

Hippocampal volume and cognitive function in anorexia nervosa

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Abstract

We hypothesised that hippocampal volume would be reduced in underweight anorexia nervosa (AN) and associated with impaired hippocampus-dependent cognitive function. Hippocampal and whole brain volumes were measured in 16 women with AN and 16 matched healthy women using magnetic resonance imaging (MRI) and a manual tracing method. Participants also completed the Doors and People Test of hippocampus-dependent memory and an IQ test. After adjustment for total cerebral volume, there was significant bilateral reduction in hippocampal volume in the AN group (8.2% right; 7.5% left). There was no evidence of impaired hippocampus-dependent cognitive function and no evidence of a relationship between hippocampal volume and clinical features of AN. The reduced hippocampal volume in anorexia nervosa is not associated with changes in cognitive function. To understand the cause and consequence of hippocampal size and function, it will be important to integrate endocrine, neuropsychological and neuroimaging studies.

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1. Introduction

In women with anorexia nervosa (AN), an enlarged ventricular volume and dilated sulci have been consistently found (Dolan et al., 1988; Krieg et al., 1988, 1989; Kingston et al., 1996; Swayze et al., 1996, 2003). Reductions in both white and gray matter have also been observed (Katzman et al., 1996; Swayze et al., 2003). Brain metabolism studies parallel the structural findings, showing global reductions in brain metabolism (Delvenne et al., 1995) and perfusion (Krieg et al., 1989).

Regional perfusion studies of children and adolescents with AN demonstrated unilateral reduced perfusion in the temporal lobe (in which the hippocampus is located) in the majority of those studied (Gordon et al., 1997; Chowdhury et al., 2003). In contrast, one unreplicated study reported relative hyperperfusion of the thalamus and the amygdala–hippocampal complex in adults with active AN (Takano et al., 2001). Structural deficits tend to improve with weight gain (Dolan et al., 1988; Krieg et al., 1988, 1989; Kingston et al., 1996; Swayze et al., 1996; Golden et al., 1996), although gray and white matter volume may remain significantly reduced following recovery (Lambe et al., 1997; Katzman et al., 1997; Swayze et al., 2003) and temporal lobe hypoperfusion may also persist (Rastam et al., 2001). Significant reductions in the volume of the hippocampal–

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amygdala formation have also been reported (Giordano et al., 2001). It is unclear whether these various persisting abnormalities reflect premorbid vulnerability factors for AN or scars of the illness. One possible pathogenic mechanism is hypercortisolaemia, which along with other factors related to malnutrition may contribute to the differential recovery rates of the various structural abnormalities in AN (Naruo, 2002; Swayze et al., 2003). Cortisol is known to specifically endanger hippocampal neurones (Sapolsky et al., 1986), and is associated with both global hypometabolism (Brunetti et al., 1998) and significant hippocampal atrophy in Cushing's disease (Starkman et al., 1992).

The hippocampus is involved in learning and memory (Zola-Morgan and Squire, 1990), and discrete hippocampal lesions give rise to impaired recall with relative sparing of recognition (Baddeley et al., 2001; Mayes et al., 2002). An association between reduced hippocampal volume and impaired verbal recall has been observed in Cushing's disease (Starkman et al., 1992), depressive disorder (Sheline et al., 1999), post-traumatic stress disorder (PTSD) (Bremner et al., 1995) and normal aging (Lupien et al., 1998). Significant deficits of learning and memory have been demonstrated in AN (Jones et al., 1991; Mathias and Kent, 1998; Kingston et al., 1996), with some weak evidence of an association between memory impairment and structural brain abnormalities (Kingston et al., 1996).

The aim of the study was to test the hypothesis that hippocampal volume would be reduced in underweight AN and that it would be associated with impaired hippocampus-dependent cognitive function. Furthermore, hippocampal volume would be inversely related to the duration of the disorder, supporting the hypothesis that structural deficits are a scar of the illness.

2. Methodology

2.1. Participants

Sixteen female inpatients with AN were recruited from the specialist eating disorders (ED) inpatient unit at the Bethlem Royal Hospital, London. All had no significant medical or psychiatric history, other than that associated with AN. The study took place during the weight-restoration phase of treatment.

Sixteen healthy comparison women, with no history of an ED or psychiatric illness, were recruited by advertisement from the staff and students of the Bethlem and Maudsley NHS Trust and Institute of Psychiatry, King's College London (KCL). All had stable healthy weight (Body Mass Index (BMI) 20–25 kg/m²). Comparison

women were matched pair-wise to AN participants for height (± 5 cm), age (± 5 years) and handedness.

All participants were aged 16–45 years and spoke English as their first language. All had no significant medical or psychiatric history, other than that related to AN, and no history of head injury, seizures, alcohol or substance misuse, steroid medication use or contraindications for MRI.

The Ethics Committee of the Institute of Psychiatry, KCL and Bethlem and Maudsley NHS Trust Hospitals approved the study, and written informed consent was obtained from all participants.

3. Procedures

3.1. Clinical assessment

Clinical diagnoses (DSM-IV) and characteristics were obtained from routine clinical assessment. Age of onset was defined as the age at which an individual first fulfilled standard diagnostic criteria for AN (DSM-IV). Duration of amenorrhoea was estimated as an objective index of duration of disorder and of oestrogen deficiency. Lowest ever BMI was used as an index of severity of illness. Weight and BMI on the day of scanning were measured for all participants.

3.2. Neuropsychological assessment

Cognitive functioning was assessed using a short form of the Wechsler Adult Intelligence Scale-Revised (WAIS-R), containing the Vocabulary, Comprehension, Block Design and Object Assembly subtests (Wechsler, 1981; Canavan and Beckmann, 1993). Discrete hippocampal lesions give rise to impaired recall with relative sparing of recognition. Hippocampus-dependent cognition was therefore tested using a memory battery that is specifically designed to measure recall and recognition, namely the Doors and People Test (Baddeley et al., 1994). Subscale scores were computed according to a standard protocol.

One participant from each group did not complete either neuropsychological test. One further AN participant failed to complete the WAIS-R and another the Doors and People Test.

3.3. Neuroimaging procedure

A coronal 1.5-mm contiguous, interleaved 3D spoiled grass (SPGR) sequence covering the whole head was collected on a 1.5-T neuro-optimised General Electric (GE Healthcare, Milwaukee, USA) magnetic resonance

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