a source of antibodies involved in humoral immunity.

In the original study, hypnosis also buffered the decline in NK cell numbers; indeed, this was the stronger of the effects ($p<0.008$) which, with elevation of CD8 T-cells, is part of a typical immune response stress profile (Evans et al., 2000). However, enumerative estimates of NK cells have sometimes proved difficult to interpret in hypnosis studies which have involved first-year medical students (Kiecolt-Glaser et al., 1985; Whitehouse et al., 1996). In support of this inference, comparisons of first-year with second-year students indicated that immunosuppression in first-year students may well mask the effects of the examination stressor due to immunosuppressed baselines. However, it was not clear why the decline in NK cells in the second-year students was not buffered by self-hypnosis training as it was in the original study. Functional assays, had they not suffered attrition, may have helped to elucidate this.

In the previous study, aside from the buffering effect of hypnosis on NK cells and CD8 cells, there was an increase in cortisol. This appeared to be more than accidental, manifesting as it did as part of an integrated pattern of examination–baseline change scores together with NK cell and CD8 cell parameters. The present results further support what was seemingly a paradoxical increase in cortisol, for here too the conventional associations between cortisol and negative affect were no longer in evidence following self-hypnosis training. In fact, they went beyond an absent relation, suggestive of dissociation, going as far as reversal of the common association. Speculatively, it may be that hypnotic instructions to mobilize resources that were common to the various induction procedures, were apposite: cortisol plays an essential role in maintaining normal metabolism, a function sometimes lost sight of in psycho-neuro-immunological investigations. Consider, for example, the nadir in cortisol level reached towards the later stages of sleep, followed by the surge in cortisol on normal and habitual re-awakening and resumption of daily activity (Hucklebridge, Clow and Evans, 1998). The higher energy ratings following hypnosis is in keeping with an energy mobilization interpretation.

Mobilization in the form of cognitive activation relates to our favoured interpretation of the preferential effects of immune-related hypnotic imagery on the immune system. Attributing this to the power of suggestion is unlikely, as both hypnosis approaches were believed to be beneficial, as they proved to be in different ways. Individual differences in cognitive activation, a personality dimension, proved to be predictive of increases in lymphocyte counts and both NK cell counts and functional activity in the previous study with medical students and a concurrent study with patients with herpes simplex virus-2 (Gruzelier et al., 1998; Gruzelier et al., 2001). In

other contexts, a fighting spirit and action-oriented approaches have been beneficial in diseases which involve immune compromise (Greer, 1983; LaPierre, Antoni, Schneiderman, Ironson et al., 1990). On this basis, one possible explanation is that the greater alert cognitive involvement in the hypnotic protocol with immune imagery, which was required for conjuring up and generating images of adversarial dynamics in the battle against invaders of the body, was fundamental to the preferential effects of the immune directed imagery over passive relaxation imagery. It is also the case that, at a mechanistic level, there is a compelling commonality between left hemispheric versus right hemispheric underpinning in:

- Approach/cognitive activation versus withdrawal behaviour.
- The expression of positive versus negative affect.
- Immune up- versus down-regulation (Gruzelier, 1989; Evans et al., 2000; Gruzelier et al., 2001).

In conclusion, the two main contributions of the present study were the demonstration of less reported illness at examination time of the students receiving self-hypnosis with immune imagery, and the preferential effects of immune imagery when compared with relaxation imagery on T- and B-lymphocytes. The field of psychological intervention studies and immunity has been characterized by small-scale studies, done on a shoestring, with a small selection of immune parameters, seldom assayed more than twice, and without long-term follow-up. The present study is no exception. Despite these limitations, these preliminary results are not without interest. In a general sense they support earlier investigations showing the value of self-hypnosis training in moderating stressful influences on the immune system. They also contribute to the small literature showing that in some respects guided imagery evoking advantageous interactions within the immune system may have benefits beyond imagery that evokes deep relaxation. Most importantly, these results fill a gap in the literature by demonstrating that health advantages may indeed accompany a psychological intervention which produces changes in immune function in healthy subjects faced with a real life stressor. Until recently, this inference lacked an evidential base; self-hypnosis may play a valuable future role in the prevention of illness.

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