

Review: psychological interventions have a narrow application in influencing immune response

Miller GE, Cohen S. *Psychological interventions and the immune system: a meta-analytic review and critique*. *Health Psychol* 2001 Jan;20:47–63.

QUESTION: Do psychological interventions positively influence immune response?

Data sources

Studies were identified by searching Medline and PsycINFO, using combinations of the terms intervention, psychotherapy, disclosure, hypnosis, relaxation, biofeedback, conditioning, stress management, leukocyte, lymphocyte, natural killer cell, psychoneuroimmunology, and immune function. Further studies were identified using the ancestry method. Post 1960 issues of 7 journals in the field of psychoneuroimmunology were handsearched.

Study selection

Studies were selected if they were English language randomised controlled trials with multiple subject designs of psychological interventions for modulating immune functions. Studies that aimed to improve wellbeing by manipulating anatomical or physiological processes were excluded.

Data extraction

Data were extracted on study design, patient background characteristics, type of intervention (stress management, relaxation, disclosure, hypnosis, and conditioning), and immune system parameters (enumerative and functional measures). Aggregate effect sizes (ESs) were calculated using the fixed effects model, and heterogeneity and publication bias (file drawer problem) were considered.

Main results

59 trials (2135 patients) were included of which 16% examined stress management, 26% relaxation, 10%

disclosure, 31% hypnosis with immune suggestion, 10% conditioning, and 7% relaxation and hypnosis. Of 11 immune response measures, stress management showed a positive influence in only 1; relaxation in 1 of 14; disclosure in 1 of 3 (and a negative influence in 1 [reduction in 1 cell count measure]); hypnosis in 3 of 8; and conditioning in 1 of 1. The table shows the aggregate ESs for the statistically significant findings. Only the relaxation data were not subject to a file drawer problem and heterogeneity existed among trials for several measures.

Conclusion

Insufficient evidence exists at present to support the broad application of psychological interventions in positively influencing immune response.

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Psychological interventions to elicit immune response after treatment

Intervention	Immune measure	Number of trials	Aggregate effect size (95% CI)
Stress management	Lymphocytes	2	0.28 (0.01 to 0.51)
Relaxation	Total secretory immunoglobulin A	6	0.37 (0.25 to 0.47)
Disclosure	T helper lymphocytes	2	-0.31 (-0.5 to -0.08)*
	Epstein Barr virus	2	-0.29 (-0.44 to -0.10)
Hypnosis	Total secretory immunoglobulin A	4	0.15 (0.01 to 0.28)
	Neutrophil adherence	2	0.50 (0.27 to 0.68)
	Immediate type hypersensitivity erythema	8	0.23 (0.04 to 0.41)
Conditioning	Natural killer cell cytotoxicity	4	0.57 (0.36 to 0.73)

*Result does not favour intervention.

COMMENTARY

Psychoneuroimmunology is an interdisciplinary field integrating current knowledge and research methods of diverse disciplines such as basic immunology and endocrinology, neurosciences, and psychiatry and psychology.^{1, 2} It focuses on the interaction between the main information transmitting and processing subsystems of the body, in particular the central and peripheral nervous systems, the endocrine system, and the immune system. Accumulating evidence that various chronic stressors may negatively influence the immune system and have detrimental health effects have inspired a new area of research examining the potentially protective or ameliorative effects of interventions aimed at stress reduction.

The review by Miller and Cohen features 2 important sections. Firstly, the authors propose a theoretical framework for possible mechanisms mediating the effects of psychological interventions on immune functions. Most of the included studies lack such a theory driven approach and thus, the design and parameters that have been used are often inappropriate. Secondly, the authors skilfully stress the methodological weaknesses of the studies and derive important requirements for future research in the field.

The meta-analysis, however, has several limitations because few studies could be analysed. For various interventions or parameters, the authors could analyse only 2 studies (eg, disclosure, stress management, and Epstein Barr virus). Furthermore, the 4 classical conditioning studies, the latest of which was published in 1994, were all done by one research group. It remains to be shown whether other groups can replicate the findings, a necessary condition for external validity.

A further question arises as to whether the interventions studied are comparable within the groups the authors have aggregated. The lack of standardisation of most of the interventions and their heterogeneity adds a further problem to this meta-analysis.

In general this review shows that the empirical basis for the assumption that psychological interventions can change immune functions, especially with regard to illnesses such as cancer or HIV infection, is scarce. In addition, there is scant evidence to date that immune enhancing effects of psychological interventions are large or persistent enough to be of biological relevance. On the other hand, to give psychological interventions in the belief that psychological (in contrast to medical) interventions can do no harm biologically also is questionable, because the number of helper T cells decreased in the disclosure interventions. At this point, we must adopt the Scottish verdict of “not proven.”

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1 Ader R, Felten D, Cohen N. *Psychoneuroimmunology*. 3rd edition. New York: Academic Press, 2001.

2 Schedlowski M, Tewes U. *Psychoneuroimmunology: an interdisciplinary introduction*. New York: Plenum Press, 1999.