ADHD and dysthymic disorder in children and adolescents: emerging evidence from behavioural and fMRI memory and working memory tasks

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Introduction

Dysthymic disorder (DD) - most prevalent pre-pubertal depressive disorder; a major risk factor for major depressive disorder (MDD). Currently, it is unknown whether there are developmental stage-dependent neurobiological risk factors underlying DD. Further, both ADHD and DD - main drivers for oppositional defiant disorder; the most common reason for referral to mental health services. It is also known that ADHD and early onset depressive disorders such as DD have a ‘greater than chance’ association. Indeed, impairing levels of inattentive type ADHD symptoms - key symptom dimension within the nosological construct of DD.
Introduction (continued)

Yet, to date, little or no systematic research examining the association between ADHD, inattentive type and DD using robust cognitive neuroscience probes with well defined brain behaviour relationships. In this study, we address known key limitations by using spatial memory and spatial working memory tasks constrained by known specific brain behaviour relationships based on non-human primate data to examine 8-12 year old pre-pubertal children with DD (N=26) and 28 matched healthy control participants. Eight post-pubertal and 12 pre-pubertal boys with DD and age-, gender-, handedness- and FSIQ-matched healthy control participants also completed a spatial working memory (mental rotation) fMRI paradigm.
Method

DD defined by
(1)-parent and child structured clinical interview;
(2)-parent and child dimensional report subscale
scores - core symptom domains of DD -
greater than 1.5 standard deviations above the mean
for a given child’s age and gender
- medication and formal psychological treatment naïve -
Healthy control participants - age-, gender,
-fullscale IQ, and - handedness matched

-comorbid diagnoses of learning disorders, DCD, speech/language disorders, major depressive disorder and conduct disorder excluded;

DD children –
consecutively referred for assessment because they were not responding to usual school psychological management approaches delivered at a community primary care level; met the inclusion criteria of living in a family home and attending normal primary schools. All IQs > 80; none had overt neurological disease or psychotic symptoms
The children with DD demonstrated impaired spatial memory abilities compared to the healthy control group (Figure 1). In particular, dysfunction in the attentional processes of encoding stimulus information was implicated rather than retention and recall processes.

Group $F(1,50) = 10.12$, $p = .003$, partial $\eta^2 = .17$; co-varying for the simultaneous MTS condition, $F(1,50) = 6.02$, $p = .02$, partial $\eta^2 = .11$, no significant interaction bw condition and group, Wilks’ $\lambda = .91$, $F(2,49) = 2.35$, $p = .11$.

Further, the children with DD demonstrated spatial working memory (VSWM) deficits compared to the healthy control group (Figure 2). VSWM deficits, including deficits to both the ‘spatial span’ and strategy components of VSWM, as well as associated symptoms of inattention, taken together, implied dysfunction to dorsolateral and ventrolateral fronto-striatal-parietal neural networks.

These memory and working memory impairments correlated with inattentive symptoms.
The adolescent boys with DD demonstrated deceased activation of the right dorsolateral prefrontal cortex and right parietal/precuneus regions (Table 1), while the prepubertal DD boys had additional decreased activation in the right ventrolateral prefrontal cortex, right striatal, right inferior temporal and right insula regions (Table 2). Right frontal-parietal decreased activation correlated with inattentive symptoms.
Discussion – Research Implications

-inattentive symptoms in the DD group correlated with memory (mainly) encoding and working memory deficits and right frontal-parietal dysfunction
-right frontal-parietal dysfunction developmental stage independent finding in DD
-these findings are qualitatively similar to those in children and adolescents with ADHD, combined type
-further (1) pre-pubertal children with DD demonstrated decreased activation in right frontal, striatal and insular brain regions associated with depressed and/or irritable mood and (2) all the above results reflect a dysfunctional use of the same/and or a different SWM strategy in boys with DD because activation differences occurred while behavioural performance did not differ. Therefore DD, apart from the associated inattentive symptoms may also contribute to these aberrant findings. In future, DD with and without inattentive symptoms need to be compared.
Discussion – Clinical Implications

- Early identification of DD is imperative because it is common, an independent driver of ODD – a main driver for referral to public mental health services, working memory deficits contribute to learning difficulties and language acquisition difficulties, it increases the risk of MDD and self harm potential, ADHD and DD share common deficits, such as spatial memory encoding, working memory and right frontal-striatal-parietal under-activation, but they also differ in the specific cognitive and neurological processes affected that comprise these common deficits.

- A specialist multi-disciplinary team needs to comprehensively assess DD and prioritise specific and targeted psychological and/or medication treatments.
Discussion – Clinical Implications

-Specific and targeted psychological and/or medication treatments need to be trialled and evaluated; eg working memory training, comprehensive parent and teacher management training and child skills training run in conjunction, encoding strategies, task persistence strategies and organising and prioritising strategies, educational and/or language remediation

-Further, the potential synergism between (1) medication treatments, for example, stimulant medication for inattentive symptoms and SSRI medication for DD mood symptoms, and (2) the implemented psychological treatments needs to be assessed and maximised through RCTs