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Research report

Atopic disorders and depression: Findings from a large, population-based study

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ABSTRACT

Background: Atopy, a common disorder characterized by a sensitivity to allergic reactions, affects a large proportion of the adult population and, as with depression, is associated with immune-inflammatory pathway changes. We sought to determine the role of atopic disorders in depression using data from a randomly-selected, population-based study of men and women.
Methods: Cross-sectional data derived from the Geelong Osteoporosis Study for 942 males and 1085 females were analyzed. Depression [major depressive disorder (MDD), minor depression and dysthymia] was assessed using the Structured Clinical Interview for DSM-IV-TR Research Version, Non-patient edition. Data on medical conditions, including atopic disorders (asthma, hay fever and eczema), smoking status, alcohol consumption, socioeconomic status, and physical activity were documented by self-report. Logistic regression modeling was used to explore the associations between atopic disorders and depression.
Results: Atopic disorders were associated with a 59% increased likelihood of depression [gender and smoking-adjusted odds ratio (OR) 1:50, 95% CI 1.20–1.97]. Sub-group analyses revealed a similar pattern for those with MDD [gender and smoking-adjusted OR 1:54, 95% CI 1.22-1.94]. These associations were independent of socio-demographic characteristics, clinical and lifestyle factors.
Limitations: Reliance on self-report for allergic symptoms and cross-sectional nature of study.
Conclusion: This population-based study provides evidence of the potential contribution of allergic disorders to depression. Further research is required to elucidate the direction of this association and to further explicate its underlying physiology, including immune-inflammation markers.

1. Introduction

Atopy is defined as the presence of elevated immunoglobulin E (IgE) levels associated with exposure to allergens commonly occurring in the environment (Johansson et al., 2004). This disorder typically results in the development of allergic symptoms such as eczema, dermatitis, allergic rhinitis/hay fever, allergic conjunctivitis or asthma. Interestingly, its prevalence has increased over the past 20 to 30 years in many parts of the world, including Western nations like the United States and Australia (Jarvis and Burney, 1998); the cause of which is relatively unknown. Historically, atopic disorders have been considered to be "psychosomatic" in origin (Niemeier et al., 2002), but recently the concept of psycho-neuro-immune-endocrinology, a discipline that studies the close relations between mind, brain, immune and hormonal system, has reformulated perspectives on these relationships

Abbreviations: 5-HT, 5-hydroxytryptamine; ABS, Australian Bureau of Statistics; BMI, body mass index; CI, confidence intervals; CMI, cell-mediated immune; CRP, C-reactive protein; GOS, Geelong Osteoporosis Study; ICAM-1, intracellular adhesion molecule-1; IgE, immunoglobulin E; IL, interleukin; IRSAD, Index of Relative Socioeconomic Advantage/Disadvantage; MDD, major depressive disorder; NHANES III, Third National Health and Nutrition Examination Survey; O&NS, oxidative and nitrosative stress; OR, odds ratio; SCID-I/NP, Structured Clinical Interview for DSM-IV-TR Research Version, Non-patient edition; SES, socio-economic status; SEIFA, Socio-Economic Index for Areas; TNFα, tumor necrosis factor α; Treg, T regulatory

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(Liezmann et al., 2011) and atopic disorders are now considered to be primarily due to immune dysregulation.

Studies investigating immune system functioning in patients with depression have observed activated inflammatory, cell-mediated immune (CMI) and oxidative and nitrosative stress (O&NS) pathways in these individuals (Maes et al., 2011; Maes, 2011; Dowlati et al., 2010). This evidence comprises signs of inflammation, such as increased levels of pro-inflammatory cytokines [e.g. interleukin-1 (IL-1), IL-6 and tumor necrosis factor-α (TNFα)], acute phase proteins [e.g. haptoglobin and C-reactive protein (CRP)] and complement factors; CMI and Th1 cell activation, with increased levels of interferon-(IFN)γ and neopterin, lower concentrations of T regulatory (Treg) cells, oxidative damage to membrane fatty acids and DNA, and nitrosative modifications of proteins (Maes, 1995; Pasco et al., 2010; Maes et al., 2011; Li et al., 2010). Furthermore, the incidence of depression is considerably higher among medically ill patients, particularly in those diseases associated with immune activation (Clarke and Currie, 2009; Sanna et al., 2013), thus providing a rationale for this study.

Antidepressants, such as tricyclic antidepressants and selective serotonin reuptake inhibitors, have specific negative immune-regulatory effects by lowering the production of IFNγ and IL-1β, and increasing the production of IL-10 and the levels of Treg cells (Maes et al., 1999; Himmerich et al., 2010). Many drugs with anti-inflammatory effects augment the clinical efficacy of antidepressants in the treatment of depression (Maes et al., 2012). For example, TNFα blockers, such as etanercept, may reduce depressive symptoms in patients with psoriasis suffering from depression and in animal models of depression (Tyring et al., 2006; Krugel et al., 2012). In a randomised clinical trial, infliximab a TNF antagonist failed to separate from placebo, although an interaction between higher baseline TNF levels and greater reduction in depression scores with treatment was seen (Raison et al., 2013).

Depression has been linked with several atopic disorders within clinical and some population-based samples of individuals with asthma (Hurwitz and Morgenstern, 1999; Gunn et al., 2012; Afari et al., 2001; Loerbroks et al., 2012; Chun et al., 2008), eczema (Klokk et al., 2010; Yang et al., 2010), dermatitis (Hashiro and Okumura, 1997; Gunn et al., 2012) and allergic rhinitis (Cuffel et al., 1999; Hurwitz and Morgenstern, 1999; Marshall et al., 2002). These comorbidities appear to have an additive negative effect on functional status (Afari et al., 2001) and quality of life (Ford et al., 2003; Slattery et al., 2011; Lu et al., 2013; Goldney et al., 2003; Adams et al., 2004). Depression can compromise treatment adherence (Lehrer et al., 2002) and is thought to influence decision making in self-managed treatment (Adams et al., 2004) in patients with asthma.

Many of the previous studies investigating the relationship between depression and atopic disorders have been limited by an age range (Lu et al., 2013; Timonen et al., 2003; Hurwitz and Morgenstern, 1999; Klokk et al., 2010), restricted to clinical settings (Afari et al., 2001; Hashiro and Okumura, 1997), or reliant on self-report inventories to measure depression (Adams et al., 2004; Goldney et al., 2003; Marshall et al., 2002). The purpose of this study was to investigate whether an association exists between a lifetime diagnosis of allergic disorders and history of depression in a population-based sample of adult men and women, using a gold standard psychiatric measure and adjusting for potential confounders.

2. Method

2.1. Participants

The Geelong Osteoporosis Study (GOS) (Pasco et al., 2012) is a prospective, cohort study comprising an age-stratified random sample of residents from the Barwon Statistical Division, recruited from the Commonwealth of Australia Electoral Rolls. Female participants were recruited between 1994 and 1997 and males between 2001 and 2006. For the purpose of this study, we utilized cross-sectional data collected at the 10-year follow up assessment for women and the 5-year assessment for men.

Of those enrolled at baseline (1494 women and 1540 men), 82% ($n=881$) and 81% ($n=978$) of eligible women and men, respectively, returned for follow-up assessments. A further 246 women aged 20–29 year (71% response) consented to participate between 2004 and 2008 and were incorporated into the female cohort, retaining the full adult age range (20+ years). Reasons for non-participation have been detailed elsewhere (Williams et al., 2010; Sanna et al., 2013).

From the pool of 2105 participants, those who did not undergo psychiatric assessment ($n=49$; 17 men and 32 women) or did not provide a medical history ($n=29$; 19 men and 10 women) were excluded from the analyses, resulting in a sample of 2027 participants (1085 women and 942 men). Written informed consent was obtained from all participants and this study was approved by the Barwon Health Human Research Ethics Committee.

2.2. Study measurements

The presence of lifetime allergic disorders, including asthma, hay fever and eczema was self-reported. Participants were asked if they had ever been diagnosed with medical conditions from a list of disease groups including metabolic, cardiovascular, psychiatric, cancer, childhood and respiratory; asthma, hay fever and eczema were listed as medical conditions. Research has shown a reasonable correlation between self-reported chronic diseases, including asthma, diabetes and coronary heart disease, and those identified in medical records (Kriegsman et al., 1996).

Trained personnel with qualifications in psychology conducted the Structured Clinical Interview for DSM-IV-TR Research Version, Non-patient edition (SCID-I/NP) (First et al., 2002) to determine the presence of depression. Data derived from diagnostic interviewing are considered gold-standard for classification of mood disorders. The SCID-I/NP has been used extensively for epidemiological research, demonstrating sound validity and reliability for depression diagnoses as well as inter-rater reliability for depressive disorders. The term depression encompasses those meeting criteria for a lifetime history of major depressive disorder (MDD), minor depression and/or dysthymia.

Body Mass Index (BMI; kg/m^2) was calculated from height, measured to the nearest 0.1 cm, and body weight, measured to the nearest 0.1 kg. Participants were classed as active if they reported participation in light to vigorous activity on a regular basis compared to sedentary behavior. Tobacco smoking was documented and grouped as current or not. The Index of Relative Socio-economic Advantage/Disadvantage (IRSAD), grouped into quintiles, was used to indicate a participant's socio-economic status (SES). This index was calculated using data from the Socio-Economic Index for Areas (SEIFA) and the 2006 Australian Bureau of Statistics (ABS) census (Australian Bureau of Statistics, 2006). IRSAD values take into account educational and income level, type of occupation, and some measure of wealth (such as owning a car, or number of bedrooms in a dwelling).

2.3. Statistical analysis

Statistical analysis was performed using Minitab (version 16; Minitab, State College, PA). Differences between those with and without allergic diseases were compared using chi-square and Kruskal–Wallis analyses. Univariate regression models were performed to assess unadjusted associations between dependent and independent variables. Binary logistic regression techniques were