

HYPNOTIZABILITY AND IMMUNOLOGICAL RESPONSE TO PSYCHOLOGICAL INTERVENTION IN HIV

Tannis M. Laidlaw, Ryan Kerstein, Bryan M. Bennett, Akira Naito, Prabudha Dwivedi and John Gruzelier

Imperial College London, UK

Abstract

Objective: This pilot study related hypnotizability to changes in HIV immune blood markers after two psychological interventions.

Design: The mean of two blood assays prior to intervention was compared to the results of the blood assay after the intervention.

Intervention: A course of four weekly 2-hour training sessions coupled with daily self-hypnosis practice was given to 13 participants with diagnosed HIV and for a further 9 participants a similar course was given in a Japanese healing method called Johrei (a total of 22 participants). All were naïve to anti-retroviral medication.

Main outcome measures: CD4+ T cell counts, viral load of the HIV virus in blood.

Results: When highly hypnotizable subjects were compared to those of lower hypnotizability in a repeated measures analysis, their CD4+ t-lymphocyte counts were significantly higher ($p = 0.007$). This was achieved by the highly hypnotizable subjects non-significantly raising their CD4+ counts while the CD4+ counts of the less hypnotizable subjects declined significantly (mean change = -79.4 $p = 0.006$). The differences in CD4+ T cell % of lymphocytes and the viral loads did not differ.

Conclusions: This pilot study indicates that hypnotizability may predict immunological response to psychological interventions in HIV.

Key words: CD4, energy healing, HIV infection, hypnotizability, immune response, self-hypnosis

Introduction

In this preliminary study we investigate the possibility of hypnotizability affecting immunological response to treatment. Participants are a sub-sample of what will be a larger project comparing the efficacy of self-hypnosis training with training in a Japanese method of energy healing on participants with an HIV infection but who have never been prescribed anti-retroviral medication.

Hypnotizability is relatively normally distributed throughout the population. The reason why we posit that this may influence response to treatment, and immunological function in particular, is because of several neuro-psychophysiological considerations. These will be briefly mentioned here and in more detail in the discussion. First, empirical

studies have shown that one of the key determinants of high hypnotizability is cognitive and physiological flexibility (Evans, 1991; Crawford and Gruzelier, 1992). This responsiveness may not only facilitate response to treatment, but also signify a vulnerability to pathology (Gruzelier in press). Second, the balance of activity between the hemispheres, especially anterior hemispheric functions, has been shown to relate to both immune competence and mood valence, such that a left hemispheric dominance both advantages immune function and underpins positive affect, which in turn is advantageous for a healthy immune system (see for review, Gruzelier, 2002a, 2002b). A left lateralized functional asymmetry has on occasion been demonstrated in highly hypnotizable subjects in the everyday state prior to hypnosis (Gruzelier, Brow, Perry, Rhonder and Thomas, 1984; Gruzelier, 1998; Egner, Jamieson and Gruzelier, submitted) and has been theorized to facilitate the induction process. Finally, of particular relevance to the current report, a left hemispheric functional advantage in men at early stages of HIV infection was found to be predictive of higher CD4+ T cell counts up to three years later, whereas those with a right hemispheric advantage had lower CD4+ T cell counts (Gruzelier, Burgess, Baldeweg, Riccio, Hawkins, Stygall, Catt, Irving and Catalan, 1996). For these reasons it follows that high hypnotizability may confer a similar advantage on CD4+ T cell counts, the subject of this report.

HIV is an increasing problem worldwide with nearly 60 000 people in the UK alone harbouring the virus. There is increasing evidence that psychological interventions can prolong the asymptomatic period of HIV infection before the highly effective, but side effect-laden, anti-retroviral medications are deemed necessary (Nott, Vedhara and Spickett, 1995). Response to treatment is variable. The mechanisms are complex. According to theory, one important immunological dynamic in HIV is when the HIV virus attaches itself to an otherwise normal resting CD4+ T cell, so that when the cell transfers back and forth from the blood to the lymph nodes, the cell gets a message to self-destruct and so the CD4+ T cell count declines (Cloyd, Chen, Adegboyega and Wang, 2001). Another mechanism appears to account for the increase in viral load. The resting CD4+ T cells are not replicating the virus, but other activated CD4+ T cells become infected in order to replicate (Korin and Zack, 1998). When inside a cell, the virus is hidden from immune surveillance while the HIV virus replicates itself and further viral particles are released.

When the CD4+ T cell count is below 200, the immune system is deemed unable to handle opportunistic infection, thus putting the person at risk, so that anti-retroviral medication is commenced, usually with good results. This medication is expensive, requires good compliance to prevent drug resistance, and is accompanied by side effects such as nausea, pancreatitis and anaemia. Thus, anything that prolongs the non-medicated period is desirable and advantageous to the person with HIV.

Psychological intervention techniques, which have ranged from relaxation to hypnosis, have been effective in maintaining immune function during a period of stress. Stress and negative affect are well-researched aspects of influences on immunity. Stress disrupts normal physiology in the production of adrenaline, noradrenaline and glucocorticoids (Yang and Glaser, 2003). In a series of studies on medical students in both the UK and the USA, students experiencing stress showed immunosuppression which was buffered by interventions including hypnosis (Kiecolt-Glaser, Glaser, Strain, Stout, Tarr, Holliday and Speicher, 1986; Glaser, Rice, Speicher, Stout and Kiecolt-Glaser, 1986; Gruzelier, Smith, Nagy and Henderson, 2001b; Naito, Laidlaw, Henderson, Farahani, Dwivedi and Gruzelier, 2003). An important component of treatment has been guided imagery, mostly in the context of hypnosis, which has been a technique used clinically with

some research backing for its efficacy (Fox, Henderson, Barton, Champion, Rollin and Catalan, 1999; Gruzelier, Levy, Williams and Henderson, 2001a; Gruzelier, 2002a). In the Gruzelier et al. (2001b) study, groups having immune imagery were directly compared to those having hypnosis without immune imagery and a control group (Gruzelier et al., 2001a). The self-hypnosis intervention group with immune imagery showed continued immune efficacy during exam stress compared to the two other groups.

HIV studies have shown equivocal results in linking HIV progression with stress or depression (Burack, Barrett, Stall, Chesney, Ekstrand and Coates, 1993; Lyketsos, Hoover, Guccione, Senterfitt, Dew and Wesch, 1993; Mayne, Vittinghoff, Chesney, Barrett and Coates, 1996), although one of the leading research groups in the field has found strong evidence for both the connection between HIV progression and stress and its effective treatment (Antoni, Baggett, Ironson, LaPerriere, August, Klimas, Schneiderman and Fletcher, 1991; Antoni, Cruess, Cruess, Lutgendorf, Kumar, Ironson, Klimas, Fletcher and Schneiderman, 2000; Antoni, 2003a, 2003b). Treatments included relaxation, visualization, coping strategies and other cognitive-behavioural stress management techniques.

In the present study there were two interventions: self-hypnosis and the Johrei healing method. Johrei is a Japanese non-touch therapy based upon traditional techniques of laying-on-of-hands or 'channelling' subtle energies (Clarke, 2000). One person 'channels' subtle energies by imagining that they are transmitting healing energy in the form of light to a recipient, who passively accepts the energy. Johrei teaches that both channellers and recipients benefit from this quiet procedure. Practitioners claim medical benefits, and indeed, immunological and psychological benefits have been recorded when this technique was used with non-ill subjects (Laidlaw, Naito, Dwivedi et al., 2003; Naito, Laidlaw, Henderson et al., 2003; Laidlaw, Naito, Dwivedi et al., in press).

Self-hypnosis, on the other hand, has a long history of documented beneficial effects on both non-ill and ill subject samples (Kiecolt-Glaser, Glaser, Shuttleworth et al., 1987; Fox, Henderson, Barton et al., 1999; Gruzelier et al., 2001b; Miller and Cohen, 2001). Self-hypnosis for the HIV participants in the present study included training in immediate and deeper stress relief techniques and they were given audio CDs that contained many different tracks all with immune-enhancing imagery. Some clinical trials have indicated that hypnotizability has some predictive value clinically (Collison, 1975; Fox, Henderson, Barton et al., 1999) and others, little value (Shertzer and Lookingbill, 1987). This leads us to the question as to whether interpersonal differences, like hypnotizability, exert sufficient influence to be detectable in physiological measures in HIV infection. In this preliminary study we found support for this proposition.

Methodology

Participants

Twenty-two participants with HIV infection (3 females, 19 males; mean age 37.0, 27–53 years) agreed to take part in the study. All were naïve to anti-retroviral medication. Their mean CD4+ T cell count before starting training was 414.9, the percentage of lymphocytes that were CD4+ T cell t-cells was 25.5% and their mean viral load was 74 457. Thirteen of the 22 had been trained in self-hypnosis and 9 in Johrei. Ethical approval was obtained and all participants signed informed consent.

Measures

Three related tests were included: the Stanford Hypnotic Clinical Scale (SHCS, $n = 22$; Morgan and Hilgard, 1978); the Jamieson version of the Tellegen Absorption Scale

(J-TAS, $n = 20$; Tellegen and Atkinson, 1974; Jamieson, 1987); and the Creative Imagination Scale (CIS, $n = 17$; Wilson and Barber, 1978).

The SHCS is a standard clinical method of assessing hypnotizability although it has been used in hypnosis research and has a 0.72 correlation with the parent Stanford Susceptibility Scales, considered to be the 'gold standard' of measuring hypnotizability (Morgan and Hilgard, 1978). This is an individually administered test that takes less than half an hour, with ratings that range from 0 to 5. Highly hypnotizable subjects (4, 5) were separated from those of more moderate abilities (0–3) to form two separate groups that could then be compared. The two other scales were included as they often are correlated with hypnotizability scores. Absorption measures the ability to become engrossed, and the CIS measures how vividly a person can use their imagination.

Blood samples were also taken from participants as part of their usual care for the monitoring of their HIV status. Measures included the number of CD4+ T cells (count/_L), their percentage of other lymphocytes, and the viral load of the HIV virus (cRNA/mL).

The interventions learned by the participants included a course of four weekly 2-hour training sessions in self-hypnosis techniques for 13 of them and a similar length training in the Johrei healing method. All participants were asked to practise their technique daily. There were no differences in the groups on any of the measures prior to the intervention, nor were there significant differences between the groups after the intervention learning period. This allowed the groups to be collapsed for further statistical analysis using hypnotizability ratings. The data was analysed using SPSS v11.0 with analyses conducted to a standard 0.05 level of significance.

Results

Raw values of the blood variables for the whole group before and after the intervention period are shown in Table 1. The values were examined using a GLM Repeated Measures analysis. The comparison of CD4+ T cell counts before and after the intervention disclosed a highly significant disparity between those with high compared to lesser hypnotizability ratings (hypnotizability groups \times time, $F = 8.9$, $p = 0.007$, see Figure 1). A Mann-Whitney test confirmed this relationship ($z = 2.5$, $p = 0.01$).

Table 1: Means and standard deviations of the blood variables for HIV+ participants

Participants	Blood variables	Pre-intervention		Post-intervention	
		Mean	(s.d.)	Mean	(s.d.)
Total($n=22$)	CD4+ count	414.9	(151.3)	389.4	(175.5)
	CD4+%/lymph	25.5	(7.8)	24.6	(8.1)
	Viral Load	74456	(95367)	81726	(117786)
Highs ($n=8$)	CD4+ count	393	(98.1)	430.6	(158.5)
	CD4+%/lymph	26.2	(6.9)	26.4	(5.0)
	Viral Load	72961	(84100)	72958	(78097)
Others ($n=14$)	CD4+ count	441.1	(172.5)	361.7	(190.8)
	CD4+%/lymph	26.0	(7.9)	24.6	(9.0)
	Viral Load	77319	(107294)	91003	(140152)

When the hypnotizability groups were analysed separately, the more moderately hypnotizable subjects showed a significant loss in their CD4+ T cell counts over the intervention period ($n = 14$; mean change: -79.4 , $t = 3.3$, $p = 0.006$). In contrast, the highly hypnotizable subjects showed a small non-significant rise in their CD4+ T cell counts ($n = 8$; mean change: 37.6 , $t = 1.25$, $p = ns$).

The results of the same analyses for the CD4+ T cell percentage of lymphocytes and the viral load did not show any significant differences, although the direction of change was consistent with the CD4+ T cell count data (see Table 1).

A Pearson's correlation analysis was carried out between SHCS ratings and the mean CD4+ T cell count. This showed a positive trend ($r = .41$, $p = 0.06$: see Figure 2).

No significant correlations with SHCS were found between the CD4+ T cell percentages or the viral load changes. The J-TAS and the SHCS showed inter-correlations similar to those found in the literature ($n = 19$, $r = 0.35$, $p = ns$) and the CIS correlated with the J-TAS ($n = 15$, $r = 0.45$, $p = 0.09$). However, the CIS and the SHCS were not correlated, nor were there further correlations with the blood variables.

Discussion

This pilot study has provided an indication that hypnotizability does have an influence on immunological responses to psychological interventions. During a period when participants were practising self-hypnosis or Johrei, those with higher hypnotizability maintained their levels of the important diagnostic HIV marker, the CD4+ T cell count, while those with lower hypnotizability ratings saw a significant decline.

The literature contains many examples of the influence of psychological interventions on immunological variables in stressful conditions (Glaser et al., 1986; Kiecolt-Glaser, Glaser, Strain et al., 1986; Kiecolt-Glaser, Glaser, Shuttleworth et al., 1987; Burack, Barrett, Stall et al., 1993; Gruzelier et al., 2001b; Naito, Laidlaw, Henderson et al., 2003). Transferring these results into the clinical sphere has importance for those suffering immunological disease. Specifically, Burack's team (Burack, Barrett, Stall et al., 1993) found that HIV-infected persons suffered higher stress levels than a matched group without HIV infection. Accordingly stress-control psychological interventions appear to have a place in the treatment of HIV. Indeed, self-hypnosis training was found to be highly effective in ameliorating a chronic viral infection, HSV-2, in patients in whom it was not only chronic, but highly virulent; recurrence rate was reduced by half with only six weeks of training (Fox, Henderson, Barton et al., 1999). However, psychological interventions are usually provided to treat psychological symptoms or pain (e.g. Laidlaw and Willett, 2002; Dalton, 2004; van Eijk, Diederiks, Kempen, Honig, Meer and Brenninkmeijer, in press), but are rarely used to treat the disease itself.

Here the results indicate that hypnotizability, which has a long history of predicting response to hypnotic interventions, appears to be a valid personality construct to investigate in HIV treatment and research. A fall in the CD4+ T cell count in HIV is the most important marker for HIV progression towards AIDS, and indeed, if the count reaches the benchmark of $200/\text{L}$, anti-retroviral medication is recommended. Of direct interest for this investigation is the Ruzyla-Smith study (Ruzyla-Smith et al., 1995), which compared the effect of two different psychological interventions (hypnosis and flotation-relaxation) on immunological variables. Only the highly hypnotizable subjects saw any beneficial effects of these interventions (Ruzyla-Smith et al., 1995).

Various hypotheses that bear on the relationship between hypnotizability and immune function can be considered. Most salient perhaps is the construct of cognitive and physio-

logical flexibility, putatively instrumental in the ability to respond to the differential requirements of psychological interventions such as self-hypnosis or Johrei training. This proposition was first entertained by Evans who from 1969–91, with a total of 640 participants, carried out studies on hypnotizability and the flexible control of sleep (see for review, Evans, 1991). The ease of falling asleep, of staying asleep, and the flexibility of sleep patterns were associated with high hypnotizability, as well as the ability to respond to suggestion in the REM phase of sleep. Evans and Graham went on to show that random number generation was a facility associated with high hypnotic susceptibility (Evans and Graham, 1980).

Subsequently Crawford and Gruzelier and colleagues (Malott et al., 1989; Crawford and Gruzelier, 1992; Crawford, 1994; Gruzelier, 1998) used this concept as an explanatory construct for cognitive and neurophysiological findings that have differentiated high from low hypnotic susceptibility. Among these were responsiveness to visual illusions and reversible figures, susceptibility to autokinetic movement, stronger attentional filtering abilities, the ability to shift from analytic to holistic strategies and the ability to display requisite hemispheric specificity in alignment with task demands. Neuro-cognitive flexibility has been invoked to account for associations found between high hypnotizability and schizotypal features, aside from the ability to shift both cognitive strategies and states of awareness, as in sleep, and to undergo functional neuro-cognitive changes following instructions of hypnosis (Gruzelier, 2002; *in press*). These associations have included a rapid, free-flowing association of thoughts and ideas (Santarcangelo and Sebastiani, 2004) and other aspects of the cognitive activation syndrome of schizotypy as well as the perceptual flexibility and magical thinking of the unreality syndrome (Gruzelier, 2001; Gruzelier, Jamieson, Croft et al., *in press*; Jamieson, Laidlaw et al., *under review*; Laidlaw, Naito, Dwivedi et al., *under review*).

A second strand of evidence on the relationship between hypnotic susceptibility and immune function concerns the importance of left hemispheric functional dominance. Left hemispheric functional advantages have been associated with immune competence (see for review, Gruzelier, 2002a). There is evidence in animals where, to give one example, lesions in the neocortex produced opposite effects on various immune parameters depending upon which side of the brain was lesioned. When the right hemisphere was removed leaving an intact left hemisphere, increased lymphoproliferation was seen (Neveu, 1993). Among human evidence was our finding that HIV-infected people with a greater right hemispheric dominance compared with those with a left hemispheric activation dominance showed a larger decline in CD4+ T cell counts (Gruzelier et al., 1996).

Second, as mentioned above, evidence has been reviewed showing left lateralized functional advantages in highly hypnotized individuals outside of hypnosis (Gruzelier, 1998). These results have been supported by our recent fMRI evidence comparing volunteers with high and low hypnotizability on a stroop-like task (Egner et al., *submitted*). However, whether this laterality dynamic is central to our present results remains unclear in the light of a recent EEG analysis (Dwivedi et al., *in preparation*) from an earlier stress intervention study first published in this journal (Laidlaw, Naito, Dwivedi et al., 2003). In the run up to exams university students were randomly assigned to four weeks of self-hypnosis training, Johrei or a neurofeedback relaxation procedure. Johrei and self-hypnosis both proved not only to be advantageous in improving mood compared to a relaxation control group, but also advantageous in various immune parameters (Naito, Laidlaw, Henderson et al., 2003). When changes in EEG power were examined, the more striking pattern of changes concerned shifts in the balance of anterior hemispheric activation (Dwivedi et al., *in preparation*). In keeping with our present hypotheses, there

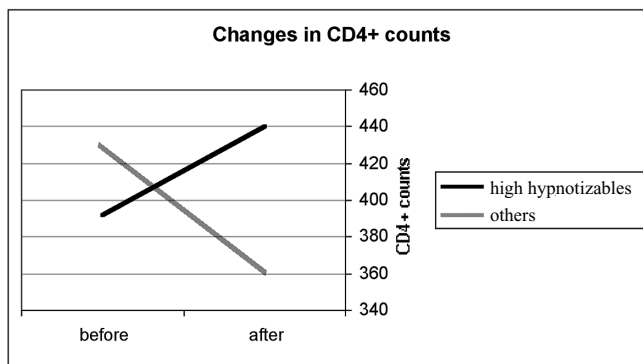


Figure 1. Change in CD4+ T cell counts of highs (n = 8) and those of more moderate hypnotizability (n =14).

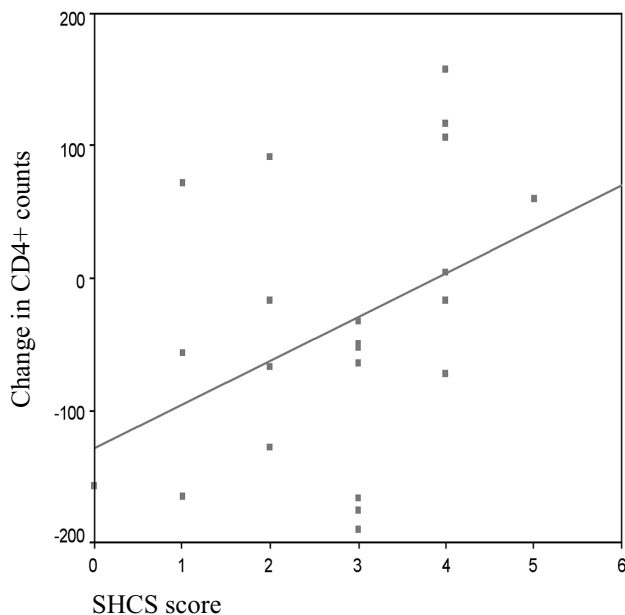


Figure 2. Mean change in CD4+ T cell counts and SHCS scores.

was an increase on the left following self-hypnosis with a concomitant increase in CD8+ cells, and to a lesser extent following relaxation training. However, the result following Johrei training contradicted this hypothesis. Johrei training, which was an intervention that clearly influenced immunology, indexed by a significant increase in natural killer cell counts, produced an increase in *right* anterior EEG power. Opposite effects on anterior asymmetry, though in contradiction with the laterality-immune hypothesis would be in keeping with the different cognitive strategies inherent in hypnosis and Johrei. Hypnosis requires focussed, inner-directed attention (left hemisphere) and Johrei, broader, outer-directed attention (right hemisphere). This indicates that the laterality-immune hypothesis may prove to be too simplistic given the complexity in brain-immune connections. Therefore, of our initial

neurophysiological hypotheses as to the nature of the relationship between hypnotizability and response to treatment, neuro-cognitive flexibility may be the more appropriate one.

Though there were limitations to this pilot study which in view of the small sample size made it impossible to compare the two interventions, hypnotizability, a measurable personality dimension, appeared to be a factor in determining response to the psychological interventions, here evinced by a significant difference in CD4+ T cell counts between the high and less hypnotizable participants with HIV. It is proposed that the highly hypnotizable are more accepting of psychological interventions and possibly have neuro-cognitive differences that potentiate their response to treatment and their immunological response. Hypnotizability may be a salient individual difference with which to explain the uncertain nature of response to psychological interventions.

Conclusion

This pilot study indicates that hypnotizability may predict immunological response to psychological interventions in HIV.

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Address for correspondence:

Dr TM Laidlaw

Division of Neuroscience and Psychological Medicine

Imperial College London

St Dunstan's Road

London W6 8RF

England

Email: t.laidlaw@ic.ac.uk