

Psoriasis and Psycho-Dermatology

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ABSTRACT

Introduction: Psoriasis is a common, long-term skin condition associated with high levels of psychological distress and considerable life impact. The impact of psoriasis, beyond the skin, is often not recognised and under-treated.

Methods: This paper explores the relationship between psychological distress and psoriasis including reference to the 'brain–skin access'. The life impact of psoriasis is discussed and pharmacological interventions which affect distress associated with psoriasis and psychological interventions are reviewed. Evidence from peer-reviewed journals and controlled trials inform the text.

Results: Psoriasis has a profound impact on mental health and well-being which is under-

recognised by clinicians. The sympathetic adrenal medullary axis and hypothalamic pituitary adrenal axis are likely to be involved in the onset of psoriasis and there may also be an effect from inflammation in the skin on the central release of corticotrophin-releasing hormone. Psoriasis can be stigmatising and may affect all aspects of life including relationships, employment, social life and leisure activities. There is some evidence for psychological interventions being effective in the management of distress associated with psoriasis and psoriasis itself. Studies, however, have used disparate outcomes and methods and largely involve low numbers of patients. There is very limited access to psychological support for the patients with psoriasis despite evidence of high levels of psychological distress and considerable life impact.

Conclusions: Psoriasis is a long-term skin condition associated with high levels of distress and considerable life impact, both of which are under-recognised. Routine screening for distress with access to effective treatment is required. There is a need for high-quality studies to assess the effect of psychological intervention in patients with psoriasis both to

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inform guidance and facilitate the provision of effective psychological support services.

Keywords: Brain–skin axis; Psoriasis; Psycho-dermatology; Psychological distress; Psychological impact; Psychological intervention; Psycho-neuroimmunology; Stress

INTRODUCTION

Psoriasis affects approximately 1.2 million people in the UK [1]. The profound impact of psoriasis on mental health, well-being and quality of life is increasingly recognised [2–4]. The burden of living with psoriasis is equivalent or greater than that of other long-term conditions such as congestive cardiac failure and chronic lung disease [5], but tends to be under-recognised [6]. There is limited evidence regarding the management of stress and distress associated with psoriasis [7] and even less scope within our present health system for psychological intervention [8].

This article reviews the relationship between distress and psoriasis, exploring the life impact of psoriasis and the current evidence for pharmacological and psychological interventions in this population. Papers from peer-reviewed journals have been used to inform the text and all interventional studies cited are from controlled trials.

PSYCHOLOGICAL IMPACT OF PSORIASIS

Stress and Psoriasis

Distress, in the form of excessive worrying, impairs clearance of psoriasis during phototherapy [9]. Retrospective studies have demonstrated that 37–88% of patients believe

that their psoriasis is caused or exacerbated by stress [10–12]. In prospective studies, Verhoeven et al. [13] confirmed that daily stressors trigger increased itch and psoriasis severity, and that patients with high levels of worrying are most vulnerable to the impact of stressors [14].

Psychoneuroimmunology: The Brain–Skin Axis (Fig. 1)

The stress response is an evolutionary mechanism enabling both a rapid (fight or flight) response to an acute stressor (e.g. avoiding a predator) and a response to chronic stress by saving energy [15]. Modern day stressors trigger established pathophysiological pathways, which can act as exacerbating or causative factors in inflammatory disease [16].

Hypothalamic–Pituitary–Adrenal Axis

Activation of neuro-hormones by stress is predominantly via the hypothalamic–pituitary–adrenal (HPA) axis with up-regulation of corticotrophin-releasing hormone (CRH), adrenocorticotrophic hormone and glucocorticoids [17], alongside neuropeptide stress response mediators [18]. The immune system is profoundly altered: glucocorticoids inhibit interleukin (IL)-12, interferon-gamma and tumour necrosis factor (TNF) via antigen-presenting cells and T-helper (Th)1 cells. IL-4, IL-10 and IL-13 are up-regulated via Th2 cells. Cortisol exerts an immunosuppressive effect shifting Th1 to Th2-mediated immunity [19]. CRH also directly affects localised inflammatory responses [20]. Skin has a fully functional peripheral HPA axis that translates and co-ordinates the peripheral stress response from the central HPA axis, creating its own cutaneous homeostasis [21]. Neuropeptides, substance P and nerve growth

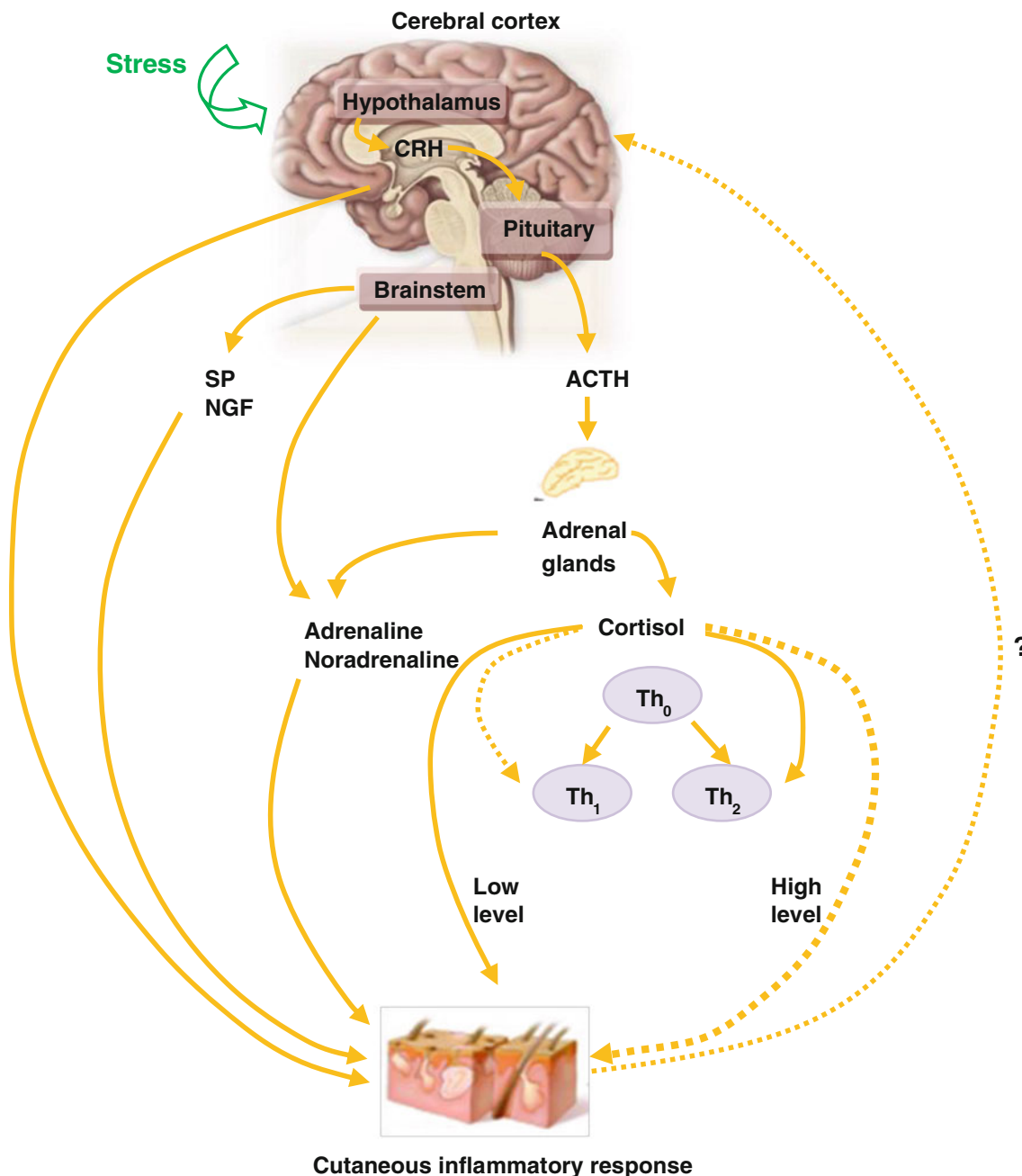


Fig. 1 The brain–skin axis. *ACTH* adrenocorticotrophic hormone, *NGP* nerve growth factor, *SP* substance P, *Th* 0-2 Thelper 0-2 cells, ? up-regulation of CRH by the cutaneous inflammatory response

factor facilitate communication between neuronal and immune cells, and promote migration of macrophages and monocytes through vascular endothelium. [22].

Very interestingly, the cutaneous immune system may also regulate the central nervous

system. Mast-cell histamine increases the expression of CRH messenger RNA in the hypothalamus of dogs [23], and IL-1 and IL-6 (elevated in psoriasis) trigger CRH release [24]. Furthermore, pro-inflammatory cytokines can induce sickness behaviour and depressive

symptoms [25]. This raises the question of whether psoriasis triggers stress or stress triggers psoriasis, or both.

Low cortisol levels in people with psoriasis who describe themselves as stress responders and who have a blunted HPA axis response to acute social stress in psoriasis [26] may result in hypocortisolism and partly explains the immune overactivity involved in psoriatic flares.

Sympathetic–Adrenal–Medullary Axis

While the HPA axis tends to be involved in slow and sustained responses to stressors [27], the sympathetic–adrenal–medullary axis is activated within seconds of a stressful stimulus. Catecholamines are released, activating CD4+ lymphocytes and trafficking of lymphocytes into the skin; an event that precedes the development of psoriatic plaques [28].

Psychiatric Co-Morbidity

The prevalence of depression in psoriasis is estimated to be up to 30% [29]. Fortune et al. [30] identified 38% of 140 patients with psoriasis as pathological worriers, while Gupta and Gupta [31] found that 5.5% of patients with psoriasis had active suicidal ideation and that 9.5% expressed a death wish.

A UK population-based cohort study of 146,042 patients [4] demonstrated an increased incidence of diagnoses of depression, anxiety and suicidality in psoriasis; the authors estimated that over 10,400 diagnoses of depression, 7,100 diagnoses of anxiety, and 350 diagnoses of suicidality were attributable to psoriasis each year.

Accurate epidemiology of psychiatric comorbidity is limited by disparities in methodologies, with some studies using symptom questionnaires to diagnose

depression and others employing clinical diagnosis alone. Most studies lack a control group and are cross-sectional in nature, preventing determination of causal relationships.

A recent study suggests that maladaptive schema-level cognitions may underlie the psychological distress experienced by people with psoriasis [32]. Mizara et al. [32] investigated the relationship between maladaptive schemas and psychological distress in patients with psoriasis. Three schemas—vulnerability to harm, defectiveness and social isolation—predicted anxiety and depression.

Despite evidence for psychiatric morbidity, most guidelines regarding psoriasis do not include screening for anxiety and depression; hence patients may not receive appropriate intervention.

Disease Severity and Psychological Impact

Psychological and psychiatric symptoms are generally in keeping with disease severity [33, 34], but not universally [33, 35]. In a prospective study of 72 patients undergoing phototherapy, Fortune et al. [36] demonstrated significant improvement in psoriasis, without change in anxiety, depression or worrying. In another prospective study, Gupta et al. [35] found that 16 of 98 patients receiving phototherapy had persistent or worsening psoriasis disability index scores despite an improvement in psoriasis. Sampogna et al. [33] reported persistent psychiatric disorder with clearance of psoriasis in one-third of subjects.

The lack of correlation between psychological impact and physical severity in some patients may be due to the cumulative impact of living with psoriasis [2], maintenance of distress by established maladaptive schemas and coping responses [32], or by psoriasis

affecting ‘high impact’ sites [37]. Lower levels of distress have been reported with longer disease duration [38, 39], which may indicate psychological acceptance, or reflect long-term adaptation [40] and avoidance of activities that trigger distress. The latter hypothesis is supported by Kleyn et al. [41] in a study using functional magnetic resonance imaging, which demonstrated reduced signal responses to disgusted faces in patients with psoriasis compared with controls, suggesting coping mechanisms among those with psoriasis to prevent distress when seeing disgusted facial expressions.

Recognition of Distress by Clinicians

Clinicians and patients may differ in their assessment of disease severity and health-related quality of life (HRQoL). In a study comparing a checklist completed by both dermatologists and patients [42], patients ranked “embarrassment over one’s appearance” as the most severe feature of psoriasis, whereas dermatologists ranked it the lowest feature. Patient-, rather than clinician-rated severity is the strongest predictor of HRQoL impairment [2, 33, 43]. Richards et al. [44] assessed 43 outpatient consultations where self-report questionnaires indicated that 37% and 12% of patients had clinical anxiety and depression, respectively. The dermatologist discussed psychological difficulties in only 39% of consultations with significantly distressed patients. There was poor correlation between the patient and clinician regarding the presence of anxiety and depression.

The discrepancy between patients and clinicians is probably multi-factorial. Patients’ own underlying perceptions of illness, coping strategies [43–46], personality traits [32], and body shame contribute to distress and are

factors often unexplored by clinicians. Richards et al. [47] found that 33% of 300 patients with psoriasis had alexithymia (impaired ability to build mental representations of emotions and express emotions). This may limit a patient’s ability to communicate emotions effectively and lead to the misinterpretation of emotional arousal as physical illness. People with psoriasis may be reluctant to disclose personal information through fear of rejection and previous experience of clinicians’ lack of empathy [3, 45].

SOCIAL IMPACT OF PSORIASIS

Stigmatisation

Psoriasis may attract attention, and cause avoidance, public rejection and reactions of disgust. Ginsburg and Link [48] identified six main areas associated with stigma: anticipation of rejection; feelings of being flawed; sensitivity to others’ attitudes; guilt and shame; secretiveness; and positive attitudes. The main predictors of stigma were: younger age at onset; extent of bleeding; employment status; duration of disease; and rejection experience. Hrehorów et al. [49] repeated the study in 2012 and found that over 78% of patients had high levels of stigmatisation. Stigmatising experiences appear to be very common. Ginsburg et al. [50] found that 99 of 100 patients described experiencing stigmatising events and Gupta et al. [51] reported that 26% of patients had experienced public rejection. Recently, Sampogna et al. [3] found that 37% of patients experienced humiliation often or all the time, and that shame was one of the most frequently reported emotions.

Feelings of shame and stigmatisation can lead to avoidance of sporting activity, social

opportunities, intimacy and public places. It may also affect access to health care, with patients reluctant to expose their skin even to a doctor.

Relationships

Eghlileb et al. [52] interviewed family members of patients with psoriasis; 57% described psychological distress, 55% social disruption, 44% limitations to leisure activities and 37% deterioration of close relationships. The patient's level of distress was more closely related to the family members' level of distress and social disruption than the severity of psoriasis. In a multicentre, case-controlled study, Poot et al. [53] found severe family dysfunction to be 16-fold more likely in patients with psoriasis than in families without a skin condition.

Psoriasis also affects sexual functioning. In Gupta and Gupta's cross-sectional survey of 120 inpatients, 40% reported a decline in sexual activity since the onset of psoriasis. This decline was associated with joint pains, but not psoriasis severity [54]. Sampogna et al. [55] confirmed the impaired sexual life of 936 inpatients with psoriasis. Using individual questions relating to sexual functioning from dermatology- and psoriasis-specific questionnaires, they found that 35.571.3% of patients reported sexual problems. In contrast to the Gupta and Gupta findings, psoriasis severity and psychological problems were associated with sexual functioning. In neither study was the presence of genital lesions determined.

In a cross-sectional study of 92 male patients with psoriasis, Goulding et al. [56] found an increased prevalence of erectile dysfunction (ED) (58%) compared with controls with other skin conditions (49%). Psoriasis was not an independent risk factor for ED. The link between

psoriasis, ED and atherosclerosis was suggested as a mechanism for sexual dysfunction.

Difficulties in relationships are unsurprising in a condition with high levels of distress and stigma. Despite this, the quality of relationships and sexual functioning are not routinely included in consultations or as outcomes of studies.

Employment and Financial Burden

The choice of employment or career, and therefore income, is affected by psoriasis [57–59]. In one study, 40% of patients reported experiencing major difficulties at work [52] and in another, 2% stopped work due to psoriasis [57]. There is an inverse relationship between psoriasis severity, employment and income [59–62]. In a study of 601 patients by Horn et al., 31.2% of patients with severe psoriasis had a low income (less than US\$30,000) compared with 18.1% of patients with mild psoriasis [59]. Approximately 20% were unemployed. Significantly more patients with severe psoriasis (17%) reported their psoriasis as the reason for unemployment compared with patients with mild psoriasis (6%). Though the results were consistent with other studies [60–62], its cross-sectional design prevents determination of causal relationships.

Recently, biological intervention studies have incorporated broader 'life impairment' outcomes into their study designs. Psoriasis-related work productivity and activity impairment (WPAI) are significantly improved by treatment with adalimumab [61]. Treatment with ustekinumab is linked with an improvement in productivity and reduced absenteeism [60]. Both studies show strong correlations between disease severity and work disability. Kimball et al. [61] reported that a reduction in Dermatology Life Quality Index (DLQI) was more highly correlated with WPAI

outcomes than an improvement in Psoriasis Area Severity Index (PASI) score, and Reich et al. [60] reported a greater improvement in WPAI outcomes in patients with higher DLQI scores and Hospital Anxiety and Depression Score at baseline, suggesting that a reduction in work disability may only be partially attributable to an improvement in disease severity.

Alcohol and Smoking Misuse

Alcohol and cigarette misuse are common among patients with psoriasis [63, 64]. Kirby et al. [65] reported excess alcohol consumption to be up to 50%. Mills et al. [66] found that twice as many patients with psoriasis smoked compared with controls. Alcohol exacerbates psoriasis severity and pruritus, and impairs treatment response [67]. Poikolainen et al. [68] demonstrated an increased standardised mortality ratio in all parameters of alcohol- and smoking-related causes in people with psoriasis. Naldi et al. [69] found that the risk of psoriasis was higher (but not significantly) for current smokers and drinkers, and a trend for increased risk of psoriasis with increased usage of cigarettes and alcohol [70].

TREATMENT OF PSYCHOLOGICAL DISTRESS IN PSORIASIS

Pharmacological Interventions

Biological Agents

TNF- α antagonists are safe and effective in improving both the physical severity of psoriasis and HRQoL [71–73]. Patients with depression also have increased levels of TNF- α [74]. It is speculated that TNF is related to fatigue and sleepiness, and may account for the coexistence of depression with fatigue [75, 76].

TNF- α antagonists may reverse depressive symptoms and fatigue in patients with psoriasis [61, 74, 77]. Reductions in anxiety and depression scores have also been demonstrated with ustekinumab (an anti-IL-12/23 agent used to treat psoriasis) [78].

Psychotropic Medications

Few studies have investigated the role of psychotropic medications in psoriasis. A double-blind, placebo-controlled study by Alpsy et al. [79] compared treatment with moclobemide (a monoamine oxidase inhibitor antidepressant) plus topical corticosteroid to treatment with topical corticosteroid alone in 60 patients. Improvements in PASI, depression and anxiety scores were significantly greater in the moclobemide group at 6 weeks compared with topical corticosteroid alone. Baseline PASI scores, however, were low (<5) in both groups, making it difficult to evaluate changes in scores. A recent retrospective open study of 38 patients with moderate/severe psoriasis and depressive and/or anxiety disorders who recently started anti-TNF α therapy compared treatment with escitalopram (a serotonin selective reuptake inhibitor) plus psychotherapeutic support with psychotherapeutic support alone [80]. Reduced depression and anxiety scores, and pruritus and PASI scores were seen in the escitalopram plus psychotherapeutic support group compared with psychotherapeutic support only. No details of the 'psychotherapeutic support' were given and randomisation was by patient preference.

The evidence for psychotropic medications and psoriasis is conflicting, with several case-reports of fluoxetine-induced or -exacerbated psoriasis [81–83], while the atypical antidepressant, bupropion, has been linked to exacerbations of psoriasis [84]. In addition, the mood stabiliser, lithium, commonly precipitates or aggravates psoriasis [85].

Psychological Interventions

Despite the association of distress with psoriasis, evidence for a ‘brain–skin axis’ and the effect of stress on immune functioning and disease severity, there have been few high-quality studies investigating the effectiveness of psychological interventions. A recent meta-analysis of psychological interventions designed to improve skin condition outcomes identified only eight studies involving psoriasis that fulfilled the criteria of having a control group, being published in a peer-reviewed journal and written in English [7]. The majority of these studies had small sample sizes and non-randomised study designs. A diverse range of psychological interventions with differing outcomes were included, making comparisons impossible.

Psychological interventions can be divided into those addressing cognitive and behavioural processes—cognitive behaviour therapy (CBT)—and those targeting a reduction in stress (arousal reduction).

Arousal Reduction

A prospective, randomised, single-blinded study by Kabat-Zinn et al. [86] introduced a mindfulness meditation-based stress reduction audio-tape intervention as an adjunct to phototherapy and compared it to phototherapy alone. A significant improvement in the rate of psoriasis clearance and a non-significant reduction in stress levels were found. The duration of remission was not assessed.

Gaston et al. [87] performed a single-blinded, randomised, controlled trial comparing 20 weeks of meditation or meditation plus imagery with a waiting list control group or treatment-free group. A significant improvement in psoriasis severity ($P \leq 0.01$) was seen in the meditation intervention

groups, with no additional benefit of imagery. Psychological outcomes were not evaluated and patient numbers were small.

Vedhara et al. [88] evaluated the effects of an emotional disclosure programme. Patients with psoriasis were asked to spend 20 min writing or talking about their thoughts or the most upsetting times of their lives on four consecutive days. A control group wrote a factual (non-emotional) account of the previous day. They found no difference in psoriasis severity between the two groups; however, changes in mood predicted psoriasis severity in the intervention group only. Assessments were at 12 weeks after the intervention. Paradisi et al. [89] compared the efficacy of two different written emotional disclosure techniques performed on three consecutive days with a control group in patients undergoing phototherapy. The results were difficult to interpret, but appeared to demonstrate a slightly longer duration of remission in one of the emotional disclosure groups. Both of these studies had a very short duration of intervention. The inclusion of emotional disclosure techniques on a more regular basis may warrant further investigation.

Hypnosis

A potential role for hypnosis has been demonstrated in two studies [90–92]. Tausk and Whitmore [91] randomised highly or moderately hypnotisable patients with psoriasis to either hypnosis with active suggestions of improvement or neutral hypnosis. No difference in PASI scores was found between the two groups, although there was a suggestion that highly hypnotisable patients in both groups demonstrated a greater percentage reduction in PASI score than moderately hypnotisable patients ($P = 0.01$). Patient numbers, however, were very low and there was no non-intervention

control group. Price et al. [92] employed self-hypnosis, together with relaxation and support group discussions over eight weekly sessions in a matched-controlled trial. A significant reduction in anxiety and neuroticism, and an increase in self-esteem, maintained at 6 months, were demonstrated. No significant improvement in psoriasis severity was found. Both studies are limited by small group size and the improvement seen in the study by Price et al. cannot be concluded as the sole benefit of self-hypnosis training. Hypnosis may, however, be a therapeutic modality that warrants further testing.

Cognitive Behaviour Therapy

Individual coping strategies, illness perceptions, beliefs about control and curability of illness, and individual personality traits are closely linked with health outcomes and psychological distress in psoriasis [46, 93–95]. Only two studies, however, have investigated CBT as an adjunctive treatment for psoriasis. A high-quality, case-controlled study by Fortune et al. [96] involving 40 patients with psoriasis receiving adjunctive group CBT demonstrated a significant reduction in PASI scores at 6 weeks and 6 months follow-up, with 64% of patients achieving >75% psoriasis clearance at 6-month follow-up compared with 23% of the control group. The CBT group also showed reductions in anxiety and depression scores, and almost double the reduction in self-reported disability and life stress scores at 6-week and 6-month follow-ups.

In a randomised, controlled trial, Zacharie et al. [97] compared the effect of seven individual psychotherapy sessions—which included imagery, stress management and relaxation training over a 12-week period—with a control therapy in 51 patients with psoriasis. Slight, but significant, reductions in reference lesion severity and a non-significant trend for overall

reduction in psoriasis severity were observed in the psychotherapy test group. Perceived stress remained unchanged. This study, however, combined arousal reduction with a cognitive intervention. Further studies investigating the effectiveness of CBT, including work- and relationship-related outcomes, are warranted.

DISCUSSION

Psoriasis is a common, visible, long-term condition with a considerable psychological and life impact, potentially affecting every aspect of an individual's existence including work, recreation, relationships, sexual functioning, family and social life.

Increasing awareness of the life impact of psoriasis has led to clinical guidelines that include the evaluation of patients' HRQoL in addition to physical severity [98–100]. European evidence-based (S3) clinical guidelines propose a DLQI of 0 or 1 as a treatment goal [99], and Scottish Intercollegiate Guidelines Network guidance states that the “assessment of patients with psoriasis or psoriatic arthritis should include psychosocial measures, with referral to mental health services as appropriate”, and recommends at least annual screening for depressive symptoms [100].

Despite high levels of psychological distress, the provision of psychology services in the UK for patients with skin disease is, at best, limited. In spite of clear demand, only 4% of dermatology units in the UK provide a dedicated counselling service [101]. Despite attempts to increase awareness and the provision of resources by groups such as the British Association of Dermatologists and Psoriasis Association, psychology services provision has, in fact, deteriorated since 2004 [101].

Good-quality evidence to support the instigation of dedicated psychology services for patients with psoriasis and other skin conditions is presently limited. Existing data for psychological interventions mainly come from studies that lack consistency in design and outcome measurements. The effect of psychological intervention on work, relationships and the need for systemic therapies, which would make these services cost-effective, has not been investigated adequately. The degree of heterogeneity in the studies prevents further extrapolation of results. There is a need for well-designed, adequately powered and well-controlled interventional studies to investigate the optimal psychological interventions for people with psoriasis. These data are required not only to inform future provision of psychological services for this population of patients who are presently under-supported, but also to provide hard evidence for the efficacy of such interventions as part of the successful management of psoriasis.

However, there is cause for optimism. Routinely measuring PASI and DLQI and asking about the life impact of psoriasis in clinics is a manageable start, even without dedicated psychology resources. Screening for psychological distress would detect undiagnosed cases of anxiety and depression, enabling patients to be directed towards services that may offer treatment. Increased recognition of the psychological and life impact of psoriasis among clinicians is the first step towards improving care.

An understanding of the links between physical and psychological health is increasing. Government initiatives, such as 'No Health Without Mental Health' may help transform understanding into service improvement [102]. The future management of psoriasis may routinely involve multi-disciplinary teams to

manage physical, psychological and social aspects of the condition in line with other systemic long-term conditions.

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