AN EXAMINATION OF WORRY, PHYSIOLOGICAL ANXIETY, AND SOCIAL ANXIETY AS POTENTIAL MODERATORS OF WORKING MEMORY DEFICITS IN CHILDREN WITH ADHD

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Submitted to the Faculty of the
Graduate College of the
Oklahoma State University
in partial fulfillment of
the requirements for
the Degree of
DOCTOR OF PHILOSOPHY
July, 2018

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Date of Degree: JULY, 2018

Title of Study: AN EXAMINATION OF WORRY, PHYSIOLOGICAL ANXIETY, AND SOCIAL ANXIETY AS POTENTIAL MODERATORS OF WORKING MEMORY DEFICITS IN CHILDREN WITH ADHD

Major Field: PSYCHOLOGY

Abstract: Attention Deficit/Hyperactivity Disorder (ADHD) is a pervasive, multifaceted, and complex neurocognitive disorder characterized by problems with inattention, hyperactivity, and impulsivity that effects 3 to 7% of children worldwide. The functional working memory (WM) model of ADHD suggests that WM deficits are a core feature of the disorder, and is supported by extant findings of large-magnitude ADHD-related WM deficits. WM deficits are not unique to ADHD, however, as they have be associated with other problems of psychopathology such as general anxiety and social anxiety. Given extensive literature that has found multiple deficits in WM associated with ADHD and anxiety, and the high comorbidity of anxiety in children affected with ADHD, there has been an increased interest in determining if individuals with comorbid ADHD and anxiety symptoms experience neurocognitive deficits above and beyond deficits exhibited by children with ADHD alone. However, findings from studies examining children with comorbid ADHD and anxiety have yet to yield a clear understanding of how the relationship between ADHD and various anxiety symptom clusters affect WM performance. Although initial studies have failed to detect more severe WM deficits in children with comorbid ADHD and anxiety compared to children with ADHD alone, limitations in the measurement of WM in the studies may have failed to capture the potential "additive effect" of this comorbidity. Furthermore, the use of broadband anxiety measures may mask the effects of specific anxiety symptoms on WM. This study aimed to examine if high levels of self-reported anxiety moderate PH-WM performance differences between children with ADHD and their typically developing peers. Moreover, this study addresses limitations of previous studies by utilizing (1) a PH-WM task (i.e., Letter-Number Sequencing subtest of the WISC-IV) that is expected to place higher demands on CE functioning, (2) children's self-reported anxiety levels in lieu of parent and teacher scales that are expected to more accurately measure internal distress, and (3) three unique self-report scales of anxiety: worry, physiological anxiety, and social anxiety.

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	ADHD (*n* = 25)	**TD (*n* = 15)**		
	M (SD)	*M (SD)*	*t*	χ^2
Ethnic Composition				3.00
Age	9.33 (1.43)	9.51 (1.19)	.41	
SES	45.75 (9.13)	50.10 (13.30)	1.91	
WISC-IV GAI	102.68 (11.58)	109.53 (15.87)	.124	
RAN	96.75 (14.35)	104.60 (14.01)	1.68	
CBCL DSM-ADHD	65.84 (7.77)	50.80 (1.78)	-7.35***	
TRF DSM-ADHD	64.08 (6.84)	51.40 (2.35)	-6.90***	
C3P DSM-ADHD-I	75.76 (9.03)	47.67 (8.76)	-9.63***	
C3P DSM-ADHD-HI	72.56 (13.89)	47.80 (7.61)	-6.33***	
C3T DSM-ADHD-I	71.64 (9.06)	45.66 (4.65)	-10.28***	
C3T DSM-ADHD-HI	66.36 (15.92)	46.80 (6.36)	-4.53***	
RCMAS PHY	5.36 (2.81)	2.26 (2.60)	-3.46**	
RCMAS WOR	5.80 (4.86)	1.33 (2.23)	-3.35**	
RCMAS SOC	3.36 (2.60)	0.87(1.92)	-3.22**	
LNS RAW	14.72 (3.61)	17.67 (3.04)	2.64**	

Note. M = Mean; SD = Standard deviation; ADHD = Attention-deficit/hyperactivity disorder; TD = Typically developing; SES = Socio economic status; WISC-IV GAI = Wechsler Intelligence Scale for Children, Fourth Edition General Ability Index; RAN = Naming Facility; CBCL = Child Behavior Checklist; TRF = Teacher Report Form; C3P = Conners-3 Parent Rating Scale; C3T = Conners-3 Teacher Rating Scale; DSM-ADHD = Attention-deficit/hyperactivity problems scale; DSM-ADHD-I = DSM ADHD inattention subscale; DSM-ADHD-HI = DSM ADHD hyperactive/impulsive subscale; RCMAS = Revised Children's Manifest Anxiety Scale; PHY = Physiological Anxiety; WOR = Worry; SOC = Social Anxiety; LNS RAW = Letter-Number Sequencing Raw Score.
*** p < .01, ***p < .001*

Table 1. Sample Characteristics

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
(1) Group	1.00	-0.27	-0.25	-0.29	-0.39*	0.47**	0.49**	0.46**
(2) RAN		1.00	0.33*	0.06	0.43**	-0.01	-0.07	-0.17
(3) GAI			1.00	0.14	0.45**	0.11	-0.08	0.01
(4) SES				1.00	0.30	-0.33*	-0.16	-0.27
(5) LNS					1.00	-0.33*	-0.30	-0.26
(6) WOR						1.00	0.69**	0.85**
(7) PHY							1.00	0.68**
(8) SOC								1.00

Note. RAN = Naming Facility; GAI = General Ability Index; SES = Socioeconomic Status; LNS = Letter-Number Sequencing Raw Score; WOR = Worry Raw Score; PHY= Physiological Anxiety Raw Score; SOC = Social Anxiety Raw Score.

** $p < .05$, ** $p < .01$*

Table 2. Correlations

	B	*SE B*	*t*	*95% C.I.*	R^2	ΔR^2
Moderation 1					0.26	0.79
Group	-3.79	1.44	-2.64	-6.71, -0.88		
WOR	-0.87	0.39	-2.21	-1.67, -0.07		
Group x WOR	0.82	0.42	1.95	0.11, 1.54		
Moderation 2					0.19	0.02
Group	-3.89	1.91	-2.03	-7.77,-0.01		
PHY	-0.46	0.35	-1.30	-1.17,0.25		
Group x PHY	0.44	0.43	1.02	-0.43, 1.31		
Moderation 3					0.26	0.10
Group	-4.32	1.43	-3.02	-7.22,-1.42		
SOC	-0.10	0.46	-2.19	-1.92, -0.07		
Group x SOC	1.15	0.52	2.19	-3.98, 4.96		

Note. LNS = Letter-Number Sequencing Raw Score; WOR = Worry Raw Score; PHY= Physiological Anxiety Raw Score; SOC = Social Anxiety Raw Score.

Table 3. Moderating Effect of Anxiety on LNS Score

	B	*SE B*	*t*	*95% C.I.*	R^2	ΔR^2
Moderation 1					0.47	0.02
Group	-1.35	1.47	-0.92	-4.33, 1.64		
WOR	-0.60	0.36	-1.65	-1.34, 0.14		
GAI	0.07	0.04	1.67	-0.01, 0.16		
SES	0.07	0.04	1.43	-0.03, 0.17		
RAN	0.07	0.04	1.88	-0.01, 0.14		
Group x WOR	0.48	0.40	1.18	-0.35, 1.30		
Moderation 2					0.44	0.01
Group	-1.64	1.81	-0.91	-5.33, 2.04		
PHY	-0.45	0.32	-1.38	-1.10, 0.21		
GAI	0.06	0.04	1.46	-0.02, 0.15		
SES	0.09	0.05	1.88	-0.01, 0.19		
RAN	0.08	0.04	2.12	0.01, 0.15		
Group x PHY	0.36	0.41	0.89	-0.47, 1.18		
Moderation 3					0.45	0.04
Group	-2.24	1.48	-1.51	-5.25, 0.78		
SOC	-0.71	0.44	-1.65	-1.60, -0.17		
GAI	0.05	0.04	1.11	-0.04, 0.14		
SES	0.08	0.05	1.60	-0.02, 0.18		
RAN	0.08	0.04	2.10	0.01, 0.15		
Group x SOC	0.82	0.52	1.56	-0.25, 1.89		

Note. LNS = Letter-Number Sequencing Raw Score; WOR = Worry Raw Score; PHY= Physiological Anxiety Raw Score; SOC = Social Anxiety Raw Score; GAI = General Ability Index; SES = Socioeconomic Status; RAN = Naming Facility.

Table 4. Moderating Effect of Anxiety on LNS Score with Covariates

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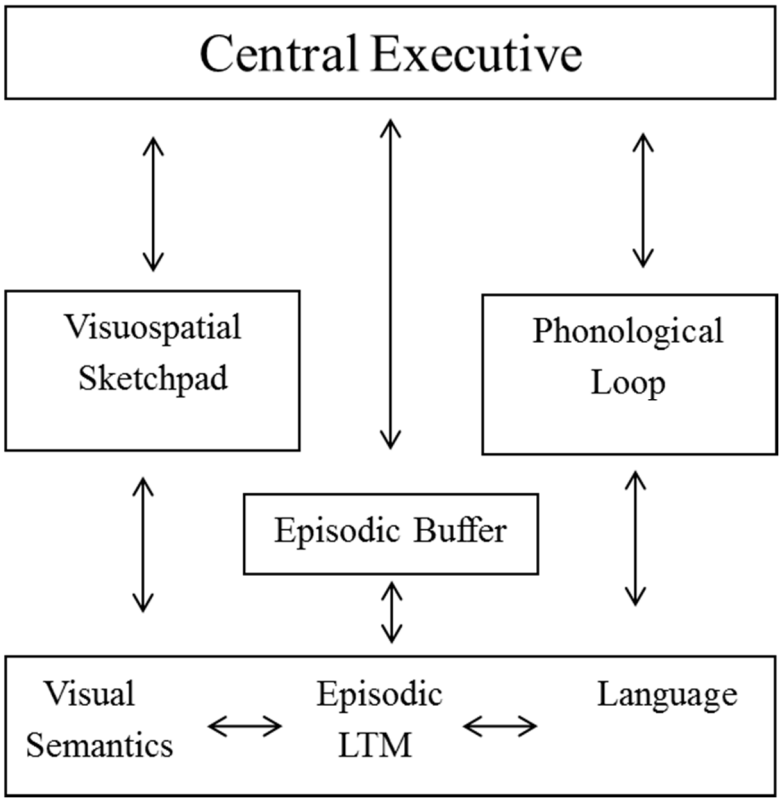


Note. LTM= Long term memory.
Figure 1. Visual schematic of Baddeley's (2007) multi-component model of working memory

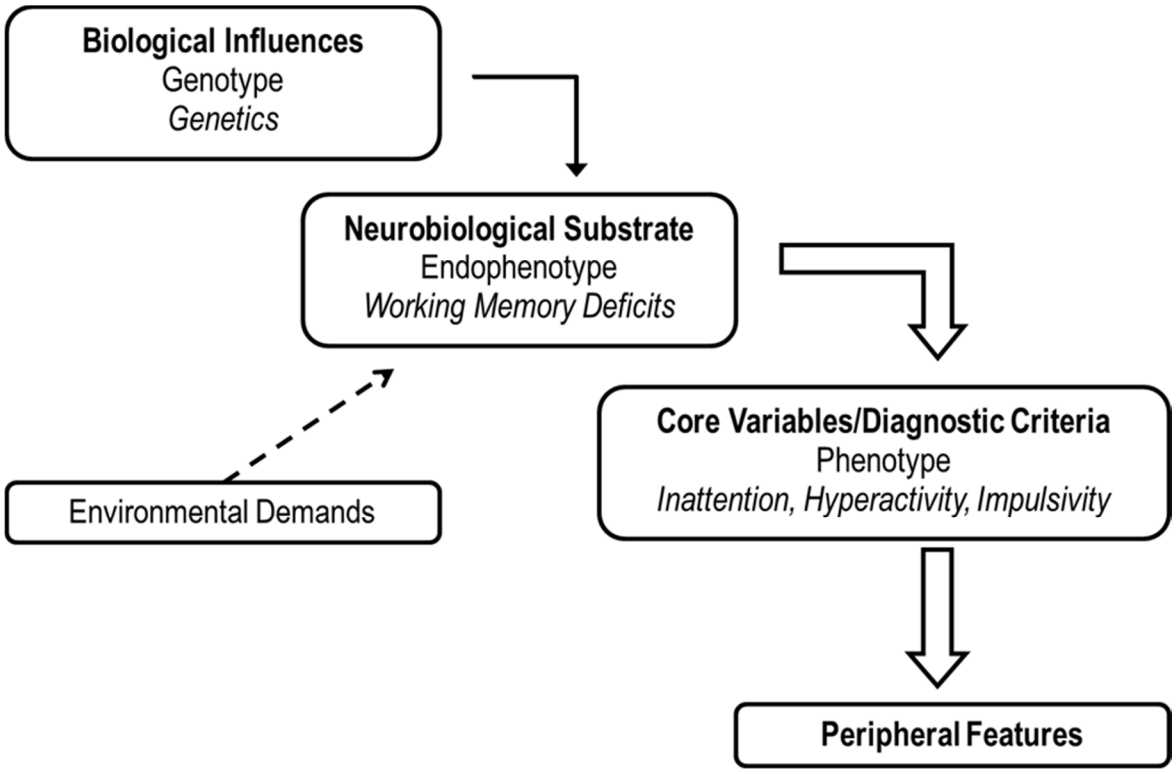
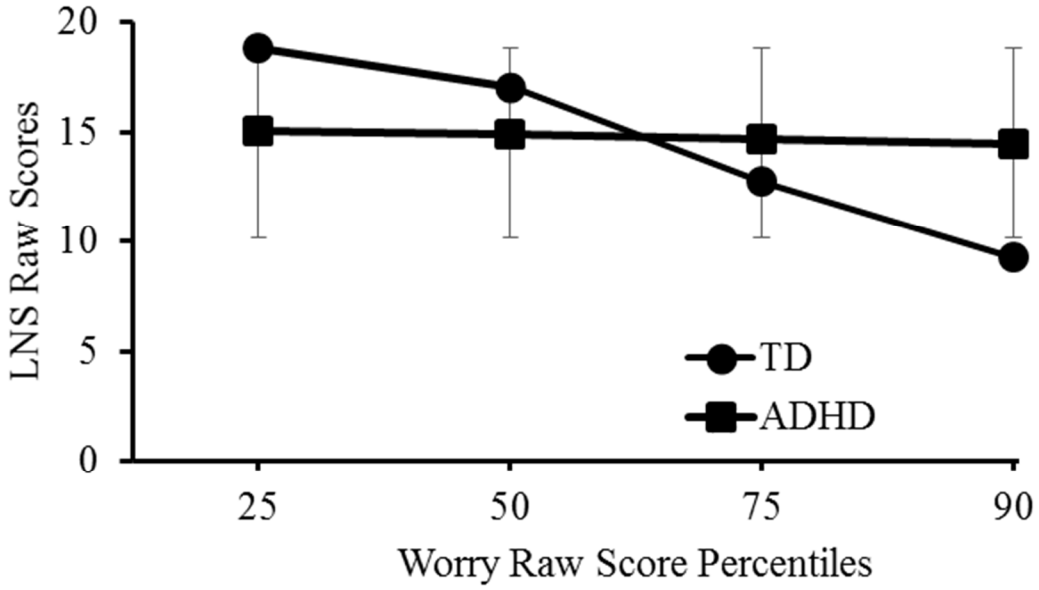


Figure 2. Visual schematic of Rapport and colleagues' (2008) functional working memory model of ADHD



Note. ADHD = Attention-deficit/hyperactivity disorder; TD = Typically developing; Error bars = standard deviation; LNS = Letter- Number Sequencing.

Figure 3. Letter-Number Sequencing raw scores comparison at various levels of self-reported worry.

CHAPTER I

INTRODUCTION

Attention Deficit/Hyperactivity Disorder (ADHD) is a pervasive, multifaceted, and complex neurocognitive disorder characterized by problems with inattention, hyperactivity, and impulsivity that effects 3 to 7% of children (American Psychiatric Association, 2013; Barkley, 2006: Polanczyk, de Lima, Horta, Biederman, & Rohde, 2007). Evidence derived from community-based samples suggest that 44% of children with ADHD meet criteria for at least one additional DSM-V (APA, 2013) diagnosis (Mash & Barkley, 2014), and 43% meet criteria for two or more diagnoses (Willcutt et al.., 2012). For example, an estimated 25 to 50% of children with ADHD also experience clinically significant anxiety symptoms (Barkley, 2014; Costello, Egger & Angold, 2004) that convey increased risk for greater attention deficits (Jarret et al., 2016; Jenson et al., 2001), increased rates of oppositional behaviors (Humphreys, Aguirre, & Lee, 2012; Newcorn et al.,2001; Tannock, 2000), and greater academic underachievement (Biederman, Faraone, & Chen, 1993), compared to children with ADHD or anxiety alone.

Models of ADHD have begun to converge and identify impaired executive functions, including behavioral inhibition (Barkley, 1997), planning and decision making (Sergeant, 2005), delay aversion (Songue-Barke, 2005), and working memory (Rapport et

al., 2008), as core deficits or associated neurocognitive deficits associated with the disorder. The functional working memory (WM) model of ADHD (Rapport et al., 2008), for example, suggests that WM deficits serve as a core feature that underlies other deficits in executive functioning such as behavioral inhibition, delay aversion, and self-regulation. Baddeley's (2007) multi-component model of WM serves as the theoretical basis for the functional WM model, and divides WM into four subcomponents: the phonological (PH) loop, the visuospatial (VS) sketchpad, the domain-general central executive (CE) system, and the episodic buffer. The PH loop is responsible for the temporary storage, rehearsal, and processing of auditory information, whereas the VS sketchpad is responsible for the temporary storage, rehearsal, and processing of visual and spatial information. The CE is responsible for the division, switching, and maintenance of attention, the manipulation of information in the VS and PH rehearsal systems, and the allocation of resources to the VS and PH systems. Finally, the episodic buffer is responsible for the temporary storage of information presented via multiple modalities and provides a link between short term and long-term memory. Figure 1 provides a visual schematic of Baddeley's multi-component model of WM.

Experimental and meta-analytic examinations have provided support for Rapport and colleagues' model predictions, such that deficits in the CE, PH, and VS subsystems of WM have been reliably observed in both children (Alderson et al., 2010; Kasper, Alderson, & Hudec, 2012; Kofler, Rapport, Bolden, Sarver, & Raiker, 2010; Martinussen, Hayden, Hogg-Johnson, & Tannock, 2005; Rapport et al., 2008; Rapport et al., 2009) and adults (Alderson, Hudec, Patros, & Kasper, 2013; Alderson, Kasper, Hudec, & Patros, 2013; Hervey, Epstein, & Curry, 2004; Hudec, Alderson, Patros, &

Kasper, 2014) with ADHD. Moreover, a growing body of literature suggests that WM deficits underlie DSM-5-defined core and secondary features of the disorder. For example, findings from carefully controlled lab-based studies suggest that ADHD-related hyperactivity is functionally related to WM demands in both children (Alderson et al., 2012; Hudec, Alderson, Patros, Lea, Tarle, & Kasper, 2015; Porrino et al., 1983; Rapport et al., 2009) and adults (Hudec et al., 2014; Lea, Alderson, Patros, Tarle, Arrington, & Grant, under review; Lis et al., 2010). Secondary outcomes such as ADHD-related academic underachievement in reading, have been associated with significant PH-WM impairments, while academic underachievement in mathematics appears to be associated with impairments in both the PH and VS WM subsystems (Alloway, Gathercole, & Elliot, 2010; Rogers, Hwang, Toplak, Weiss, & Tannock, 2011). Further, CE and VS-WM deficits have been found to mediate the relationship between group membership (ADHD, typically developing: TD) and performance on behavioral inhibition (Alderson et al., 2010) and impulsivity tasks (Patros et al., 2015; Raiker, Rapport, Kofler, & Sarver, 2012). Finally, WM deficits have been found to mediate the indirect relationship between ADHD and parent/teacher reports of social skills deficits (Alloway et. al., 2005; Kofler et al., 2011; Phillips, Tunstall, & Channon, 2007). Figure 2 displays a visual schematic of the functional WM model of ADHD.

Paralleling ADHD models, models of anxiety have begun to focus on the relationship between anxiety symptoms and executive functions. Theoretical explanations of WM deficits suggest that anxiety decreases the CE's attentional control and focus (Eysenck, Derakshan, Santos, & Calvo, 2007). Specifically, the attentional control theory identifies two distinct attentional systems (Corbetta & Shulman, 2002): a goal directed

system focused on current goals, and a stimulus directed system focused on directed attention to relevant stimuli. The model hypothesizes that high anxiety increases focus on the stimulus driven system, rather than the goals driven system, resulting in inhibition (i.e., ability to inhibit prepotent responses and inhibit attention away from task irrelevant stimuli), shifting (i.e., using attentional control to switch between multiple tasks), and updating (i.e., updating and modifying stimuli within the WM system; Miyake et al., 2000). Studies of anxiety symptoms have increasingly begun to provide support for these theoretical predictions. For example, several examinations of WM in individuals with high state and/or trait anxiety have identified multiple deficits in both storage/rehearsal and CE WM systems (Darke, 1988; MacLeod & Donnellan, 1993; Miyake et al., 2000; Ikeda, Iwanaga & Sweiwa, 1996; Sorg & Whitney, 1992). Further, a recent meta-analytic review found that higher levels of self-reported general anxiety are reliably related to poor WM capacity across simple, complex, and dynamic span tasks in both children and adults (Moran, 2016). Another meta-analytic review aimed at identifying the relationship between WM and academic performance in individuals with anxiety found that high levels of worry are associated with deficits in CE-WM, which ultimately leads to poor academic performance (Owens, Stevenson, Hadwin, & Norgate, 2012). Lastly, socially anxious individuals have been shown to have difficulties disengaging from goal-irrelevant stimuli as WM load increases (Judah, Grant, Lachner, & Mills, 2013; Moriya & Sugiura, 2012).

Given the substantial body of literature that has found multiple deficits in WM associated with ADHD and anxiety, and the relatively high comorbidity of anxiety in children affected with ADHD, there has been an increased interest in determining if

individuals with comorbid ADHD and anxiety symptoms experience behavioral and neurocognitive deficits above and beyond deficits exhibited by children with ADHD alone (Bloemsma at al., 2013; Ferrin & Vance, 2014; Manassis, Tannock, Young, & Francis-John, 2007). For example, Manassis, Tannock, Young, and Francis-John (2007) found that children with ADHD and comorbid anxiety did not perform significantly worse than children with ADHD alone. Another study utilizing structural equation modeling (SEM; Bloemsma at al., 2013) aimed to examine the effect of anxiety and ADHD on executive functioning and found that there was no relationship between WM functioning and parent, teacher, or self-reported anxiety. Finally, Ferrin and Vance (2014) recently examined anxiety and depression as potential moderators of ADHD-related WM deficits, and found that PH-WM was impaired in children with ADHD regardless of their level of anxiety/depression, while typically developing children who experienced high levels of anxiety/depression made more search errors during the VS-WM task.

Although these initial data do not support a cumulative risk hypothesis, there are several limitations of these studies that warrant consideration and further research. For example, Bloemsma et al. (2013) and Ferrin and Vance (2014) utilized simple-span WM tasks that are not expected to place high demands on the *working component of working memory* (i.e., CE). That is, previous findings from SEM (Engle et al., 1999) and factor analytic (Cantor et al., 1991; Moleiro et al., 2013) studies suggest that both forward and backward span tasks place few demands on CE processes and consequently provide indices of short-term storage (i.e., short-term memory: STM) rather than WM. Moreover, findings from meta- analytic (Kasper et al., 2012, Martinussen et al., 2005) and

experimental (Rapport et al., 2008; Alderson et al., 2015; Tarle et al., 2017) studies provide compelling evidence that impaired CE functioning represents the greatest deficit in affected children (Alderson et al., 2010; Dovis, Van der Oord, Wiers, & Prins, 2013; Martinussen et al., 2005; Rapport et al., 2008). Thus, using a PH-WM task that places higher demands on CE functioning, like the Letter-Number Sequencing subtest of the WISC-IV; Wechsler, 2003; Tarle et al., 2017) may provide a better test of the cumulative risks associated with comorbid ADHD and anxiety.

Findings from previous studies are also limited due to their method of anxiety measurement. For example, the use of parent-report anxiety rating scales in previous studies (Bloemsma at al., 2013; Ferrin & Vance, 2014) reflects a potential limitation due to expected discrepancies between parent and child reports of internalizing symptoms (Weems, Feaster, Horigian, & Robbins, 2011). Moreover, all previous studies utilized only broadband anxiety or combined anxiety/depression self-report scales (Bloemsma at al., 2013; Ferrin & Vance, 2014; Manassis, Tannock, Young, & Francis-John, 2007). This methodology potentially obscures interpretations, due to the heterogeneous mix of anxiety symptom clusters that present with varying phenotypes of WM deficits in both anxiety-only and ADHD/anxiety groups. For example, individuals with social anxiety have been shown to exhibit changes in performance on WM tasks depending on the presence or absence of "threat" related stimuli, whereas individuals with generalized anxiety exhibit deficits when feeling worried (Amir & Bomyea, 2011; Eysenck, Derakshan. Santos, & Calvo, 2007). In using children's own reports on narrow-band measures to capture specific anxiety phenotypes, future studies may be able to determine

which, if any, anxiety phenotypes contribute to greater WM deficits in children with ADHD.

Collectively, despite similar WM deficits noted among children with ADHD (Alderson et al., 2010; Kasper et al., 2012; Kofler, Rapport, Bolden, Sarver, & Raiker, 2010; Rapport et al., 2008; Rapport et al., 2009) and children with anxiety (Moran, 2016), findings from studies examining children with comorbid ADHD and anxiety (Bloemsma at al., 2013; Ferrin & Vance, 2014; Manassis, Tannock, Young, & Francis-John, 2007) have yet to yield a clear understanding of how the relationship between ADHD and various anxiety symptom clusters affect WM performance. Although initial studies have failed to detect more severe WM deficits in children with comorbid ADHD and anxiety compared to children with ADHD alone, limitations in the measurement of WM in the studies may have failed to capture the potential "additive effect" of this comorbidity. Specifically, children with ADHD exhibit the greatest deficit in CE component of WM (Alderson et al., 2010; Kasper, Alderson, & Hudec, 2012; Kofler, Rapport, Bolden, Sarver, & Raiker, 2010; Martinussen, Hayden, Hogg-Johnson, & Tannock, 2005; Rapport et al., 2008; Rapport et al., 2009), whereas anxiety is theoretically more closely linked with deficits in inhibition, shifting, and updating (Miyake et al., 2010). A recent meta-analysis found children with anxiety experience greater deficits in WM capacity or storage/rehearsal processes (Moran, 2016). Furthermore, the use of broadband anxiety measures may mask the effects of specific anxiety symptoms on WM.

Ultimately, the examination of a WM task that places greater demands on the CE while also placing demands on WM storage/rehearsal systems (i.e., increasing set sizes) could yield new results on the cumulative effect of ADHD and anxiety related deficits.

This study aimed to examine if high levels of self-reported anxiety moderate PH-WM performance differences between children with ADHD and their typically developing peers. Moreover, this study addresses limitations of previous studies by utilizing (1) a PH-WM task (i.e., Letter-Number Sequencing subtest of the WISC-IV; Wechsler, 2003) that is expected to place higher demands on CE functioning, (2) children's self-reported anxiety levels in lieu of parent and teacher scales that are expected to more accurately measure internal distress (Bloemsma at al., 2013), and (3) three unique self-report scales of anxiety: worry, physiological anxiety, and social anxiety.

CHAPTER II

HYPOTHESES

Hypothesis I (Examination of the Moderation of Worry on Groups' WM Performance)

Based on previous experimental (Alderson et al., 2010; Kofler, Rapport, Bolden, Sarver, & Raiker, 2010; Rapport et al., 2008; Rapport et al., 2009) and meta-analytic (Kasper et al., 2012: Martinussen et al., 2005; Willcutt, 2005) studies that reported medium to large magnitude ADHD-related WM deficits, children with ADHD are expected to perform significantly worse on the Letter-Number Sequencing task compared to typically developing children. Further, given that WM deficits are often associated with high levels of anxiety (Darke, 1988; MacLeod & Donnellan, 1993; Miyake et al., 2000; Moran, 2016; Ikeda, Iwanaga & Sweiwa, 1996, Sorg & Whitney, 1992), self-reported worry is expected to moderate the magnitude of the relationship between group (ADHD vs. TD) and WM performance. Specifically, both children with ADHD and typically developing children were expected to perform worse when high levels of self-reported worry are present, relative to when lows levels of worry are present. However, children with ADHD were expected to perform disproportionately worse compared to their typically developing peers.

Hypothesis II (Examination of the Moderation of Physiological Anxiety on Groups' WM Performance)

Based on previous literature that suggests anxiety in children often manifests as somatic symptoms or complaints (e.g. headaches, stomachaches, muscle tension; Eisen and Engler, 1995), and that WM deficits are associated with high anxiety, self-reported physiological anxiety is expected to moderate the magnitude of the relationship between group (ADHD vs. TD) and WM performance. Specifically, it was expected that both children with ADHD and typically developing children will perform worse when high levels of self-reported physiological anxiety are present relative to when low levels of physiological anxiety are present. However, children with ADHD were expected to perform disproportionately worse compared to their typically developing peers.

Hypothesis III (Examination of the Moderation of Social Anxiety on Groups' WM Performance)

Given previous literature that has outlined WM deficits related to social anxiety (Judah, Grant, Lachner, & Mills, 2013; Moriya & Sugiura, 2012), and that the Letter-Number Sequencing task was administered in a manner that might elicit social anxiety (i.e., the task is administered by a live examiner and scored in real time), it is expected that self-reported social anxiety will moderate the magnitude of the relationship between group (ADHD vs. TD) and WM performance. Specifically, it is expected that both children with ADHD and children who are typically developing will perform worse when high levels of self-reported social anxiety are present relative to when low levels of social anxiety are present. However, children with ADHD were expected to perform disproportionately worse compared to their typically developing peers.

CHAPTER III

METHODOLOGY

Participants

Participants were boys between the ages of 8 and 12 years old recruited by or referred to a university-based child assessment clinic in the southwestern United States. The sample was recruited through community resources, such as local pediatricians, schools, community mental health clinics, posting flyers at local businesses, and communicating with faculty and staff at the university. All children received a comprehensive psychological evaluation consistent with gold standard procedures used to identify children with ADHD (Gualtieri & Johnson, 2005), and caregivers of all children received a psychoeducational report as compensation for participation in the study. Caregivers and children provided consent and assent before participating in the study. The university's Institutional Review Board (IRB) approved the study prior to the onset of data collection. The final sample of 40 children was comprised of 80% Caucasian, 7.5% Biracial, 7.5% Native American, and 5% Hispanic children.

Group Assignment. Children were included in the ADHD group if they met all of the following criteria: (1) a diagnosis of ADHD (any presentations) by the directing clinical psychologist, based on a clinical interview with the caregiver and child, and diagnostic criteria outlined in the DSM-5 (American Psychiatric Association, 2013);

(2) parent ratings of at least two *SD*s above the mean on the DSM-ADHD scale of the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001), or 1.5 *SD*s above the mean on the DSM-ADHD scale of the Conners-3 Parent (C3P; Conners, 2008); and (3) teacher ratings of at least two *SD*s above the mean on the DSM-ADHD scale of the Teacher Report Form (TRF; Achenbach & Rescorla, 2001), or 1.5 *SD*s above the mean on the DSM-ADHD scale of the Conners-3 Teacher (C3T; Conners, 2008). Twenty-five children comprised the ADHD group and had an average age of 9.33 (*SD* = 1.43) years.

Children were included in the Typically Developing (TD) group if they met all of the following criteria: (1) no clinical diagnosis based on rating scales and a clinical interview with the caregiver and child; and (2) a normal developmental history based on a psychosocial interview with the caregiver. Fifteen children comprised the TD group and had an average age of 9.52 (*SD* = 1.19) years.

This study excluded children that presented with (1) a history of seizure disorders, (2) psychosis, (3) gross neurological, sensory, or motor impairments, (5) a comorbid learning disorder, or (5) a General Ability Index (GAI) score of less than 80. The GAI was used as an estimate of IQ in this study since it does not include variance associated with WM subtests from the WISC-IV. Children that were currently taking prescribed psychostimulant medications also were excluded in this study.

Measures

Psychosocial Interview

A psychosocial interview aimed at gathering developmental, medical, educational, and social background information was administered to all caregivers of participating children. This information was used in combination with other diagnostic

measures to examine symptom impairment. Information obtained on developmental history was examined to determine potential exclusion from this study due to medical or sensory-motor impairment.

Clinical Interview

In addition to a psychosocial interview, caregivers and children completed the Kiddie Schedule for Affective Disorder and Schizophrenia for School-Aged Children-Present and Lifetime version (K-SADS-PL; Kaufman et al., 1997). This comprehensive, semi-structured clinical interview assesses onset, course, frequency, duration, and severity of current and past emotional and behavioral difficulties based on DSM-IV-TR diagnostic criteria. The K-SADS-PL is routinely used in research protocols and clinical evaluations and has good to excellent test-retest reliabilities (k = 0.63 to 1.00; Kaufman et al., 1997) as well as good overall convergent and discriminant validity with other clinical measures (r = 0.39 – 0.45; Birmaher et al., 2009).

ADHD Rating Scales

Child Behavior Checklist and Teacher Report Form. The CBCL and TRF are broadband rating scales that screen for internalizing and externalizing difficulties in children (ages 6-18) as measured by parent and teacher report. The CBCL and TRF exhibit strong test-retest reliabilities (0.95-1.00) and inter-rater reliabilities (0.93-0.96) as well as acceptable validity scores (Achenbach, 1991). Caregivers and teachers completed the rating scales independently to assess functioning in multiple settings.

Conners-3 Parent and Teacher Rating Scales. The C3P and C3T are narrowband ratings scales that assess behavioral problems in children (ages 6-18) via parent and teacher report. These rating scales primarily focus on assessing ADHD

symptomology (i.e. inattention, hyperactivity, impulsivity) and obtaining information on possible comorbid emotional or behavioral difficulties (e.g. Oppositional Defiant Disorder; Conners, Sitarenios, Parker, & Epstein, 1998). The C3P and C3T have excellent psychometric properties, such as good internal consistency (r = 0.60) and strong test-retest reliabilities (r = 0.52- 0.67; Conners et al., 1998). Again, caregivers and teachers completed the rating scales independently to assess functioning in multiple settings.

Anxiety Rating Scale

Revised Children's Manifest Anxiety Scale- Second Edition. The Revised Children's Manifest Anxiety Scales- Second Edition (RCMAS-2; Reynolds & Richmond, 2012) was used as a narrowband measure to assess a variety of anxiety symptoms in participating children. The RCMAS-2 includes worry, physiological anxiety, and social anxiety subscales. These subscales are then combined to create a total anxiety symptoms scale. This self-report measure has exhibited acceptable construct validity and strong test-retest reliabilities (0.52 – 0.77; Reynolds & Richmond, 2012).

Intellectual Functioning

All participating children were administered the Wechsler Intelligence Scale for Children - Fourth Edition (WISC-IV; Wechsler, 2003). The WISC-IV provides measures of fluid and crystalized intelligence less sensitive to WM and processing speed via the General Ability Index (GAI). The WISC-IV has strong psychometric properties including construct and criterion validity (0.61 – 0.83) and test-retest reliabilities (0.69 – 0.90; Wechsler, 2003).

Academic Achievement

The Kaufman Test of Educational Achievement- Second Edition (KTEA-II; Kaufman & Kaufman, 2004) is a standardized measure commonly administered to assess academic achievement in children. The KTEA-II has strong psychometric properties such as high internal consistency (all composites have an $\alpha > .82$), inter-rater reliability (range from 0.82-0.97; Kaufman & Kaufman 2004), and convergent validity with other measures of achievement ($r > 0.70$ for all composite scores; Kaufman & Kaufman, 2004). The KTEA-II was administered to rule-out any potential comorbid learning disabilities in the children included in the final sample.

Reading ability. The Rapid Automatized Naming (RAN) task of the KTEA-II is a timed naming facility task that examines how quickly children can identify visually presented letters. The RAN task is highly correlated with reading ability and specifically aims to identify deficits in word identification or reading fluency (Kaufman & Kaufman, 2004). Standardized administration procedures of the RAN task were used. The RAN was administrated to control for reading ability in the follow up covariate analyses.

Working Memory Measure

The WISC-IV provides three tasks as reified measures of WM that load on the WM Index; Digit Span Forward, Digit Span Backward, and Letter-Number Sequencing (LNS). For the purposes of this study, the LNS task of the WISC-IV was used as a measure of WM as it is expected to place higher demands on the CE than the Digit Span tasks that reflect predominately storage/rehearsal WM processes (Oberauer, Süb, Scheulze, Wilhelm, & Wittmann, 2000; Tarle et al., 2017). Standardized administration procedures of the LNS task were used. Children heard a string of aurally presented numbers and letters in a scrambled order. They were then asked to verbally repeat the

numbers from least to greatest, followed by the letters in alphabetical order. Set sizes range from two to eight stimuli and the tasks includes a maximum of 30 trials, with three trials per set size. Correct responses are trials in which the child repeats all stimuli in the correct order. Children were required to obtain at least one correct trial per set size to move on to the next set size. Set sizes were administered beginning with set size two and proceeding in ascending order until the children completed all 30 trials or discontinued due to three incorrect responses within one set size. The raw score of the LNS task were computed to represent WM tasks performance. Raw scores were used rather the standard scores to examine greater variability between children.

Moderating Variables

Three moderating variables were assessed using the children's RCMAS-2. The worry subscale, physiological anxiety subscale, and the social anxiety subscale raw scores were used to examine the potential moderating effects of each domain of anxiety on group and WM performance. Raw scores were used rather the standard scores to examine greater potential variability between children.

Covariates

The relationship between group (TD versus ADHD) and WM performance as moderated by self-reported worry, physiological anxiety, and social anxiety was further examined by controlling for three additional variables that could potentially account for group differences in WM. Specifically, children's intellectual functioning as measured by the GAI, socioeconomic status as measured by the Hollingshead Four-Factor Index of Socioeconomic Status (Hollingshead, 1975), and reading ability as measured by the RAN task were examined as potential covariates. These variables were chosen for the covariate

analyses based on previous literature that has found that lower GAI (Cornoldi, Orsini, Cianci, & Pezzuti, 2013), lower SES (Leonard, Mackey, Finn, & Gabrieli, 2015), and reading deficits (Jacobson, et al., 2010) are associated with poorer WM performance.

Procedure

Prior to data collection, caregivers of children interested in participating in the study completed a phone screener aimed at gathering basic information on the child, such as age, grade level, and academic performance. After obtaining this information, caregivers were mailed packets that included both parent and teacher ADHD rating scales. Once the completed measures were received from both the parent and the teacher, assessment sessions were scheduled for weekday mornings. During the first assessment session, a session administrator reviewed an informed consent form with the child's caregiver and obtained their consent to participate. The session administrator also reviewed a child assent form and gained the assent of the child.

Data was collected as a component of a larger battery of assessment and experimental measures. Children completed two three-hour assessment sessions during which they completed the WISC-IV (Wechsler, 2003) and the KTEA-II (Kaufman & Kaufman, 2004) according to standardized administration procedures. While children completed the assessment protocols, caregivers were administered both the psychosocial and clinical interviews. Children were provided breaks between the tasks' administrations and as needed to minimize potential testing fatigue. Children completed the RCMAS-2 during one of the longer breaks between task administrations.

CHAPTER IV

FINDINGS

Analytic Strategy

The effect of each moderating variable (i.e. worry, physiological anxiety, and social anxiety) on the relationship between group status and WM performance was examined via procedures outlined in Hayes (2013, 2015). This procedure involves examination of a simple moderation model via the PROCESS macro (Hayes, 2013) and evaluation of 95% bias-corrected confidence intervals. Confidence intervals were calculated after the generation of 10,000 bootstrapped estimates of the relationships in each of the three models. Confidence intervals are considered statistically significant if they do not contain zero.

Preliminary Analyses

Raw scores for the LNS task were screened for values ≥ 3.29 standard deviations (corresponding to $p < .001$) above or below the group mean. No outliers were identified during this screening. Children with ADHD and TD children did not differ in race/ethnicity ($p = .554$), age ($p = .522$), intelligence ($p = .293$), socioeconomic status ($p = .097$), or reading ability ($p = .109$). All parent and teacher rating scales were significantly higher for children with ADHD compared to the TD group (see Table 1.).

Further, children with ADHD had significantly lower LNS raw scores compared to their typically developing peers (p = .012). Children with ADHD reported higher levels of self-reported worry (p = .002), physiological anxiety (p = .001), and social anxiety (p = .003) compared to their TD peers. Sample and demographic variables are presented in Table 1.

Initial Pearson bivariate correlations revealed a moderate negative correlation between group (ADHD, TD) and WM performance (r = -0.39, p = 0.01). Furthermore, group was moderately positively correlated with self-reported worry (r = 0.47, p < 0.01), physiological anxiety (r = 0.49, p < 0.01), and social anxiety (r = 0.46, p < 0.01). GAI were also found to be moderately positively correlated with RAN (r = 0.33, p = 0.39) and WM performance (r = 0.45, p < 0.01). All subscales of the RCMAS were found to be strongly positively correlated (r = 0.68- 0.85, p < 0.01). Finally, SES was found to be moderately negatively correlated with self-reported worry (r= -0.33, p = 0.04). The correlation matrix is provided in Table 2.

Tier 1: Examination of the Moderation effect of Worry on WM Performance

A linear regression was used to examine the moderating effect of self-reported worry on the relationship between group (ADHD vs TD) and WM performance. Results indicated that group (ADHD, TD) significantly predicted LNS scores, b = -3.80, t (39) = -2.64, 95% CI [-6.71-0.88], such that children with ADHD had lower scores than TD children. Additionally, the relationship between group assignment and WM performance was moderated by self-reported worry, b = .817, t (39) = 1.95, 95% CI [0.11, 1.54]. The Johnson-Neyman technique (Johnson &Neyman, 1936), as recommended by Hayes (2013), was used to probe this interaction by examining the relationship between group

and WM performance at the 10th, 25th, 50th, 75th, and 90th percentiles of the distribution of self-reported worry scores in the sample. It was found that group significantly predicted WM performance when self-reported worry scores fell at or below the 25th percentile (t (39) = -2.64, p = 0.01, d = -0.85), such that children with ADHD had lower scores than TD children at low levels of worry. The groups' LNS scores did not differ at the 50th (t (39) = -1.77, p = 0.08), 75th (t (39) = .77, p = 0.44), and 90th (t (39) = 1.29, p = 0.21) percentiles of the distribution of self-reported worry. These findings indicate that TD children with higher levels of self-reported worry perform similarly to children with ADHD. Table 3 Displays the regression values and Figure 3 displays LNS raw score comparisons.

A follow-up linear regression was used to examine the moderating effect of self-reported worry on the relationship between group (ADHD vs TD) and WM performance while controlling for GAI, SES, and RAN. GAI (b = 0.07, t (39) = 1.67, 95% CI [-0.01, 0.16]), SES (b = 0.07, t (39) = 1.43, 95% CI [-0.03, 0.17]), and RAN (b = 0.07, t (39) = 1.88, 95% CI [-0.01, 0.14]) were non-significant covariates in the model. Further, group did not significantly predict LNS scores, b = -1.35, t (39) = -0.92, 95% CI [-4.33, 1.64], and the relationship between group and WM performance was not moderated by self-reported worry, b = 0.48, t (39) = 1.18, 95% CI [-0.35, 1.30], when the covariates were included in the model. Table 4 displays the regression and covariate values.

Tier 2: Examination of the Moderation effect of Physiological Anxiety on WM Performance

A linear regression was used to examine the moderating effect of self-reported physiological anxiety on the relationship between group (ADHD vs TD) and WM

performance. Results indicated that group (ADHD, TD) significantly predicted LNS scores, b = -3.89, *t* (39) = -2.03, 95% CI [-7.77, -0.01], such that children with ADHD had lower scores than TD children. However, the relationship between group assignment and WM performance was not moderated by self-reported physiological anxiety b = .44, *t* (39) = 1.03, 95% CI [-0.60, 1.06]. Table 3 displays the regression values.

A follow-up linear regression was used to examine the moderating effect of self-reported physiological anxiety on the relationship between group (ADHD vs TD) and WM performance while controlling for GAI, SES, and RAN. GAI (b = 0.06, *t* (39) = 1.46, 95% CI [-0.02, 0.15]), SES (b = 0.09, *t* (39) = 1.88, 95% CI [-0.01, 0.19]), were non-significant covariates in the model, whereas RAN (b = 0.08, *t* (39) = 2.12, 95% CI [0.01, 0.15]) was a significant covariate. Further, group did not significantly predict LNS scores, b = -1.64, *t* (39) = -0.91, 95% CI [-5.33, 2.04] and the relationship between group and WM performance was not significantly moderated by self-reported physiological anxiety, b = 0.36, *t* (39) = 0.89, 95% CI [-0.47, 1.18], when the covariates were included in the model. Table 4 displays the regression and covariate values.

Tier 3: Examination of the Moderation effect of Social Anxiety on WM Performance

A linear regression was used to examine the moderating effect of self-reported social anxiety on the relationship between group (ADHD vs TD) and WM performance. Results indicated that group (ADHD, TD) significantly predicted LNS scores, b = -4.32, *t* (39) = -3.06, 95% CI [-7.22 -1.41], such that children with ADHD had lower scores than TD children. However, the relationship between group assignment and WM performance was not moderated by self-reported social anxiety b = 1.15, *t* (39) = 2.20, 95% CI [-3.97, 4.97]. Table 3 displays the regression values.

A follow-up linear regression was used to examine the moderating effect of self-reported social anxiety on the relationship between group (ADHD vs TD) and WM performance while controlling for GAI, SES, and RAN. GAI (b = 0.05, *t* (39) = 1.11, 95% CI [-0.04, 0.14]), SES (b = 0.08, *t* (39) = 1.60, 95% CI [-0.02, 0.18]), were non-significant covariates in the model, whereas RAN (b = 0.08, *t* (39) = 2.10, 95% CI [0.01, 0.15]) was a significant covariate. Further, group did not significantly predict LNS scores, b = -2.25, *t* (39) = -1.51, 95% CI [-5.25, 0.78], and the relationship between group and WM performance was not moderated by self-reported physiological anxiety, b = 0.82, *t* (39) = 1.56, 95% CI [-0.25, 1.89], when the covariates were included in the model. Table 4 displays the regression and covariate values.

CHAPTER V

CONCLUSION

The current study examined three self-report scales of anxiety: worry, physiological anxiety, and social anxiety, as potential moderators of PH-WM performance differences between children with ADHD and their typically developing peers. Previous literature examining the effects of anxiety on WM performance in children with and without ADHD have failed to identify greater WM deficits in children with ADHD and anxiety compared to children with ADHD alone. (Bloemsma at al., 2013; Ferrin &Vance, 2014; Manassis, Tannock, Young, & Francis-John, 2007). These null findings may be due to a variety of potential methodological confounds, such as utilization of WM tasks that fail to place sufficient demands on the CE (Bloemsma at al., 2013; Ferrin & Vance, 2014), failure to include self-report anxiety rating scales (Bloemsma at al., 2013; Ferrin & Vance, 2014), and utilization of only broadband anxiety or combined anxiety/depression self-report scales (Bloemsma at al., 2013; Ferrin & Vance, 2014; Manassis, Tannock, Young, & Francis-John, 2007). The current study addressed these limitations by using children's self-reported anxiety levels in lieu of parent and teacher scales, examining three unique subscales that reflect various symptom cluster of anxiety, and by utilizing a PH-WM task (i.e., Letter-Number Sequencing) that places higher demands on CE functioning compared to forward or backward span tasks.

Overall, as expected, children with ADHD exhibited significantly lower PH-WM performance compared to their TD peers, as measured by raw scores on the LNS subtest of the WISC-IV. These findings are consistent with various experimental examinations (Alderson et al., 2010; Kofler, Rapport, Bolden, Sarver, & Raiker, 2010; Rapport et al., 2008; Rapport et al., 2009) and meta-analytic reviews (Alderson et al., 2013; Kasper, Alderson, & Hudec, 2012; Martinussen, Hayden, Hogg-Johnson, & Tannock, 2005; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005) that have reliably observed WM deficits in children with ADHD. Together, these results continue to support Rapport and colleagues' (2008) functional working memory model of ADHD; in particular, the hypothesis that impaired CE functioning and limited storage rehearsal capacity in the PH system serve as core features of ADHD.

Children with ADHD, compared to children in the TD group, reported significantly higher levels of worry, as measured by the worry subscale of the RCMAS-2. This is not surprising given the body of literature that suggests 25 to 50% of children with ADHD also suffer from elevated anxiety, relative to unaffected peers (Barkley, 2014; Costello, Egger & Angold, 2004). Children with ADHD also had higher levels of self-reported physiological anxiety and social anxiety compared to their TD peers. These findings are consistent with previous literature that indicated children with ADHD often experience significant social concerns or deficits (Kofler et al., 2011) and experience higher rates of social anxiety symptoms (Koyuncu et al., 2015). These findings are also consistent with regard to physiological anxiety symptoms, as previous literature suggests that children with ADHD often report more frequent somatic complaints compared to their TD peers (Egger, Costello, Erkanli, & Angold, 1999).

The examination of the three moderation analyses yielded several important findings. Consistent with our *a priori* hypothesis, children's self-reported worry significantly moderated the relationship between group and WM performance, such that typically developing children performed better than children with ADHD at low levels of anxiety, but similarly at high levels of anxiety. When further probed, the nature of this relationship was somewhat surprising. Specifically, high levels of self-reported worry were associated with decreased WM performance, but only for TD children. Although these findings are consistent with those from previous experimental (Darke, 1988; MacLeod & Donnellan, 1993; Miyake et al., 2000; Ikeda, Iwanaga & Sweiwa, 1996, Sorg & Whitney, 1992) and meta-analytic (Moran, 2016; Owens et al., 2012) studies that suggest heightened levels of anxiety and worry are generally associated with deficits in WM, they do not support our *a priori* hypothesis that the presence of worry would result in a disproportionate/compounded decrease in WM performance among children with ADHD. One potential explanation for these unexpected findings is that children with ADHD exhibited a floor effect , whereas children in the typically developing group had greater room to vary. Alternatively, the LNS task used in this study may lack sufficient sensitivity to detect within group variability in ADHD-related WM deficits due to the task's low number of trials. Specifically, findings from experimental (Tarle et al., 2017) and meta-analytic (Kasper et al., 2012) studies suggest that WM tasks that administer a greater number of trials (e.g., $\geq$ 10) are associated with larger between group effects. Although these results are consistent with findings from Bloemsma et al. (2013), Ferrin and Vance (2014), and Manassiss et al. (2007), the limitations with the WM task may in part explain the null results, suggesting additional work in this area is needed.

Contrary to expectations, neither self-reported physiological anxiety nor social anxiety significantly moderated the relationship between group and PH-WM performance. These findings were unexpected given findings from previous studies that suggest anxiety in children often manifests as somatic symptoms or complaints (Eisen & Engler, 1995), and that WM deficits are associated with high state and/or trait anxiety (Darke, 1988; MacLeod & Donnellan, 1993; Miyake et al., 2000; Ikeda, Iwanaga & Sweiwa, 1996, Sorg & Whitney, 1992) and social anxiety (Moruya & Sugiura, 2012; Segal, Kessler, & Anholt, 2014). Although, it should be noted that in several examinations of anxiety, ADHD, and WM performance in children, no differences in performance were observed between anxious children and controls (Bloemsma et al., 2013; Manaiss et al., 2007). Nonetheless, several potential factors may explain these findings. First, it is likely that limited variability in physiological and social anxiety scores obtained from children in this study contributed to the null findings, as only five children with ADHD and four TD children reported physiological and/or social anxiety above the normal range. Another potential explanation is that physiological anxiety and social anxiety are more closely associated with impairments in other executive functions, such as inhibition (Miyake et al., 2000), not examined via the LNS task.

Notably, when controlling for GAI, SES, and reading ability (i.e. RAN), group status (ADHD, TD) no longer predicted WM performance and no significant moderations were found across all three models. That is, when controlling for other factors that have been associated with WM deficits in previous literature (Cornoldi et al.,2013; Jacobson et al., 2010; Leonard et al., 2015), ADHD no longer accounted for a significant proportion of variance associated with WM performance. The simplest explanation for this finding is

that the relatively poor WM performance exhibited by children in the ADHD group does not solely reflect a neurocognitive deficit central to ADHD, but rather, the influence of ADHD-related secondary outcomes such as academic underachievement in reading (Alloway, Gathercole, & Elliot, 2010; Rogers, Hwang, Toplak, Weiss, & Tannock, 2011), lower SES (Litt, 2004), and lower intellectual functioning. This explanation, however, contrasts the wealth of extant findings published in the last two decades (see Kasper et al., 2012 for a meta-analytic review) that provide strong support for ADHD-related WM deficits, as well as changes in the current iteration of the DSM-5 that list ADHD as a neurodevelopmental deficit (APA, 2013). An alternative explanation is that the GAI, SES, and RAN variables are not appropriate covariates for the current study, and consequently, findings from the covariate analyses should be considered with caution. Specifically, the preliminary analysis indicated no significant differences in GAI, SES, or RAN scores between the ADHD and TD groups. Previous ADHD literature has indicated that when groups do not differ on a potential covariate, simple models with no covariates are preferred (Friedman, Rapport, Raker, Orban, & Eckrich, 2016; Raiker et al., 2012). This is particularly salient to the current study, as inclusion of the covariates is expected to increase risk of Type II errors, and consequently, obscure interpretations (i.e., Are non-significant findings due to the covariates accounting for significant variance, or are the non-significant findings due to underpowered analyses?). Moreover, Dennis and colleagues (2009) suggest that it is inappropriate to examine covariates in neurocognitive studies when the covariates reflect outcomes of the independent or dependent variables. That is, to the extent that variability in a potential covariate reflects variability associated with the neurodevelopmental disorder, removing such variability via covariate analyses is

not theoretically justified and results in "…overcorrected, anomalous, and counterintuitive findings about neurocognitive function." To that end, Dennis and colleagues (2009) indicate it is not possible or appropriate to attempt to separate intellectual abilities from a neurodevelopmental disorder as IQ "postdates" not "predates" the disorder. In a similar vein, findings from a recent study revealed that CE WM deficits mediate reading deficits in children with ADHD (Freidman et al., 2016), and several previous studies have suggested that ADHD leads to lower SES and greater economic burden (Doshi et al., 2012; Liss, 2014; Pelham, Foster, & Robb, 2007). Nonetheless, findings from the covariate analyses warrant consideration and convey the need for provide future research on additional variables that may influence the relationship between ADHD, anxiety, and WM performance.

Although findings from this study yielded important information about the influence of various anxiety symptom clusters on the relationship between ADHD and PH-WM performance, this study is not without limitations. First, this study did not include a group of children with ADHD and clinically significant comorbid anxiety, or a group of children with clinically significant anxiety alone. The inclusion of children with clinically significant anxiety is expected to increase variability in scores and consequently may yield additional significant findings. Future studies are needed to test this hypothesis. Further, this study's sample size precluded an examination of how self-reported anxiety symptoms differentially affect the three ADHD presentations. Future examinations of this nature are important given previous research that has suggested ADHD-C and ADHD-I exhibit different EF deficits (Barkley, 1998; Nigg, Blaskey,

Huang-Pollock, & Rappley, 2002), and anxiety may improve correct strategy usage in children with ADHD-C, but not in children with ADHD-I (Ferrin & Vance, 2013).

Collectively, findings from the current study suggest that self-reported worry is associated with decreased PH-WM performance in children who are TD, but not in children with ADHD. It is notable that the anxiety-related decrease in WM performance was observed in non-treatment seeking, typically developing children that did not meet criteria for a formal anxiety diagnosis, indicating that subclinical levels of worry can substantially affect cognitive performance. Moreover, our observation that children with high levels of worry exhibited WM impairments similar to children with ADHD suggests that WM deficits may represent a universal core deficit or transdiagnostic feature associated with general psychopathology. To that end, these findings may help explain potential phenotypic similarities (i.e. forgetfulness and inattention) observed in children with anxiety and children with ADHD. Lastly, these findings may provide clarity to the poor academic performance frequently observed in children with diagnosed and non-diagnosed anxiety (Owens, Stevenson, Hadwin, & Norgate, 2012), as WM performance has been previously linked to academic underachievement achievement (Aronen, Vuontela, Steenari, Salmi, & Carlson, 2004).

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APPENDICES

Appendix A

Overview of Attention Deficit/Hyperactivity Disorder

Attention Deficit/Hyperactivity Disorder (ADHD) is a pervasive, multifaceted, and complex neurocognitive disorder that interferes with the daily functioning and overall development of children and adults (American Psychiatric Association, 2013; Barkley, 2006). Epidemiological estimations of ADHD prevalence rates suggest that 3 to 7% of the current childhood population (Polanczyk, de Lima, Horta, Biederman, & Rohde, 2007) are affected by the disorder. Previous factor analytic studies indicate common ADHD symptom manifestations fall within three primary symptom clusters; inattention, hyperactivity, and impulsivity. Inattentive symptoms include frequent off task behaviors, forgetfulness, poor attention, and concentration difficulties (Bauermeister et al., 2005). Hyperactive symptoms include developmentally inappropriate or excessive motor activity and fidgeting (Barkley, 1998), while impulsive symptoms include acting without foresight and the inability to delay gratification (Gaub & Carlson, 1997a; Williams & Dayan, 2005; Winstanley, Eagle, & Robbins, 2006). These symptom clusters are reflected in the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; DSM-5; American Psychiatric Association, 2013), which currently identifies three presentations of the disorder; predominately inattentive presentation (ADHD-I), predominately hyperactive/impulsive presentation (ADHD-H), and combined

presentation (ADHD-C). While meta-analytic reviews suggest that ADHD-I is the most common presentation in the general population (Baumgartel, Wolraich, & Dietrich, 1995; Wolraich, Hannah, Pinnock, Baumgaertal, & Brown, 1996), prevalence rates of ADHD-C in clinical samples equal or exceed the rates of the ADHD-I presentation (Faraone, Biederman, Weber, & Russell, 1998). These differences suggest that children with the ADHD-C presentation are more likely to be referred for treatment (Carlson, Shin, Booth, 1999). Further, hyperactive symptoms have been noted as the primary reason for clinical referrals in comparison to inattentive or impulsivity symptoms (Sayal, Taylor, Beecham, & Byrne, 2002).

Gender differences in prevalence rates of ADHD diagnoses have been frequently noted, with male diagnoses exceeding female diagnoses by 2:1 in the childhood population, and 1.6:1 in the adult population (Gershon, 2002; Lee, Oakland, Jackson, & Glutting, 2008). Notably, males are more likely to receive an ADHD-H or ADHD-C diagnosis, while females are more likely to receive an ADHD-I diagnosis (Biederman et al., 2002). The gender differences in clinical diagnostic rates likely reflect referral biases from parents, teachers, and physicians (Gaub & Carlson, 1997b). For example, hyperactive behavior or hyper-talkativeness in females is often seen as less disruptive than hyperactive behaviors seen in males with the disorder, which may result in a gender bias in the observation or reporting of hyperactive symptoms (Gaub & Carlson, 1997b; Quinn, 2005).

A variety of negative outcomes have been associated with ADHD in both children and adults with the disorder. For example, children with ADHD, compared to their typically developing peers, are more likely to underachieve in reading, writing, and

mathematics (Barry, Lyman, & Klinger, 2002; Mannuzza, Klein, Bessler, & LaPadula, 1993; Marshall, Hynd, Handwerk, & Hall, 1997). Adults with ADHD are at an increased risk for dropping out of high school and college (Harpin, 2005). Children and adults with ADHD are also more likely to experience impairments in social functioning which can result from noncompliance with authority and overbearing or intrusive behaviors toward peers (Harpin, 2005, Pelham, et al., 2007; Keown & Woodard, 2006). In addition, symptoms associated with ADHD are predictive of a number of lifelong negative outcomes, such as violent criminal behavior (Klinteberg, Andersson, Magnusson, & Stattin, 1993), increased rates of substance use disorders (Bierderman el al., 1995), increased rates of sexually transmitted infections, increased rates of traffic violations or accidents, increased rates of workplace suspensions or dismissal, and increased rates of divorce (Barkley et al., 2006; Barkley, Murphy, & Fischer, 2008; Murphy & Barkley, 1996).

ADHD and Comorbid Psychological Disorders

In addition to being associated with a variety of negative outcomes, ADHD occurs frequently with other psychological disorders. Evidence derived from community-based samples suggest that 44% of children with ADHD met criteria for at least one additional psychological diagnosis and 43% met criteria for two or more diagnoses (Mash & Barkley, 2014; Willcutt et al.., 2012). Available research suggests that approximately 42.7 to 93% of children with ADHD exhibit symptoms and impairment consistent with a comorbid diagnosis of oppositional defiant disorder (ODD) and/or conduct disorder (CD; Biederman et al., 2005; Kuhne, Schachar, & Tannock, 1997; Spencer, Biederman, & Wilens, 1999). Further, studies of clinical populations indicate that between 54 to 67%

of children with ADHD will meet criteria for ODD or CD by age seven (Mash & Barkley, 2014). Children and adults with ADHD are also at an increased risk for developing substance use disorders (SUD), with 12 to 24% of individuals with ADHD meeting criteria for a SUD within their lifetime (Wilens, 2004).

While earlier research primarily focused on the comorbidity of ADHD and other externalizing and substance use disorders, recently there has been an increased interest in the relationship between ADHD and co-occurring internalizing disorders. For example, comorbid mood disorders, such as depression, are present in 20 to 30% of children and adults with ADHD (Barkley et al., 2008; Bierderman et al., 1992; Marsh & Barkley, 2014). In addition, some estimates indicate that 25 to 50% of children with ADHD also suffer from anxiety disorders (Barkley, 2014; Costello, Egger & Angold, 2004). Children with anxiety disorders are at an increased risk for additional lifelong negative outcomes, such as suicidal behavior, educational underachievement, substance dependence, and development of additional psychological disorders (Woodward & Ferguson, 2001); consequently, one might expect increased negative outcomes associated with the comorbid disorder. However, studies examining impairment associated with comorbid ADHD and anxiety are generally mixed. Examinations of the clinical presentation of ADHD and comorbid anxiety have found that children with anxiety often exhibit later age of onset of ADHD symptoms, exhibit less off-task behavior, and show fewer hyperactive symptoms than children with ADHD alone (Pliszka, 1991; Pliszka, 1992). However, some studies have found that children with comorbid ADHD and anxiety disorders exhibit greater levels of inattention (Jarret et al., 2016; Jenson et al., 2001) than children with ADHD or anxiety alone. Moreover, some research has found lower rates of

oppositional behaviors in children with ADHD and anxiety (Pliszka, 1989, Pliszka, 1992), while other studies have shown increased rates of these behaviors in children with the comorbidity (Humphreys, Aguirre, & Lee, 2012; Newcorn et al.,2001; Tannock, 2000). Children with comorbid ADHD and anxiety have also been found to report more academic problems than children with ADHD alone (Biederman, Faraone, & Chen, 1993).

Underlying Neurocognitive Mechanism of ADHD

Brief Overview. Because of the complex and pervasive nature, lifetime negative outcomes, and high prevalence rates of ADHD, numerous conceptualizations of the underlying core features of the disorder have led to several well-researched theoretical models. These models primarily aim to identify the central and secondary endophentoypes that influence the likelihood of developing or exhibiting symptoms associated with ADHD (Castellanos & Tannock, 2002). Existing models of ADHD identify many similar executive functioning and neurocognitive core deficits including behavioral inhibition (Barkley, 1997), planning and decision making (Sergeant, 2005), delay aversion (Songue-Barke, 2005), working memory (Rapport et al., 2008), and underdevelopment of the prefrontal cortex (Halperin & Schulz, 2006). However, the primary distinguishing features of each model are the differing hypotheses on the primary and secondary roles of working memory other executive functions, and their relationship to ADHD-related core (inattention and hyperactivity/impulsivity) and tertiary deficits (e.g., peer problems, academic underachievement; Rapport et al., 2008).

The functional working memory (WM) model of ADHD (Rapport et al., 2008) is a relatively recent theoretical model that has been frequently examined in an ever

growing body of literature. This model suggests that WM deficits serve as the core feature of ADHD, and underlie other deficits in executive functioning such as behavioral inhibition, delay aversion, and self-regulation. Baddeley's (2007) multi-component model of WM serves are the theoretical basis for the functional WM model. Baddeley's model of WM and Rapport's Functional WM model of ADHD are reviewed in more detail below.

Baddeley's multi-component model of WM. Baddeley's multi-component model (2007) defines WM as an executive function that is responsible for the temporary maintenance, storage, and manipulation of visually and aurally presented information. The WM system is parsed into four distinct, yet interacting subcomponents: the phonological (PH) loop, the visuospatial (VS) sketchpad, the episodic buffer (EB), and the central executive (CE) system. The PH loop and the VS sketchpad are responsible for the temporary storage, rehearsal, maintenance, and processing of auditory and visual information, respectively. Neuroimaging studies of WM have found that the PH loop is most closely associated with the left temporoparietal region of the brain, while the VS sketchpad is most closely associated with areas in the right hemisphere (Baddeley, 2007; Henson, 2001; Jonides et al., 1993; Paulesu, Frith, & Frackowiak, 1993; Smith & Jonides, 1997). The EB subcomponent of WM is hypothesized to be responsible for the temporary storage, and maintenance of bound information provided via multiple modalities (e.g. visual and auditory information presented simultaneously), and serves as the link between short-term and long-term memory (Baddeley, Allen, & Hitch, 2011).

Often conceptualized as the "working" component of WM, the CE subsystem is responsible for resource allocation, dividing, switching, and maintaining attention, as

well as manipulating information processed via the PH, VS, and EB subsystems (Baddeley, 2007). The CE has also often been identified as the key component that differentiates WM from short-term memory, as it is largely responsible for maintaining and directing attention toward relevant stimuli and manipulating information in the PH,VS, and EB during the completion of tasks (Baddeley & Hitch, 1974; Shah & Miyake, 1999). Due to the importance of the CE and its relationship to general executive functioning, interest in the nature of each unique facet of the CE has grown. Specifically, investigations of these facets aim to explain individual variability in performance across WM tasks (Daneman & Carpenter, 1980; Saito & Miyake, 2004). Examinations from correlational (Friedman, Miyake, Robinson, & Hewitt, 2011) and factor analytic (Miyake et al., 2000; Miyake & Friedman, 2012) studies, for example, have found that updating, shifting, and inhibitory processes associated with the CE are strongly correlated with one another, indicating that they share some common underlying process. However, these unique processes are also discreet, as they each relate differently to neuropsychological measures of the frontal lobe. That is, the CE subsystem of WM could perhaps be further divided into separate components which that better represent specific deficits related to various psychopathologies or brain lesions (Miyake, Emerson, & Friedman, 2000). A visual schematic of Baddeley's multi-component model of working memory is provided in Figure 1.

Rapport's Functional Working Memory Model. Rapport and colleagues' (2008) model of ADHD hypothesizes that an individual's genotype leads to the neurobiological endophenotype of impaired CE functioning and limited storage rehearsal capacity in the PH and VS subsystems. This endophenotype is identified as the core

feature of ADHD, which in turn leads to learning problems, hyperactivity, impulsivity, and inattention. A visual schematic of Rapport's functional working memory model is provided in Figure 2.

Numerous experimental examinations have supported the hypotheses proposed by Rapport and colleagues' model. Deficits in the CE, PH, and VS subsystems of WM have been reliably observed in both children (Alderson et al., 2010; Kofler, Rapport, Bolden, Sarver, & Raiker, 2010; Rapport et al., 2008; Rapport et al., 2009) and adults (Alderson, Hudec, Patros, & Kasper, 2013; Alderson, Kasper, Hudec, & Patros, 2013; Hervey, Epstein, & Curry, 2004; Hudec, Alderson, Patros, & Kasper, 2014) with ADHD. Notably the largest-magnitude WM deficits, in children with ADHD were associated with the CE and VS storage/rehearsal processes (Rapport et al., 2008), while the largest magnitude WM deficits in adults with ADHD were associated with the CE and PH storage/rehearsal processes (Alderson et al., 2013). These changes seem to indicate that deficits associated with ADHD tend to shift ontologically and are consistent with findings from basic-cognitive research that suggest children typically rely predominantly on the VS system until around the age of 10 years when the PH systems matures (Gathercole, Pickering, Ambridge, & Wearing, 2004). Moreover, these shifts are likely related to maturations of neuroanatomical areas associated with WM, as adults with ADHD tend to exhibit less pronounced cortical under arousal compared to children with the disorder (Shaw et al., 2007).

Meta-analytic reviews of WM deficits in children and adults with ADHD have yielded moderate to large magnitude PH and VS WM deficits (Alderson et al., 2013; Kasper, Alderson, & Hudec, 2012; Martinussen, Hayden, Hogg-Johnson, & Tannock,

2005; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005) that are moderated by a variety of subject and task variables (Alderson et al., 2013; Kasper et al., 2012). Specifically, Kasper and colleagues found that studies that included a low percentage of females in the sample, greater numbers of experimental trials, high demands on the CE, and recall rather than recognition tasks, were associated with larger magnitude between-group PH and VS effect sizes. Additionally, studies are expected to yield VS effect sizes of 2.15 and PH effect sizes of 2.01 in child studies (Kasper, Alderson, & Hudec, 2012), and VS effect sizes of 1.22 and PH effect sizes of 1.44 in adult studies (Alderson et al., 2013), when best-case procedures are utilized.

Converging evidence from a growing body of studies suggests that WM deficits are upstream of DSM-5 defined core and secondary features of the disorder. For example, CE and VS-WM deficits have been found to mediate differences in performance between children with ADHD and their typically developing (TD) peers on behavioral inhibition (Alderson et al., 2010) and objectively measured impulsivity tasks (Patros et al., 2015; Raiker, Rapport, Kofler, & Sarver, 2012). Similarly, ADHD related hyperactivity has been found to be functionally related to WM deficits in both children (Alderson et al., 2012; Hudec, Alderson, Patros, Lea, Tarle, & Kasper, 2015; Porrino et al., 1983; Rapport et al., 2009) and adults (Hudec et al., 2014; Lea, Alderson, Patros, Tarle, Arrington, & Grant, under review; Lis et al., 2010). These findings are consistent with predictions from Rapport et al.'s (2001; 2009) working memory model that suggest ADHD-related hyperactivity serves as a compensatory behavior to increase cortical arousal needed to improve WM performance (Rapport et al., 2009). ADHD-related academic underachievement in reading has been associated with significant PH-WM impairments,

while academic underachievement in mathematics appears to be associated with impairments in both the PH and VS WM subsystems (Alloway, Gathercole, & Elliot, 2010; Rogers, Hwang, Toplak, Weiss, & Tannock, 2011). Lastly, WM deficits have been found to mediate the indirect relationship with ADHD and parent/teacher reports of social skills deficits (Alloway et. al., 2005; Kofler et al., 2011; Phillips, Tunstall, & Channon, 2007).

Working Memory and Anxiety Disorders

Paralleling ADHD-related WM research, studies of anxiety disorders have increasingly begun to examine potential underlying neurocognitive deficits. For example, several examinations of WM in individuals with high state and/or trait anxiety have identified multiple deficits in both storage/rehearsal and CE-WM systems (Darke, 1988; MacLeod & Donnellan, 1993; Miyake et al., 2000; Ikeda, Iwanaga & Sweiwa, 1996, Sorg & Whitney, 1992). Further, a recent meta-analytic review found that higher levels of self-reported general anxiety are reliably related to poor WM capacity across simple, complex, and dynamic span tasks in both children and adults (Moran, 2016). Another meta-analytic review aimed at identifying the relationship of WM and academic performance in anxious individuals found that high levels of worry are associated with deficits in CE-WM, which ultimately leads to poor academic performance (Owens, Stevenson, Hadwin, & Norgate, 2012). Additionally, socially anxious individuals have been shown to have difficulties disengaging from goal-irrelevant stimuli as WM load increases (Judah, Grant, Lachner, & Mills, 2013; Moriya & Sugiura, 2012). Theoretical explanations of these deficits suggest that anxiety increases focus on the short-term stimulus driven system (i.e. the system responsible for attention to task relevant stimuli),

rather than the long-term goals driven system (i.e. the system responsible for identifying and maintaining current goals), resulting in deficits in CE processes such as inhibition, shifting, and updating (Miyake et al., 2000).

Working Memory in Children with ADHD and Comorbid Anxiety

Given the substantial body of literature that has found multiple deficits in WM associated with both ADHD and anxiety, there has been an increased interest in determining if individuals with this comorbidity experience behavioral and/or neurocognitive deficits above and beyond deficits exhibited by children with ADHD alone. Findings from extant studies, however, have yielded mixed results. For example, Manassis, Tannock, Young, and Francis-John (2007) examined differences in WM in children with ADHD, children with anxiety, children with comorbid ADHD and anxiety, and normal controls (Manassis, Tannock, Young, & Francis-John, 2007). Children in this study completed the Children's Paced Auditory Serial Addition Test (CHIPASAT) and the Finger Windows Backward task to assess PH and VS WM, respectively. Results from this study indicated that, compared to normal controls, children with ADHD and children with comorbid ADHD/anxiety performed more poorly on both WM tasks, but children with anxiety alone did not. Moreover, children with ADHD and comorbid anxiety did not perform significantly worse than children with ADHD alone. It is noted that the heterogeneous mix of anxiety disorders in both the anxiety-only and ADHD/anxiety groups obscures interpretations about the results, given anxiety disorders appear to present with varying phenotypes of WM deficits. For example, individuals with social anxiety have been shown to exhibit changes in performance on WM tasks depending on the presence or absence of "threat" related stimuli, while individuals with other anxiety

disorders exhibit deficits when feeling worried (Amir & Bomyea, 2011; Eysenck, Derakshan. Santos, & Calvo, 2007). It is also noted that the CHIPASAT is a timed task that relies heavily on processing speed (Diehr, Heaton, Miller, & Grant, 1998), which may confound conclusions related specifically to PH-WM. That is, between-group performance differences may reflect basic differences in processing speed rather than WM.

Another study aimed to examine the effect of anxiety on executive functioning utilizing structural equation modeling (SEM; Bloemsma at al., 2013). Anxiety symptoms were measured via parent, teacher, and self-report measures, while children completed a digit span backward task to measure PH-WM. Findings from the study indicated that there was no relationship between WM functioning and parent, teacher, or self-reported anxiety. However, these findings should be interpreted with caution as previous findings from SEM (Engle et al., 1999), factor analytic (Cantor et al., 1991; Moleiro et al., 2013), and experimental (Tarle et al., under review) studies suggest that backward span tasks do not place greater demands on CE functioning compared to forward span tasks, and consequently, backwards span tasks provide metrics of short-term memory (i.e., storage/rehearsal processes), rather than working memory (i.e., interaction of CE and storage/rehearsal processes). Not surprisingly, meta-analytic findings reveal that backward span tasks are relatively unreliable in their ability to detect WM deficits (Kasper et al., 2012), as impaired CE functioning appears to represent the greatest deficit in affected children (Alderson et al., 2010; Dovis, Van der Oord, Wiers, & Prins, 2013; Martinussen et al., 2005; Rapport et al., 2008). Studies that utilize task associated with higher CE demands, therefore, are expected to yield differences in WM performance

associated with anxiety. Lastly, this study utilized broad anxiety measures that included symptoms associated with any DSM-IV-TR (American Psychiatric Association, 2000) anxiety diagnosis. This broad measure limits any interpretations about how the nature of the children's symptoms (e.g. social phobia versus worry) affect WM performance.

A subsequent study examined if the presence of anxiety and/or depression moderated VS or PH-WM performance in children with ADHD and their typically developing peers (Ferrin & Vance, 2014). Subtypes of ADHD were also examined to determine if anxiety and depressive symptoms effect each subtype differently. Children completed the Digit Span task and the Spatial Working Memory task of the Cambridge Neuropsychological Test Automated Battery (CANTAB; Robbins et al., 1994), while anxiety and depression symptoms were measured via parent report on the anxiety and depression subscales of the Child Behavior Checklist (Achenbach & Rescorla, 2001). Findings indicated that PH-WM was impaired in all children with ADHD regardless of their level of anxiety/depression. Children with ADHD-C and higher levels of anxiety/depression exhibited higher levels of correct strategy usage, while children with ADHD-I and higher levels of anxiety/depression exhibited better spatial span compared to children with ADHD-C. Finally, typically developing children who experienced high levels of anxiety/depression made more search errors during the VS-WM task. Several limitations of the study, however, warrant consideration. In addition to the use of simple span tasks as measures of WM, a broad anxiety and depression measure was used to examine internalizing symptoms. Utilizing a single scale to examine both anxiety and depressive symptoms, rather than narrow-band scales related to anxiety or depression alone, confounds potential conclusions as depressive and anxiety symptoms may result in

differing WM deficits (Eysenck et al., 2007; Zakzanis, Leach, & Kaplan, 1998). Furthermore, this study failed to include self-report measures of internalizing symptoms, which is problematic given research indicating frequent discrepancies between parent and child reports of internalizing symptoms (Weems, Feaster, Horigian, & Robbins, 2011).

Finally, two studies have examined the effects of methylphenidate on WM performance in children with comorbid ADHD and anxiety (Bedard & Tannock, 2007; Tannock, Ickowicz, & Schachar, 1995). Findings from both studies suggest that methylphenidate improves WM performance in children with ADHD only when a comorbid anxiety disorder is not present. Specifically, methylphenidate improved performance associated with the CE and VS storage/rehearsal components of WM in the ADHD only group, but not the comorbid group. These findings suggest that WM deficits associated with comorbid anxiety and ADHD may result from a different underlying endophenotype than the deficits associated with anxiety or ADHD alone.

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