Psychological Medicine (2010), **40**, 253–261. © Cambridge University Press 2009
doi:10.1017/S0033291709990365

ORIGINAL ARTICLE

The association of visuospatial working memory with dysthymic disorder in pre-pubertal children

T. Franklin[1], A. Lee[1], N. Hall[1], S. Hetrick[1], J. Ong[1], N. Haslam[2], F. Karsz[1] and A. Vance[1]*

[1] *Academic Child Psychiatry Unit, Department of Paediatrics, University of Melbourne and Royal Children's Hospital and Murdoch Childrens Research Institute, Parkville, Victoria, Australia*
[2] *Department of Psychology, University of Melbourne, Victoria, Australia*

Background. Visuospatial working memory (VSWM) deficits have not been investigated specifically in children with dysthymic disorder (DD), although they are associated with impairments in attention that commonly occur in DD. This study investigates VSWM impairment in children with DD.

Method. A cross-sectional study of VSWM in 6- to 12-year-old children with medication-naive DD ($n=26$) compared to an age-, gender- and 'performance IQ' (PIQ)-matched healthy control group ($n=28$) was completed.

Results. The DD group demonstrated impairment in VSWM, including impairment in the spatial span and strategy components of VSWM. Furthermore, the VSWM impairment remained after controlling for spatial span. Inattentive symptoms were significantly associated with the VSWM impairment.

Conclusions. This study of children with DD found deficits in performance on VSWM tasks, suggesting that fronto-striatal–parietal neural networks that underlie processes of attention and the executive component of VSWM are dysfunctional in children with DD. These findings further our understanding of DD and suggest more specific interventions that might improve functioning.

Received 11 September 2008; Revised 11 April 2009; Accepted 18 May 2009; First published online 17 July 2009

Key words: Attention, children, dysthymic disorder, visuospatial working memory.

Introduction

Dysthymic disorder (DD) is the most common childhood depressive disorder, especially in clinically referred samples (Kovacs *et al*. 1994). In addition to the core diagnostic symptom of chronically depressed and/or irritable mood, DD is associated with impairing levels of inattention according to DSM-IV-R criteria (APA, 2000). Poor attention, difficulty concentrating and difficulty with decision making have been observed clinically in children with DD (Mitchell *et al*. 1988; Ferro *et al*. 1994; Kovacs *et al*. 1994; Masi *et al*. 2001). These symptoms of DD are thought to impair cognitive development and functioning in academic domains (Kovacs & Goldston, 1991).

Deficits in neuropsychological measures of attention (Livingston *et al*. 1996; Cataldo *et al*. 2005) and memory (Lauer *et al*. 1994) have been reported in children and adolescents with major depressive disorder (MDD) with or without DD, although MDD and DD have not been examined separately. Adolescents with MDD have shown an affective attentional bias and evidence of cognitive impulsivity (Kyte *et al*. 2005) and impaired performance on visual memory tasks (Matthews *et al*. 2008). Furthermore, there are known associations of inattentive symptoms with impaired performance on neuropsychological measures such as visuospatial working memory (VSWM) (Kempton *et al*. 1999; Barnett *et al*. 2001). This is consistent with the known overlap of the neural substrates that subserve visuospatial attention and VSWM (Smyth, 1996; Awh *et al*. 2006), specifically right hemisphere dominant activation in frontal and parietal brain regions (Awh & Jonides, 1998). A recent study found that adolescents with MDD displayed VSWM performance deficits on the Cambridge Neuropsychological Test Automated Battery (CANTAB) spatial working memory task, including significantly more between-search errors (BSEs) and poorer use of strategy compared to healthy control participants (Matthews *et al*. 2008). The depressed group did not display performance deficits on the CANTAB Spatial Span measure. This suggests impairment to 'executive' aspects of neuropsychological functioning in adolescent MDD. Evidence of 'executive' deficits associated with DD in children

* Address for correspondence: Professor A. Vance, Head, Academic Child Psychiatry Unit, Department of Paediatrics, University of Melbourne, Royal Children's Hospital, Parkville, Victoria, Australia 3052.
(Email: avance@rch.org.au)

and adolescents include poor decision making (Ferro *et al*. 1994) and poor performance on the Stroop Task (Cataldo *et al*. 2005). Adults with DD have shown performance deficits on the Trail Making Task B (Airaksinen *et al*. 2004) and the Wisconsin Card Sorting Task (Martin *et al*. 1991). However, to date, VSWM has not been investigated in children and adolescents with DD. This is important so that it can be ascertained whether VSWM impairments are developmental stage independent.

Further examination of the neuropsychological profile of DD using measures of VSWM is supported by the following findings: disruption to fronto-striatal neural networks has been associated with impairments in attention (Lange *et al*. 1992; Lawrence *et al*. 2000; Barnett *et al*. 2001) and VSWM (Owen *et al*. 1995; Pantelis *et al*. 1997). In addition, models of the brain–behaviour relationship between VSWM and the prefrontal cortex (PFC) are well evidenced by single neuronal firing rates in alert primates (Goldman-Rakic, 1987; Goldman-Rakic & Selemon, 1997), studies of behaviour following focal PFC lesions in adult humans (Owen *et al*. 1993) and studies of patterns of regional cerebral blood flow in healthy humans performing VSWM tests (D'Esposito *et al*. 1995). The experimental VSWM paradigm can be applied to studies of children and adolescents without modification (Barnett *et al*. 2001). VSWM is largely non-verbal, so that deficits in verbal functioning observed in children with depressive disorders (Kovacs & Goldston, 1991) do not confound testing. From a clinical viewpoint, the majority of children with DD develop MDD (i.e. 76%), suggesting that childhood DD is a 'window of opportunity' for early identification of and intervention for the development of MDD (Kovacs *et al*. 1994). This suggests the importance of specific studies that characterize DD in children, including clarifying associated neuropsychological impairments such as VSWM.

The CANTAB (Owen *et al*. 1996) VSWM task provides an overall measure of VSWM, measured as BSE performance, in addition to measures of two key components of VSWM: (1) the ability to maintain information 'online' in a visuospatial sketchpad (Baddeley, 1986), measured as 'spatial span', and (2) the ability to develop a systematic search strategy during task performance, measured as 'strategy' (Owen *et al*. 1990; Robbins *et al*. 1994; Pantelis *et al*. 1997; Vance *et al*. 2006*b*). This approach allows analysis of the contribution of either or both components of VSWM to observed poor BSE performance (Pantelis *et al*. 1997; Barnett *et al*. 2001; Vance *et al*. 2006*b*) and has informed the analysis of functional neural networks that subserve the construct of VSWM and its two key components. In a functional imaging study of healthy adult human subjects, Owen *et al*. (1996) found that two functionally distinct subdivisions of the lateral frontal cortex subserve different components of VSWM. During the 'online' maintenance of visuospatial information in working memory, assessed using a task identical to the CANTAB measure of spatial span, there was significant activation in the ventrolateral PFC (Brodmann Area 47), whereas the active monitoring and manipulation of spatial information within working memory was associated with significant activation in mid-dorsolateral prefrontal cortical areas 9 and 46.

Hence, the present study investigated the association of DD with VSWM in pre-pubertal children aged 6–12 years by examining the VSWM performance of medication-naïve, pre-pubertal children with DD. The CANTAB VSWM task was used to measure overall VSWM ability, and also the strategy component of VSWM, whereas the CANTAB Spatial Span task allowed a measure of the spatial span component of VSWM. It was hypothesized that VSWM performance would be impaired in the DD group compared to a healthy control group, with additional impairments in the strategy but not in the spatial span components of VSWM in the DD group.

Method

Participants

The total sample comprised 54 children aged 6–12 years. There were 28 children in the healthy control group and a group of 26 children with medication-naïve DD. The DD group children were identified from 92 children with DD referred to an out-patient clinic at a large metropolitan child psychiatry unit. They had been referred to the clinic for diagnostic review and treatment initiation from school support staff at local primary schools. These 26 male and female pre-pubertal [Tanner stage I (Tanner, 1966)] children aged 6–12 years [mean (S.D.) 9.96 (1.73) years] were identified with medication-naïve DD according to DSM-IV-R criteria (APA, 2000) during their initial clinical evaluation. These patients had no other known medical, neurological or endocrine disorders, MDD, attention deficit hyperactivity disorder, combined type (ADHD-CT), conduct disorder, developmental coordination disorder or reading/spelling learning disorders [Wide Range Achievement Test, 3rd Edition (WRAT-3); Wilkinson, 1993]. These specific psychiatric disorders were excluded because of their known independent association with VSWM.

A diagnosis of DD was defined through separate semi-structured clinical interviews with parent(s) and child [Anxiety Disorders Interview Schedule for Children (A-DISC); Silverman & Albano, 1996].

Table 1. *Group characteristics*

	DD ($n=26$)	Control ($n=28$)	$t(52)$	p
Age (years), mean (S.D.)	9.96 (1.73)	10.11 (1.26)	−0.36	0.72
Gender (M/F)	20/6	17/11	1.64[a]	0.20
PIQ, mean (S.D.)	100.08 (11.12)	105.43 (12.33)	−1.67	0.10
CBCL anx/dep, mean (S.D.)	73.00 (11.04)	54.12 (7.77)	7.13	<0.0005
CDI, mean (S.D.)	69.69 (5.82)	41.48 (7.98)	14.66	<0.0005
CBCL att, mean (S.D.)	70.88 (9.75)	52.00 (3.05)	9.43	<0.0005

DD, Dysthymic disorder; M, male; F, female; PIQ, perceptual reasoning index using the Wechsler Intelligence Scale for Children, version 4; CBCL anx/dep, Child Behavior Checklist anxiety depression subscale; CDI, Children's Depression Inventory total depression scale; CBCL att, Child Behavior Checklist attention subscale; S.D., standard deviation.

[a] χ^2 test used for categorical variables.

Symptoms of DD were also evaluated using parent report [Child Behavior Checklist (CBCL) anxiety depression subscale; Achenbach & Edelbrock, 1983] and child report [Children's Depression Inventory (CDI) total depression scale; Kovacs, 1992], where clinical-level DD symptoms were observed to be greater than 1.5 S.D. above the mean for a child's age and gender (Table 1). Inattention was also measured as part of the standard clinical assessment, through parent report of child inattentive symptoms (CBCL attention scale; Achenbach & Edelbrock, 1983).

Children in the healthy control group did not meet the diagnostic criteria for DD, as defined using the same clinical measures. The healthy control children were recruited from local primary schools and volunteered to participate in the study. These 28 prepubertal (Tanner stage I) male and female healthy control participants did not meet criteria for any other psychiatric, neurological or endocrine disorder. They did not differ from the clinical group in age, gender or 'performance IQ' (PIQ), as assessed by the perceptual reasoning index from the Wechsler Intelligence Test for Children – 4th edition (WISC-IV; Wechsler, 2003) (Table 1). All of the healthy control children were tested at home.

Computerized neuropsychological tasks

VSWM was assessed through measurement of performance on the Spatial Working Memory and Spatial Span tasks selected from the CANTAB (Owen *et al*. 1996). The computerized tests were presented on a high-resolution IBM monitor with a touch-sensitive screen. All the children reported previous experience with computers and were tested using the same apparatus.

The CANTAB Spatial Span task is a computerized version of the Corsi block-tapping test that assesses visuospatial short-memory capacity (Milner, 1971). This task measures the ability to remember a sequence of squares presented on the screen. After an incorrect attempt at choosing the squares in sequence, the next trial remains at the same difficulty level. A Spatial Span score was calculated as the highest level at which the participant successfully remembered at least one sequence of boxes.

The CANTAB Spatial Working Memory task is a self-ordered search task that measures working memory for spatial stimuli and requires the subject to use mnemonic information to work towards a goal. Participants are required to search through boxes that appear on the screen with the aim of finding the blue tokens hidden inside. The key instruction is that once a token has been taken out of a box, that box will not be used again to hide a token. There were four test trials with each of three, four, six and eight boxes. Returning to an 'empty' box, already opened and a token removed on a previous search, constituted a 'forgetting' or BSE. Performance accuracy was defined as the total number of BSEs (i.e. higher BSE rates indicate lower accuracy of VSWM performance). This was the key functional measure of VSWM. Response latencies, measured in milliseconds (ms), were obtained for each trial. This recorded the time difference between the presentation of boxes on the screen and the end of the trial when all the blue tokens have been found.

A Strategy score was calculated from each participant's performance on the six and eight box levels, to reflect how often a searching sequence was initiated from the same box during a given trial. Higher Strategy scores represent low use of strategy (i.e. many sequences beginning with a different box in a given trial). Lower scores represent efficient use of strategy (i.e. many sequences starting with the same box in a given trial).

Table 2. *Group performance on the Spatial Span task and the Visuospatial Working Memory (VWSM) task, including the between-search errors (BSEs) and the Strategy components*

	DD ($n=26$) Mean (S.D.)	Control ($n=28$) Mean (S.D.)	p
Visuospatial Working Memory			0.000[a]
BSE level 3	0.31 (0.74)	0.00 (0.00)	
BSE level 4	2.81 (2.48)	0.61 (1.13)	
BSE level 6	18.27 (7.00)	8.89 (4.94)	
BSE level 8	35.38 (7.92)	23.61 (10.31)	
Spatial Span	5.08 (1.06)	6.11 (1.34)	0.008
Strategy	37.88 (3.66)	33.75 (4.92)	0.006

DD, Dysthymic disorder; S.D., standard deviation.

[a] The significance of the repeated-measures ANCOVA across BSE levels of difficulty $p<0.0005$.

Data analysis

Performance on (1) the Spatial Working Memory BSE variable, including both the accuracy and response latency variables, and (2) the Strategy and Spatial Span variables was compared between groups using respective (1) repeated-measures and (2) one-way analysis of covariance (ANCOVA), covarying for the effects of age and PIQ, given the known sensitivity of these VSWM measures to these variables (Kravariti, 2003*a*, *b*; Barnett *et al*. 2005). Then, the Spatial Working Memory BSE variable was compared between groups using a repeated-measures ANCOVA, covarying for the effects of spatial span. To estimate effect sizes, Cohen's *d* calculation for unequal sample sizes was used to examine differences between group performance on both accuracy and latency measures. To investigate the contribution of Spatial Span and Strategy to overall VSWM, the correlations between BSE and Spatial Span and between BSE and Strategy were computed using the total number of BSEs (across all levels of difficulty). To investigate the association of VSWM with inattentive symptoms, the correlation between the total number of BSEs and inattention symptom scores was computed. Each of these correlations examined the relationships between variables in the combined sample, including healthy control and clinical participants.

Results

Descriptive statistics

Table 1 shows the mean age and PIQ for the healthy control group and the DD group. Independent samples *t* tests showed that the two groups did not differ significantly with respect to mean PIQ [$t(52)=-1.67$, $p=0.10$] and age [$t(52)=-0.36$, $p=0.72$]. Pearson χ^2 tests showed that the two groups did not differ significantly with respect to gender [$\chi^2(1)=1.64$, $p=0.20$]. In the DD group, 77% of participants were male and 23% were female. In the healthy control group, 61% of participants were male and 39% were female. DD patients exhibited significantly higher depressive symptoms according to both parent [$t(52)=7.13$, $p<0.0005$] and child [$t(52)=14.66$, $p<0.0005$] reports, and also higher inattentive symptoms [$t(52)=9.43$, $p<0.0005$] (Table 1).

VSWM task accuracy (BSEs)

Differences in accuracy of performance (BSEs) across diagnostic group were analysed using a 2 (group) × 4 (level) repeated-measures ANCOVA. Table 2 shows the mean BSEs for each group at each difficulty level on the VSWM task. There was a significant effect of condition (number of boxes) [Wilks' $\lambda=0.50$, $F(3,48)=16.30$, $p<0.0005$] and diagnostic group [$F(1,50)=37.78$, $p<0.0005$, partial $\eta^2=0.43$] on the number of BSEs, after covarying for age [$F(1,50)=8.64$, $p=0.005$, partial $\eta^2=0.15$] and PIQ [$F(1,50)=18.98$, $p<0.0005$, partial $\eta^2=0.28$], both of which had a significant independent association with the number of BSEs. The DD group made significantly more errors than the healthy control group (see Fig. 1). Cohen's *d* (1.67) showed a large effect size. There was also a significant interaction between condition and group [Wilks' $\lambda=0.57$, $F(3,48)=11.98$, $p<0.0005$] after covarying for age and PIQ. The difference between the number of BSEs for each group increased with increasing level of task difficulty (Fig. 1). Significant independent interactions were also found between condition and age [Wilks' $\lambda=0.85$, $F(3,48)=2.84$, $p=0.048$] and condition and PIQ [Wilks' $\lambda=0.73$, $F(3,48)=5.93$, $p=0.002$].

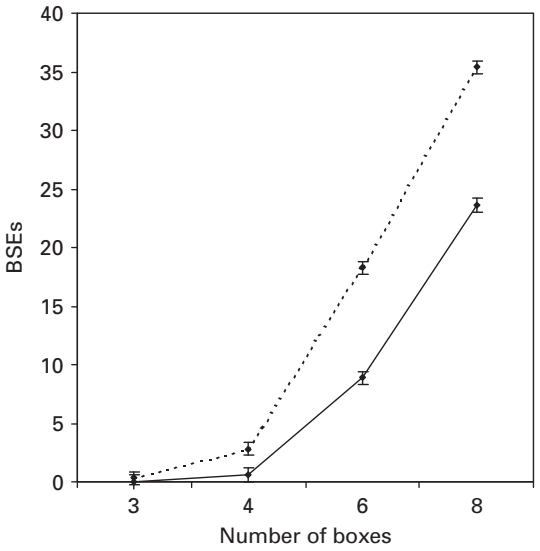

Fig. 1. The number of between-search errors (BSEs) at each level of difficulty of the visuospatial working memory task, for the healthy control group (–◆–) and dysthymic disorder group (···◆···) (standard error bars included).

None of these associations differed after the additional covariate, spatial span, was added to the analysis. There was a significant effect of condition (number of boxes) [Wilks' $\lambda = 0.49$, $F(3, 47) = 16.46$, $p < 0.0005$] and diagnostic group [$F(1, 49) = 28.21$, $p < 0.0005$, partial $\eta^2 = 0.37$] on the number of BSEs after covarying for age and PIQ. There was also a significant interaction between condition and group [Wilks' $\lambda = 0.63$, $F(3, 47) = 9.06$, $p < 0.0005$] after covarying for age and PIQ.

VSWM task response latency

Differences in the response latency (ms) on the VSWM task across diagnostic group were analysed using a 2 (group) × 4 (level) repeated-measures ANCOVA. There was a significant effect of condition [Wilks' $\lambda = 0.72$, $F(3, 48) = 6.21$, $p = 0.001$] and diagnostic group [$F(1, 50) = 4.24$, $p = 0.045$, partial $\eta^2 = 0.08$] after covarying for age [$F(1, 50) = 6.095$, $p = 0.017$, partial $\eta^2 = 0.11$] and PIQ [$F(1, 50) = 0.74$, $p = 0.39$, partial $\eta^2 = 0.02$]. Only age had a significant independent association with response latency. The DD group displayed longer response latencies than the healthy control group (see Fig. 2). Cohen's d (0.64) showed a medium effect size. There was also a significant interaction between latency and diagnostic group [Wilks' $\lambda = 0.72$, $F(3, 48) = 6.38$, $p = 0.001$] after covarying for age and PIQ. The difference in latency between groups differed with increasing level of difficulty (see Fig. 2). No significant interactions were found between latency and PIQ [Wilks' $\lambda = 0.902$, $F(3, 48) = 1.73$, $p = 0.17$] or between latency and age [Wilks' $\lambda = 0.899$, $F(3, 48) = 1.803$, $p = 0.16$].

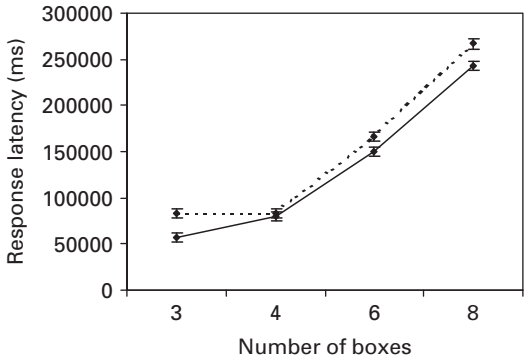

Fig. 2. Response latency on the visuospatial working memory task at each difficulty level for each group (standard error bars included). –◆–, Healthy control group; ···◆···, dysthymic disorder group.

Spatial span

A univariate ANCOVA was used to analyse the difference between the mean spatial span for each diagnostic group. There was a significant difference between the two diagnostic groups in spatial span performance [$F(1, 50) = 7.727$, $p = 0.008$, partial $\eta^2 = 0.13$] (see Table 2) after covarying for age [$F(1, 50) = 9.09$, $p = 0.004$, partial $\eta^2 = 0.15$] and PIQ [$F(1, 50) = 2.17$, $p = 0.15$, partial $\eta^2 = 0.04$]. Only age had a significant independent association with spatial span performance. The spatial span for the DD group (mean = 5.08, S.D. = 1.06) was lower than for the healthy control group (mean = 6.11, S.D. = 1.34). Cohen's d (0.85) indicated that this was a large effect.

Strategy

Univariate ANCOVA was used to analyse the difference between the mean strategy score for each diagnostic group. There was a significant difference between the two diagnostic groups in search strategy used during the VSWM task [$F(1, 50) = 8.27$, $p = 0.006$, partial $\eta^2 = 0.14$] (see Table 2) after covarying for age [$F(1, 50) = 4.02$, $p = 0.05$, partial $\eta^2 = 0.07$] and PIQ [$F(1, 50) = 13.45$, $p = 0.001$, partial $\eta^2 = 0.21$]. Only PIQ had a significant independent association with search strategy performance. The strategy score for the DD group (mean = 37.88, S.D. = 3.66) was higher, indicating a less efficient search, than for the healthy control group (mean = 33.75, S.D. = 4.92). Cohen's d (0.95) again showed a large effect size.

Correlations between VSWM, span and strategy

The relationships between VSWM (BSEs) and the spatial span and strategy components of VSWM were

assessed in the combined sample. There was a significant negative correlation between total BSEs and spatial span ($r = -0.57$, $p < 0.0005$) and a significant positive correlation between total BSEs and strategy ($r = 0.67$, $p < 0.0005$).

Correlation between symptoms of inattention and VSWM

The relationship between symptoms of inattention and VSWM performance was examined in the combined sample. The VSWM total accuracy score (as defined by the number of BSEs across all VSWM task levels) had a large positive correlation with the parent report of child inattentive symptoms (CBCL inattentive subscale score) ($r = 0.62$, $p < 0.0005$).

Discussion

Pre-pubertal children with DD demonstrated impaired VSWM performance that worsened as the cognitive demands of the VSWM task increased. Deficits were also evident in both the spatial span and strategy components of VSWM in the DD group. These findings suggest that children with DD are impaired in their ability to maintain spatial information 'online' in VSWM and in their ability to develop a systematic search strategy during task performance. Correlational analyses implied that deficits in the maintenance and manipulation of spatial information in VSWM contribute to the impairment in overall VSWM ability displayed by the DD group. Furthermore, the VSWM impairment remained after covarying for spatial span. This implies that the executive component of VSWM is dysfunctional in children with DD.

These results extend Matthews *et al.*'s (2008) findings in adolescent girls with MDD: first, pre-pubertal children, males and females, with DD also manifest impaired VSWM performance. Second, spatial span is also impaired in this younger group, unlike the adolescent sample. Third, the executive component of VSWM is also dysfunctional in this younger group, despite their spatial span deficits. Fourth, these further cross-sectional findings in a younger group may reflect depressive disorder-related processes rather than pre-morbid vulnerability alone.

Additional analyses revealed longer response times on the VSWM task for children with DD, evident at levels 3, 6 and 8 of the task. This may be due to their clinically significant inattention and manifest orienting to task difficulties (e.g. their longer response times on level 3). The similar response times between groups on level 4 suggest that motor dysfunction is unlikely to be associated with DD in pre-pubertal children. Finally, the longer response times and the lower accuracy of performance on levels 6 and 8 are consistent with the use of less efficient search strategies by the DD group. This further suggests that children with DD had difficulties with manipulating information held 'online' in VSWM.

It is known that dysfunction to fronto-striatal–parietal neural networks is associated with impaired abilities in the manipulation of spatial information in VSWM (Owen *et al*. 1995; Braver *et al*. 1997, 2001; Pantelis *et al*. 1997; Vance *et al*. 2007). The VSWM, especially strategy, performance deficits suggest that DD in children is associated with dysfunction to these fronto-striatal–parietal neural networks. In addition, deficits in spatial span ability suggest there is dysfunction involving mid-ventrolateral prefrontal and posterior parietal cortical regions in DD (Owen *et al*. 1996; Smith *et al*. 1996; Carlson *et al*. 1998).

Fronto-striatal–parietal dysfunction is also associated with clinically significant inattention (Barnett *et al*. 2001; Vance *et al*. 2007). Furthermore, dysfunction of neural networks involving the dorsolateral PFC (DLPFC), anterior cingulate cortex and striatal brain regions (Cannon *et al*. 2005; Castellanos *et al*. 2006) are thought to underpin the association of inattention and working memory. Given that the children with DD were significantly more inattentive and that inattentive symptoms were significantly associated with VSWM impairments, dysfunction to DLPFC-linked fronto-striatal neural networks is implicated in childhood DD. However, the observed deficits of VSWM may be linked to symptoms of inattention in general, rather than DD specifically (Vance *et al*. 2006*a*). Further studies should delineate whether or not VSWM deficits are associated with the neurobiology of DD *per se*, for example by examining VSWM in children with DD and no inattentive symptoms. In addition, there is need for further research examining whether dysfunction to DLPFC-linked fronto-striatal neural networks and also their connections with limbic regions (Carmichael & Price, 1995; Mayberg *et al*. 1999; Haber, 2003) are associated with the cognitive and affective symptoms of DD.

Clinical implications

Inattentive symptoms may contribute to the learning difficulties and impairments in academic functioning that have been observed in children with DD (Kovacs & Goldston, 1991; Friedman *et al*. 1995). Interventions targeting inattention may thus be helpful. The observed VSWM deficits also suggest that children with DD have trouble with holding spatial information 'online' in working memory, and manipulating this information. This may have implications for the presentation of information. For example, when children

with DD are learning or receiving instructions, they may respond better to smaller, more simple pieces of information that are presented repeatedly, particularly in high-stimulus, novel environments such as the school classroom. These interventions may also be useful in the home or in clinical settings. Stimulant medication may be helpful for this group of children, who can become severely oppositional and defiant in these contexts (Vance *et al*. 2005); however, future randomized controlled trials are needed.

Poor academic performance may exacerbate the symptoms of low self-esteem displayed by children with DD (Masi *et al*. 2001). Low self-esteem is also likely to contribute to the impaired peer relationships frequently observed during the symptomatic period of DD (Klein *et al*. 2000). Clearly, addressing cognitive, academic and social functioning is important in the treatment of childhood DD.

Study limitations

The levels of the VSWM task were presented in order of increasing cognitive demand, rather than randomized. This may suggest that the poor performance of children with DD on levels 6 and 8 of the task reflects increases in cognitive fatigue, inattention or low motivation as the task progressed. However, the order of presentation was controlled for between the two diagnostic groups. Furthermore, the CANTAB has been validated in developmental studies of children and adolescents (Luciana & Nelson, 1998; De Luca *et al*. 2003), and used in previous clinical studies of children with psychiatric disorders featuring inattentive symptoms, such as ADHD (Williams *et al*. 2000; Barnett *et al*. 2001; Cairney *et al*. 2001; Vance *et al*. 2003) and early onset schizophrenia (Vance *et al*. 2006*b*). Thus, the present findings are more likely to reflect actual deficits of VSWM and the impact of poor spatial span and strategy abilities on VSWM performance. Another limitation is that the present study was a clinical study of children with 'pure' DD. It is not certain whether the findings may be generalized to the wider community or to patients with DD and a further diagnosed co-morbid disorder. Future research should examine the neuropsychological profile of children with DD and key co-morbid disorders, particularly MDD (Kovacs *et al*. 1994).

Conclusions

In summary, the present findings support an association between VSWM and DD in pre-pubertal children. VSWM deficits, including deficits to both the spatial span and strategy components of VSWM, and also associated symptoms of inattention, taken together, imply dysfunction to dorsolateral and ventrolateral fronto-striatal–parietal neural networks. Further neuropsychological and functional neuroimaging studies are required to extend these findings.

Acknowledgements

This research was supported by project grants obtained from the University of Melbourne, Murdoch Childrens Research Institute and the Royal Children's Hospital. We thank the staff and patients at the Royal Children's Hospital.

Declaration of Interest

None.

References

Achenbach TM, Edelbrock CS (1983). *Manual for the Child Behavior Checklist and Behavior Profile*. University of Vermont: Burlington.

Airaksinen E, Larsson M, Lundberg I, Forsell Y (2004). Cognitive functions in depressive disorders: evidence from a population-based study. *Psychological Medicine* **34**, 83–91.

APA (2000). *Diagnostic and Statistical Manual of Mental Disorders*, 4th edn, text revision. American Psychiatric Association: Washington, DC.

Awh E, Jonides J (1998). Spatial selective attention and spatial working memory. In *The Attentive Brain* (ed. R. Parasuraman), pp. 353–380. MIT Press: Cambridge, MA.

Awh E, Vogel EK, Oh SH (2006). Interactions between attention and working memory. *Neuroscience* **139**, 201–208.

Baddeley A (1986). *Working Memory*. Oxford University Press: New York.

Barnett R, Maruff P, Vance A (2005). An investigation of visuospatial memory impairment in children with attention deficit hyperactivity disorder (ADHD), combined type. *Psychological Medicine* **35**, 1433–1443.

Barnett R, Maruff P, Vance A, Luk ESL, Costin J, Wood C, Pantelis C (2001). Abnormal executive function in attention deficit hyperactivity disorder: the effect of stimulant medication and age on spatial working memory. *Psychological Medicine* **31**, 1107–1115.

Braver TS, Barch DM, Kelley WM, Buckner RL, Cohen NJ, Miezen FM, Snyder AZ, Ollinger JM, Akbudak E, Conturo TE, Petersen SE (2001). Direct comparison of prefrontal cortex regions engaged by working and long-term memory tasks. *NeuroImage* **14**, 48–59.

Braver TS, Cohen JD, Nystrom LE, Jonides J, Smith EE, Noll DC (1997). A parametric study of prefrontal cortex involvement in human working memory. *NeuroImage* **5**, 49–62.

Cairney S, Maruff P, Vance A, Barnett R, Luk E, Currie J (2001). Contextual abnormalities of saccadic inhibition in

children with attention deficit hyperactivity disorder. *Experimental Brain Research* **141**, 507–518.

Cannon TD, Glahn DC, Kim J, Van Erp TGM, Karlsgot K, Cohen MS, Nuechterlein KH, Bava S, Shirinyan D (2005). Dorsolateral prefrontal cortex activity during maintenance and manipulation of information in working memory in patients with schizophrenia. *Archives of General Psychiatry* **62**, 1071–1080.

Carlson S, Martinkauppi S, Rama P, Salli E, Korvenoja A, Aronen HJ (1998). Distribution of cortical activation during visuospatial n-back tasks as revealed by functional magnetic resonance imaging. *Cerebral Cortex* **8**, 743–752.

Carmichael ST, Price JL (1995). Limbic connections of the orbital and medial prefrontal cortex in macaque monkeys. *Journal of Comparative Neurology* **363**, 615–641.

Castellanos FX, Sonuga-Barke EJS, Milham MP, Tannock R (2006). Characterizing cognition in ADHD: beyond executive dysfunction. *Trends in Cognitive Sciences* **10**, 117–123.

Cataldo MG, Nobile M, Lorusso ML, Battaglia M, Molteni M (2005). Impulsivity in depressed children and adolescents: a comparison between behavioural and neuropsychological data. *Psychiatry Research* **136**, 123–133.

De Luca CR, Wood SJ, Anderson V, Buchanan J, Proffitt TM, Mahony K, Pantelis C (2003). Normative data from the CANTAB. I: Development of executive function over the lifespan. *Journal of Clinical and Experimental Neuropsychology* **25**, 242–254.

D'Esposito M, Detre JA, Alsop DC, Shin RK, Atlas S, Grossman M (1995). The neural basis of the central executive system of working memory. *Nature* **378**, 279–281.

Ferro T, Carlson GA, Grayson P, Klein DN (1994). Depressive disorders: distinction in children. *Journal of the American Academy of Child and Adolescent Psychiatry* **33**, 664–670.

Friedman RA, Markowitz JC, Parides M, Kocsis JH (1995). Acute response of social functioning in dysthymic patients with desiplamine. *Journal of Affective Disorders* **34**, 84–88.

Goldman-Rakic PS (1987). Circuitry of primate prefrontal cortex and regulation of behavior by representational memory. In *Handbook of Physiology: Section 1, The Nervous System, Volume V, Parts 1 and 2: Higher Functions of the Brain* (ed. F. Plum), pp. 373–417. American Physiological Society: Bethesda.

Goldman-Rakic PS, Selemon LD (1997). Functional and anatomical aspects of prefrontal pathology in schizophrenia. *Schizophrenia Bulletin* **23**, 437–458.

Haber SH (2003). The primate basal ganglia: parallel and integrative networks. *Journal of Chemical Neuroanatomy* **26**, 317–330.

Kempton S, Vance A, Maruff P, Luk ESL, Costin J, Pantelis C (1999). Executive function and attention deficit hyperactivity disorder: stimulant medication and better executive function performance in children. *Psychological Medicine* **29**, 527–538.

Klein DN, Schwartz JE, Rose S, Leader JB (2000). Five-year course and outcome of dysthymic disorder: a prospective, naturalistic follow-up study. *American Journal of Psychiatry* **157**, 931–939.

Kovacs M (1992). *The Children's Depression Inventory*. Mental Health Systems: New York.

Kovacs M, Akiskal HS, Gatsonis C, Parrone PL (1994). Childhood-onset dysthymic disorder: clinical features and prospective naturalistic outcome. *Archives of General Psychiatry* **51**, 365–374.

Kovacs M, Goldston D (1991). Cognitive and social cognitive-development of depressed children and adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry* **30**, 388–392.

Kravariti E, Morris R, Rabe-Hesketh S, Murray RM, Frangou S (2003*a*). The Maudsley Early-Onset Schizophrenia Study: cognitive function in recent onset schizophrenia. *Schizophrenia Research* **61**, 137–148.

Kravariti E, Morris R, Rabe-Hesketh S, Murray RM, Frangou S (2003*b*). The Maudsley Early-Onset Schizophrenia Study: cognitive function in adolescent-onset schizophrenia. *Schizophrenia Research* **65**, 95–103.

Kyte ZA, Goodyer IM, Sahakian BJ (2005). Selected executive skills in adolescents with recent first episode major depression. *Journal of Child Psychology and Psychiatry* **46**, 995–1005.

Lange KW, Robbins TW, Marsden CD, James M, Owen AM, Paul GM (1992). L-Dopa withdrawal in Parkinson's disease selectively impairs cognitive performance in tests sensitive to frontal dysfunction. *Psychopharmacology* **107**, 394–404.

Lauer RE, Giordani B, Boivin MJ, Halle N, Glasgow B, Alessi NE, Berent S (1994). Effects of depression on memory performance and metamemory in children. *Journal of the American Academy of Child and Adolescent Psychiatry* **33**, 679–685.

Lawrence AD, Watkins LHA, Sahakian BJ, Hodges JR, Robbins TW (2000). Visual object and visuospatial cognition in Huntington's disease: implications for information processing in corticostriatal circuits. *Brain* **123**, 1349–1364.

Livingston RB, Stark KD, Haak RA, Jennings E (1996). Neuropsychological profiles of children with depressive and anxiety disorders. *Child Neuropsychology* **2**, 48–62.

Luciana M, Nelson CA (1998). The functional emergence of prefrontally-guided working memory systems in four- to eight-year-old children. *Neuropsychologia* **36**, 273–293.

Martin DJ, Oren Z, Boone K (1991). Major depressives' and dysthymics' performance on the Wisconsin Card Sorting Test. *Journal of Clinical Psychology* **47**, 684–690.

Masi G, Favilla L, Mucci M, Poli P, Romano R (2001). Depressive symptoms in children and adolescents with dysthymic disorder. *Psychopathology* **34**, 29–35.

Matthews K, Coghill D, Rhodes S (2008). Neuropsychological functioning in depressed adolescent girls. *Journal of Affective Disorders*, **111**, 113–118.

Mayberg HS, Liotti M, Brannan SK, McGinnis S, Mahurin RK, Jerbek PA, Silva JA, Tekell JL, Martin CC, Lancaster JL, Fox PT (1999). Reciprocal limbic-cortical function and negative mood: converging PET findings in depression and normal sadness. *American Journal of Psychiatry* **156**, 675–682.

Milner B (1971). Interhemispheric differences in the localisation of psychological processes in man. *British Medical Bulletin* **27**, 272–277.

Mitchell J, McCauley E, Burke PM, Moss SJ (1988). Phenomenology of depression in children and adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry* **27**, 12–20.

Owen AM, Downes JJ, Sahakian BJ, Polkey CE, Robbins TW (1990). Planning and spatial working memory following frontal lobe lesions in man. *Neuropsychologia* **28**, 1021–1034.

Owen AM, Evans AC, Petrides M (1996). Evidence for a two-stage model of spatial working memory processing within the lateral frontal cortex: a positron emission tomography study. *Cerebral Cortex* **6**, 31–38.

Owen AM, Roberts AC, Hodges JR, Summers BA, Polkey CE, Robbins TW (1993). Contrasting mechanisms of attentional set-shifting in patients with frontal lobe damage or Parkinson's disease. *Brain* **116**, 1159–1175.

Owen AM, Sahakian BJ, Semple J, Polkey CE, Robbins TW (1995). Visuo-spatial short-term recognition memory and learning after temporal lobe excisions, frontal lobe excisions or amygdalo-hippocampectomy in man. *Neuropsychologia* **33**, 1–24.

Pantelis C, Barnes TRE, Nelson HE, Tanner S, Weatherley L, Owen AM, Robbins TW (1997). Fronto-striatal cognitive deficits in patients with chronic schizophrenia. *Brain* **120**, 1823–1843.

Robbins TW, James M, Owen AM, Sahakian BJ, McInnes L, Rabbitt P (1994). Cambridge Neuropsychological Test Automated Battery (CANTAB): a factor analytic study of a large sample of normal elderly volunteers. *Dementia* **5**, 266–281.

Silverman WK, Albano AM (1996). *Anxiety Disorders Interview Schedule for DSM-IV*. Graywind: Texas.

Smith EE, Jonides J, Koeppe RA (1996). Dissociating verbal and spatial working memory using PET. *Cerebral Cortex* **96**, 11–20.

Smyth MM (1996). Interference with rehearsal in spatial working memory in the absence of eye movements. *Journal of Experimental Psychology* **49**, 940–949.

Tanner JM (1966). *Growth at Adolescence*, 2nd edn. Appleton-Century-Crofts: New York, NY.

Vance A, Arduca Y, Sanders M (2005). The associations of oppositional defiant behaviour in children with attention deficit hyperactivity disorder, combined type (ADHD-CT). *Journal of Affective Disorders* **86**, 329–333.

Vance A, Arduca Y, Sanders M, Karamitsios M, Hall N, Hetrick S (2006*a*). Attention deficit hyperactivity disorder, combined type, dysthymic disorder and anxiety disorders: differential patterns of neurodevelopmental deficits. *Psychiatry Research* **143**, 213–222.

Vance A, Hall N, Bellgrove M, Casey M, Karsz F (2006*b*). Visuospatial working memory deficits in adolescent-onset schizophrenia. *Schizophrenia Research* **87**, 223–227.

Vance AL, Maruff P, Barnett R (2003). Attention deficit hyperactivity disorder, combined type: better executive function performance with longer-term psychostimulant medication. *Australian and New Zealand Journal of Psychiatry* **37**, 570–576.

Vance A, Silk T, Casey M, Rinehart N, Bradshaw J, Bellgrove M, Cunnington R (2007). Right parietal dysfunction in children with attention deficit hyperactivity disorder, combined type: a functional MRI study. *Molecular Psychiatry* **12**, 826–832.

Wechsler D (2003). *The Wechsler Intelligence Scale for Children – 4th Edition* (WISC-IV). The Psychological Corporation: San Antonio, TX.

Wilkinson GS (1993). *Wide Range Achievement Test*, 3rd edn. Jastak Assessment Systems: Wilmington, DE.

Williams D, Stott CM, Goodyer IM, Sahakian BJ (2000). Specific language impairment with or without hyperactivity: neuropsychological evidence for frontostriatal dysfunction. *Developmental Medicine and Child Neurology* **42**, 368–375.

Author/s:
Franklin, T;Lee, A;Hall, N;Hetrick, S;Ong, J;Haslam, N;Karsz, F;Vance, A

Title:
The association of visuospatial working memory with dysthymic disorder in pre-pubertal children

Date:
2010-02

Citation:
Franklin, T., Lee, A., Hall, N., Hetrick, S., Ong, J., Haslam, N., Karsz, F. & Vance, A. (2010). The association of visuospatial working memory with dysthymic disorder in pre-pubertal children. PSYCHOLOGICAL MEDICINE, 40 (2), pp.253-261. https://doi.org/10.1017/S0033291709990365.

Publication Status:
Published