

# The relationship between fatigue and psychiatric disorders: Evidence for the concept of neurasthenia<sup>☆</sup>

Samuel B. Harvey<sup>a,\*</sup>, Simon Wessely<sup>a</sup>, Diana Kuh<sup>b</sup>, Matthew Hotopf<sup>a</sup>

<sup>a</sup>Institute of Psychiatry, King's College London, London, UK

<sup>b</sup>MRC Unit for Lifelong Health and Ageing, Department of Epidemiology and Public Health, Royal Free and UCL Medical School, London, UK

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## Abstract

**Objective:** Fatigue and psychiatric disorders frequently occur comorbidly and share similar phenomenological features. There has been debate as to whether chronic fatigue, or neurasthenia, should be considered an independent syndrome distinct from psychiatric disorders. We aimed to establish whether persistent fatigue can occur independently from psychiatric disorders and to test the hypothesis that fatigue without comorbid psychiatric symptoms has unique premorbid risk factors. We also aimed to investigate the psychological outcome of any individuals with fatigue. **Methods:** The MRC National Survey of Health and Development was used to prospectively follow 5362 participants from birth. A sample of nonfatigued individuals without psychiatric disorder was selected at age 36 and followed until age 43 years ( $n=2714$ ). At age 43, the presence of new onset fatigue and/or psychiatric disorder was assessed. Information on a number of potential premorbid risk factors was collected between ages 0 and 36 years. Individuals with fatigue but no comorbid psychiatric disorder were then followed up at age 53 years. **Results:** At age 43 years, 201 (7.4%) participants reported significant levels of new onset fatigue in the absence of

comorbid psychiatric disorder. Despite the absence of case level psychiatric disorder, these individuals did report increased levels of some psychological symptoms. Excessive childhood energy (adjusted OR 2.63, 95% CI 1.55–4.48,  $P<.001$ ) and being overweight at age 36 (adjusted OR 1.62, 95% CI 1.05–2.49,  $P=.03$ ) were specific risk factors for fatigue without psychiatric disorder but not fatigue with comorbid psychiatric illness. Neuroticism was a risk factor for fatigue both with and without comorbid psychiatric disorder. Negative life events and a family history of psychiatric illness were only risk factors for fatigue when it occurred comorbidly with psychiatric illness. **Conclusions:** A significant proportion of the adult population will suffer from fatigue without comorbid psychiatric disorder. While fatigue and psychiatric disorders share some risk factors, excessive energy in childhood and being overweight as an adult appear to be specific risk factors for fatigue. Our results confirm the significant overlap between fatigue and psychiatric disorders, while also providing evidence for neurasthenia as a separate diagnosis.

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**Keywords:** Fatigue; Chronic fatigue; Neurasthenia; Psychiatric disorder; Mental disorder; Exercise; Body weight

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\* Corresponding author. Weston Education Centre, 10 Cutcombe Road, SE5 9RJ London, UK. Tel.: +44 020 7848 0778; fax: +44 020 7848 5408.

E-mail address: [s.harvey@iop.kcl.ac.uk](mailto:s.harvey@iop.kcl.ac.uk) (S.B. Harvey).

<sup>1</sup> SH conceptualized and planned this study. SH carried out the statistical analysis and wrote this paper with MH, SW, and DK providing detailed comments on early drafts.

## Introduction

Fatigue is one of the most common symptoms encountered in medical consultations. Both primary care and community studies have found that around one quarter of all people report recent problems with fatigue [1–3]. The subjective nature of fatigue has made it difficult to define or conceptualize, although most would consider it to be an extreme and persistent form of mental and/or physical tiredness, weakness, or exhaustion [4].

Previous cross-sectional studies have demonstrated a close association between chronic fatigue and psychiatric disorders [3,5,6]. Up to two thirds of people reporting fatigue lasting longer than 6 months will also be suffering from a comorbid psychiatric disorder [7]. Prospective studies have also shown that psychiatric disorders increase the risk of later chronic fatigue [8]. While there is considerable overlap in the phenomenology of fatigue and common psychiatric disorders such as depression or anxiety, there are also some important differences. In contrast to most depressed patients, people with chronic fatigue tend to experience very little self-blame or lowered self-esteem and will often attribute their symptoms to external causes [9]. Despite this, the phenomenological similarities, together with the high rates of comorbidity, have led some authors to suggest that there is little to be gained from distinguishing medically unexplained fatigue from psychiatric disorders [10]. Others have argued that fatigue is distinguishable from depression, anxiety, or other forms of psychological distress and therefore should be considered as a separate diagnostic category [11]. The fatigue syndrome neurasthenia has been retained as a separate diagnosis within the *ICD-10* classification system [12], although it is no longer included as a separate diagnosis within the influential *DSM-IV* classification, where it is only included as undifferentiated somatoform disorder [13]. *ICD-10* classification defines neurasthenia as persistent and distressing complaints of increased fatigue after mental effort, or persistent and distressing complaints of body weakness and exhaustion after minimal effort, with accompanying somatic symptoms in the absence of a depressive illness or anxiety disorder [12].

Van der Linden et al. [14] attempted to demonstrate the existence of an independent ‘pure’ fatigue state by prospectively following 1177 patients recruited from primary care, with three separate measurements of fatigue and psychiatric disorder. While they replicated previous findings of a strong correlation between fatigue and psychiatric morbidity, they also identified a group of patients with persistent, independent fatigue, which was not associated with any increase in psychological morbidity. A similar group of individuals with fatigue, but no psychiatric comorbidity, was identified in the Baltimore sample of the Epidemiological Catchment Area study, although in this study fatigue was found to be an independent predictor of later psychiatric disorder [15]. An alternative epidemiological method of examining the differences between fatigue and psychiatric disorders is to consider shared vs. independent risk factors. Hickie et al. [16] have previously used twin studies to demonstrate that while fatigue and psychological distress share some common genetic factors, fatigue has a number of independent genetic and environmental risk factors. While previous research has identified various risk factors for both fatigue and psychiatric disorders, to our knowledge, no studies have ever attempted to identify which of these risk factors are shared and which, if any, may be independent risk factors for fatigue, but not psychiatric

disorders. Possible candidates include factors previously identified as increasing the risk of fatigue, regardless of possible psychiatric comorbidity. These include being female [8,17], emotional instability (neuroticism) [18], limiting longstanding medical conditions in childhood [19], premorbid sedentary and overactive behavior [19–21], and negative life events [22].

In this study, we used a large prospective British birth cohort to investigate the temporal associations between fatigue, psychiatric disorders, and a number of potential premorbid risk factors. The large size of this cohort and the detailed information collected over the first 53 years of each participant’s life provided us with a unique opportunity to test a number of related hypotheses. We aimed (1) to confirm previous observations that a substantial proportion of individuals with persistent fatigue do not suffer from comorbid psychiatric disorder; (2) to investigate premorbid risk factors for both fatigue and psychiatric disorders to establish which factors are shared and which are unique to fatigue; and (3) to examine the psychological outcome of those individuals with fatigue without any comorbid psychiatric disorder.

## Methods

### Sample

The Medical Research Council’s National Survey of Health and Development is based on a random social class stratified sample of 5362 participants selected from all single, legitimate births occurring in England, Wales, and Scotland in 1 week of March 1946. This sample has been prospectively followed with over 20 separate data collections up to the age of 53 years. The sampling procedure and follow-up have been described in detail elsewhere [23].

### Fatigue and psychiatric disorder

Fatigue was assessed at two separate time points in each participant’s adult life, at age 36 and 43 years. Psychiatric assessments occurred at ages 36, 43, and 53 years. At age 36 years, participants were visited at home and the 40-item version of the Present State Examination (PSE) [24] was administered by a trained nurse interviewer [25]. Psychiatric disorder was defined at a threshold level of  $\geq 5$  on the Index of Definition score [26]. The PSE contains questions about fatigue, resulting in a subscale score for fatigue and lack of energy. This subscale is calculated from the question, “Do you seem to be slowed down in your movements, or have too little energy recently? How much has it affected you?” At age 43 years, participants were again visited at home and interviewed by trained nurses using the Psychiatric Symptom Frequency scale (PSF) [27]. The PSF is an 18-item scale measuring psychiatric symptoms, particularly of depression and anxiety, over the last year. A cut-off score of  $\geq 23$  was

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