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Original article

Functional MRI investigation of verbal working memory in adults with anorexia nervosa

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ABSTRACT

Literature regarding verbal working memory (vWM) in anorexia nervosa (AN) has been inconsistent due to a misunderstanding of the key components of vWM and introduction of confounding stimuli. Furthermore, there are no studies looking at how brain function in people with AN relates to vWM performance. The present study used functional magnetic resonance imaging (fMRI) with a letter n-back paradigm to study the effect of increasing vWM task difficulty on cortical functioning in the largest AN sample to date ($n = 31$). Although the AN group had low BMI and higher anxious and depressive symptomology compared to age-matched controls (HC), there were no between-group differences in accuracy and speed at any task difficulty. fMRI data revealed no regions exhibiting significant differences in activation when groups were compared at each difficulty separately and no regions showing group x condition interaction. Although there was a trend towards lower accuracy as duration of illness increased, this was not correlated with activity in regions associated with vWM. These findings indicate that vWM in AN is as efficient and performed using the same cognitive strategy as HC, and that there may not be a need for therapies to pursue remediation of this particular neurocognitive faculty.

1. Introduction

Anorexia nervosa (AN) is a disorder characterised by extreme dietary restraint, abnormal psychosocial functioning and poor weight-related physical morbidity. With a lack of empirical support for behavioural and pharmacological treatment of AN, further research is needed to improve understanding and development of successful interventions [65].

People with AN exhibit inefficient visuo-spatial memory and processing [36], cognitive flexibility [63], long-term memory [48], attention [17] and central coherence [38]. However, the results of studies assessing verbal working memory (vWM) in AN have been inconsistent (Table 1). WM is a limited capacity store through which information is held, maintained and manipulated in order to plan and carry out behaviour [43] and to facilitate complex processes such as comprehension, learning and reasoning [3] (Fig. 1).

Specific cortical regions within the fronto-parietal brain network have been found to control these vWM mechanisms [49]. With relation to Baddeley and Hitch's model [3], the left posterior parietal cortex (PP) has been implicated in phonological storage, the left inferior frontal gyrus (IFG) in sub-vocal rehearsal and the central executive is thought to reside in the dorsolateral prefrontal cortex (DLPFC) [60].

Focal lesions in these areas give rise to vWM process-specific deficits [45] and recent neuroimaging experiments have found these same regions to show consistent abnormalities in people with AN. Voxel-based morphometric analysis of volumetric magnetic resonance imaging (MRI) [1], has localised decreases in cortical grey matter to the parietal cortex [14,25], and cerebellum [8]. The cerebellum is traditionally associated with fine motor co-ordination but has also been implicated in facilitating initial phonological encoding of verbal information [53]. Conversely, one study found a significant increase in grey matter volume in the DLPFC [8].

A timely review of positron emission tomography (PET), single photon emission computer tomography (SPECT) and functional MRI (fMRI) studies, has demonstrated a consensus of functional "disturbance" in the IFG, DLPFC and inferior parietal lobule (IPL) [50]. Effects between binge/purge and restrictor subtypes were similar, but laterality towards the left hemisphere for IPL

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Table 1
Results of a systematic review of vWM in people with anorexia nervosa (AN). PubMed, ScienceDirect and ISI Web of Knowledge were searched using the terms 'Anorexia' and 'memory'. Only cross-sectional studies including at least 1 AN group and 1 healthy control (HC) group and which provided test results pertaining specifically to verbal short-term or verbal working memory rather than "global working memory" were included. Tests of "working memory" were scrutinised and where appropriate, reappraised for classification within this table. In particular, the 1-Back task was classified as a measure of short-term retention rather than vWM as it lacks any requirement for manipulation of information [60]. Further details of each study can be found in 1 (R) = AN Restrictive subtype; (B/P) = Binge-Purge subtype.

	Direction	No. of studies	Authors	Combined number of participants
Verbal short-term memory (vSTM)	AN better than HC	1	Hatch et al. (2010) [29]	AN = 37 HC = 45
	No difference between AN and HC	7	Castro-Fornieles et al. (2010) [15] Bosanac et al. (2007) [5] Key et al. (2006) [35] Kemps et al. (2006) [34] Mathias and Kent (1998) [41] Szmukler et al. (1992) [61] Witt et al. (1985) [66]	AN = 133 HC = 130
	AN worse than HC	3	Castro-Fornieles et al. (2009) [14] Green et al. (1996) [27] Kingston et al. (1996) [36]	AN = 70 HC = 67
Verbal working memory (vWM)	AN better than HC	2	Brooks et al. (2012) [9] Dickson et al. (2008) [17]	AN = 37 HC = 44
	No difference between AN and HC	1	Nikendei et al. (2011) [48]	AN = 34 (R), 19 (B/P) HC = 30
	AN worse than HC	1	Seed et al. (2002) [57]	AN = 20 HC = 20

hyper-responsiveness and abnormal activity in IFG was mainly attributable to the restrictive subtype, with the binge/purge subtype showing bilateral disturbance in the parietal cortices and no evidence of abnormally functioning IFG.

In light of these abnormalities, it is surprising that some AN studies report superior vWM performance in comparison to healthy control participants (HC) who have no prior history of psychiatric illness (Table 1). One may hypothesise that the central executive compensates for the impaired phonological store, either directly or via the visuo-spatial sketchpad [54], the WM "slave" system dealing with visual, spatial and kinaesthetic information [3]. This would be in line with increased DLPFC grey matter volume [8] and fMRI studies showing that the DLPFC and IFG exhibit higher activation when healthy people undertake dieting behaviour [28,32].

It may also be that AN participants view vWM tasks as more of a "challenge" than simple verbal short term memory (vSTM) tasks and delegate more attentional resources to their completion [55]. For example, Dickson et al. [17] observed significantly fewer errors by AN participants compared to HC at higher loads of the N-Back task in conjunction with subliminally presented food, aversive and neutral stimuli, but no difference at lower WM loads.

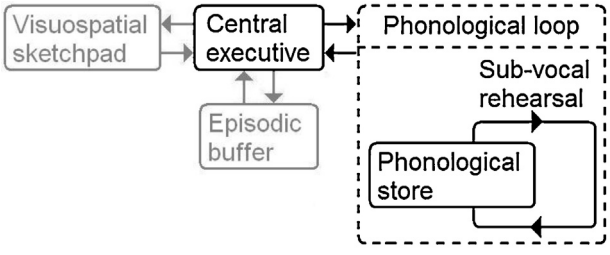

Fig. 1. Schematic diagram of the working memory model. The term "working" implies involvement of both short-term stores (phonological loop, visuo-spatial sketchpad and episodic buffer) and mechanisms that process the stored items [16]. With respect to vWM (highlighted in black), short-term retention is sub-served by the phonological loop, which is comprised of a phonological store that holds verbal information and a sub-vocal rehearsal component that maintains this information by preventing trace decay. The central executive is the attentional control mechanism that manipulates items held within the phonological loop [3]. Adapted from Baddeley, 2000 [2].

It would be useful to elaborate on these possible theories by examining associations between cortical activation and accompanying clinical demographics and performance data. To our knowledge, only one study has used fMRI with a vWM task in people with AN, without the inclusion of disorder-relevant stimuli. Castro-Fornieles et al. [15] found that whilst adolescent AN showed similar performance to age-matched controls in a verbal digit N-Back task, they exhibited increased activation in the left superior parietal lobule, an additional vWM area reportedly involved in the manipulation of information [37] and left inferior temporal gyrus, during fMRI examination.

Despite the importance of adolescent data, problems exist in analysing images from young cohorts, due to continuation of functional maturation [19]. This could explain failure to find differences in frontal executive and rehearsal regions and increased activation in the inferior temporal lobe. This area is not commonly activated in this task [49] but responds in WM paradigms during maintenance of visual objects [52], matching of an actively maintained object to a current object [18] and presentation of novel stimuli [42].

In addition, Castro-Fornieles et al. [15] only used the 1-Back condition, which is more representative of a vigilance task assessing attention and storage mechanisms and does not adequately tax prefrontal manipulation mechanisms [60]. Whereas Braver et al. [7] found a positive linear relationship between task load and hyperactivation in the DLPFC, left IFG, ACC and bilateral parietal cortices others indicate that increased activation of the DLPFC only occurs at higher cognitive loads, such as the 2-Back and 3-Back [60].

The current study aims to extend the findings of Castro-Fornieles et al. [15] by including conditions of increasing difficulty to comprehensively assess the effect of cognitive load on vWM. We use an exploratory whole-brain approach and include the largest AN fMRI sample to date, which will increase statistical robustness and enable a comparison of adult and adolescent groups with Castro-Fornieles et al. [15].

In light of the current literature regarding the N-Back task [17,9], we firstly hypothesise that the AN group will show superior