# Cognitive and Emotional Sequelae of Exposure to Maternal Depression: Memory Functioning as a Neuropsychological Correlate of Internalizing Symptomatology

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**Abstract**

Children exposed to maternal depression are at greater risk for depressive disorders later in life. Researchers have suggested that these youth experience marked stress from the care provided by parents afflicted with mental illness; in turn, chronic exposure to the toxic environment alters neural substrates involved in emotion and stress regulation, such as the hippocampus and prefrontal cortex. However, current literature on neurobehavioral functioning of these at-risk youth relative to healthy peers is sparse and conflicting. Furthermore, it is unclear whether these neurocognitive indices, such as memory functioning, are predictive of internalizing symptomatology in these youth.

Accordingly, this study examines the relationships between chronic exposure to maternal depression, severity of mother's recent symptomatology, and child's earlier internalizing symptomatology with later memory and psychological functioning (internalizing and externalizing behaviors). A total of 100 children and their parents were assessed when the child was 18 months old and followed up at 5 and 9 years of age. Of these youth, 50 child participants had mothers who had major depression at 18 months (i.e., depressed caregivers, DC), and 50 were those with nondepressed, healthy caregivers (NC). Mothers with depression were coded into three groups: chronic depression, recurrent depression, and non-recurrent depression. Children's caregiver completed the Child Behavioral Checklist (CBCL) when the child was 18 months, 5 years and 9 years to determine overall internalizing and externalizing symptomatology observed. Child participants also completed the self-report version of the Child Depression Inventory, California Verbal Learning Inventory, and subtests from the Wide Range Assessment of Memory and

Learning battery to assess their depressive symptomatology, verbal memory skills, and visual memory functioning respectively. Multiple hierarchical regressions were used to examine associations between chronic maternal depression, recent maternal depression severity, and child's earlier internalizing symptomatology with later memory and emotional functioning at 9 years. Linear mixed effects model and analysis of covariance were applied to examine the growth pattern for internalizing symptomatology based on the CBCL.

Broadly, results indicate that more chronic exposure to maternal depression, but not mothers' recent symptomatology, is associated with lower verbal memory performance and greater internalizing and externalizing symptoms in the offspring. Internalizing symptomatology of children at age 5 years was not predictive of later memory functioning at 9 years, but was associated with increased internalizing and externalizing symptoms later at 9 years. Importantly, memory functioning, a neurobehavioral index of hippocampal functioning, was not predictive of concurrent psychological functioning (i.e., both externalizing and internalizing symptoms). Finally, both DC and NC youth showed similar non-linear, developmental patterns in their internalizing symptomatology from 18 months to 5 and 9 years; however, DC youth showed elevated symptoms relative to NC peers at baseline, a disparity that persisted by 9 years of age.

These findings broadly support the postulation that chronic exposure to maternal depression may impact later hippocampal functioning, as indicated by lower verbal memory performance in offspring. However, findings also indicate that memory

performance is not a strong predictor of concurrent psychological functioning, despite that this factor behaviorally indexes the functional status of the hippocampus, a neural substrate involved in stress regulation. Findings highlight importance of engaging depressed mothers in interventions for self and parent-child relationship earlier to reduce the persistent and negative effects of maternal depression on their offsprings' development.

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## Introduction

Major depression is a debilitating mental illness with a prevalence rate of approximately 9% (CDC, 2010), and lifetime prevalence of approximately 16% (Kessler et al., 2003). Major depressive disorder is characterized by the experience of anhedonia (i.e., loss of interest/pleasure) or depressed mood, in addition to a permutation of the following symptoms: sleep and/or appetite disturbances, psychomotor change, sense of guilt/worthlessness, concentration difficulties, suicidal ideation (DSM-V, 2015). Although major depression is diagnosed typically by episodes (i.e., two month span of symptoms), this condition is often recurrent (Kessler et al., 2003). A conceptual framework, "kindling hypothesis", has been increasingly applied to research investigating stress and recurrent depression (Monroe & Harkness, 2005; Post, Rubinow, & Ballenger, 1986). Kindling hypothesis refers to the process of change, whereby initial causal factors that triggered the first depressive episode may modify or raise differential neurobiological risks for subsequent episodes, resulting with subsequent episodes being more easily triggered (Post, Rubinow, & Ballenger, 1986). Therefore, individuals with depression may be particularly more behaviorally and neurobiologically susceptible and sensitive to stressors (Monroe & Harkness, 2005).

Notably, those with a family history significant for depression are at greatest risk for more severe and recurrent depression (Hollon et al., 2006; Sullivan, Neale, & Kendler, 2000). This heightened risk of depression has been attributed to genetic influences (for a review see Nestler et al., 2002). Other researchers have argued that early adverse experience (i.e., reared in a home exposed to parent psychopathology) also provokes a pathogenesis of depression (Heim et al., 2004), although the interaction of

both genetic and environmental risks is most widely considered as the basis for onset of depression (Sullivan et al., 2000). Specifically, Heim and colleagues reviewed literature highlighting the association between early life stress (e.g., abuse, parent loss, parent psychopathology) with atypical development of neural regions (e.g., prefrontal cortex, amygdala, hippocampus) that increase heightened response to stress and emotion and abnormal emotion processing, which in turn leaves the child vulnerable to psychiatric disorders such as depression. Importantly, the effect of early life stress on depression is in part mediated by the support or dysfunction in family relationships, highlighting the role of caregivers in the development of psychopathology (Agid et al., 2000). At present, major depression in adults is an area of psychiatric research that is widely investigated with many studies directed at identifying neurobiological and behavioral risks of the development of depressive disorders and predictors of treatment response. However, much less is known regarding the intergenerational risks of depression, or the mechanisms to which *exposure to parents with depression* confers risks to their offspring. Specifically, this investigation focuses on the effect of maternal depression on child's social-emotional outcomes, as research implicates maternal depression as more strongly related to the offspring's development of mood disorder relative to paternal depression (e.g., Foley et al., 2001; Marmorstein & Iacono, 2004; Shiner & Marmorstein, 1998).

Children of depressed mothers have a significant risk for developing psychopathology (Goodman & Gotlib, 1999; Goodman & Tully, 2008). Relative to their peers with nondepressed mothers, the likelihood of experiencing depression is approximately six times greater in these children (Downey & Coyne, 1990). Importantly, the risk of developing psychopathology is not restricted to depressive disorders. Children

of depressed mothers have a significantly increased rate of panic disorder, phobias, and substance dependence (Weissman et al., 1997; 2006), attention-deficit/hyperactivity disorder (Orvaschel, Walsh-Allis, & Ye, 1988), and disruptive behaviors (Pilowsky, Wickramaratne, Nomura, & Weissman, 2006). The risk conferred by a parent with depression is not limited to childhood but across lifespan. Adolescents with parents who have a history of major depressive disorder have three to five times increase in risk of developing a depressive episode (Hammen, 2009), and the depression tends to be more severe relative to those experienced by low-risk offspring (i.e., children of parents without depression; Weissman et al., 1997). By 20 years later, offspring of depressed parents are 3 times higher in reported clinical mood or anxiety disorders and require greater mental health services than those of nondepressed parents (Weissmen et al., 2006). Longitudinal research revealed that children with early exposure to maternal depression struggle more with daily functioning, including greater reports of social maladjustment and difficulties with their occupation, relative to those with nondepressed mothers (Weissman et al., 2006). Given childhood exposure to maternal depression has pervasive effects on the ontogeny of mood disorders and augments the susceptibility of developing other psychopathology, it is imperative to characterize processes that subserve the sequelae of depression in these youth.

**Maternal Depression: Early Life Stress in the Family Context**

Further, maternal depression can have direct and indirect social influences on the child's emotional outcomes by affecting the mother-child relationship and those of other members in the family network. Individuals with a history of depression have been widely noted to show atypical attention to negative emotions (Joormann & Gotlib, 2007),

which may predispose them to access negative cognition or attributions when evaluating others or ambiguous situations (Teasdale, 1983). Depressed mothers are less responsive to distress signals of their children (Shaw et al., 2006), show less sensitivity to child's emotions (Trapolini, Ungerer, & McMahon, 2008), struggle with perspective-taking (Trapolini et al., 2008), and demonstrate more negativity in their mother-child dyads when their offspring are infants (Cohn, Campbell, Matias, & Hopkins, 1990). Further, depressed mothers use more negative emotional speech (Murray, Kempton, Woolgar, & Hooper, 1993), and harbor more negative attributions regarding their child's affective state and social-emotional adjustment (Radke-Yarrow, Belmont, Nottelman, & Bottomly, 1990; Webster-Stratton & Hammond, 1988). More severe maternal depression has been correlated with less empathic understanding of their child's affective and mental state (Coyne, Low, Miller, Seifer, & Dickstein, 2007). Importantly, investigations have consistently shown that caregivers with depression endorse a negative view of their offspring across developmental stages. Depressed mothers have been shown to view their infants as more likely to show problem behaviors (Radke-Yarrow, Belmont, Nottelman, & Bottomly, 1990; Webster-Stratton & Hammond, 1988), and view their toddlers as more negatively affective than NC parents (Coyne et al., 2007), which was associated with less engaged parenting (Gottlieb & McLeod, 1997). In effect, major depression in mothers is linked to formation of distorted cognitive states of self and their child, which in turn could adversely impact parent-child interactions at an early age.

Towards this end, in a meta-analytic investigation by Lovejoy and colleagues (2000), maternal depression was found weakly related to positive caregiver behaviors (i.e., praise and affection towards offspring), but was most strongly associated with negative parent

behaviors (i.e., irritability and hostility to the child). According to Lovejoy et al. (2000), although depressed mothers showed negative parenting behaviors across all children, younger children, particularly infants and preschool-aged children, also experienced more instances of disengagement (i.e., lack of involvement with children, frequent ignoring of the child, withdrawal) from their mothers. As such, the authors contended that exposure to caregiver psychopathology in early childhood may be potentially more deleterious to psychological health. In a review by Dix and Meunier (2009), caregivers with depression also demonstrate more negative self-perception of their parenting competency, positive appraisals for coercive parenting such as power assertion, and more negative attribution of their child's behaviors (e.g., blaming the child's behaviors to stable internal factors). Altogether, caregivers with depression expose their offspring to a stressful environment, characterized by more hostile and negative interactions, more critical forms of parent discipline, and less emotional support (Cohn et al., 1990; Coyne et al., 2007; Shaw et al., 2006).

Maternal depression has also been linked to disruptions within the family subsystems, resulting with a higher conflict and less supportive home environment for the child. According to Rogosch, Cicchetti, and Toth (2004), depressed mothers may also adversely impact levels within the family system by inciting a negative emotional environment for the child (i.e., marital discord, strain on the child's and mother's relations with others). It was reported that parents with depression show greater tendency to exhibit emotional criticism not only of the child, but also significant others. Under the family systems perspective, depressed mothers may have strained relationships with fathers, negative relationships with their offspring, and build tension within father-child

relations (Sander & McCarty, 2005). In turn, the disrupted subsystems create a family climate plagued by more family/marital discord and less cohesion, support and warmth, and act as additional risk factors for the child's emotion and stress dysregulation (Davies & Windle, 1997; Du Rocher Schudlich & Cummings, 2007; Essex et al., 2003; Fergusson et al., 1995; Sheeber et al., 1997). Indeed, mother's depressed mood has been linked to both parents' hostility towards each other and the child, and the permutations of parent-child and mother-father hostility were also associated with the offspring's internalizing symptomatology (Low & Stocker, 2005).

Furthermore, based on an integrative review by Goodman (2004), maternal depression strongly predicted depression in their husbands during the first year postpartum, and between 25 to 50% of men whose wives who have depression also experience the ailment. Current depressive symptomatology in mothers of ten-year-olds is related to that of fathers based on self-report questionnaires (i.e., Beck Depression Inventory)(Low & Stocker, 2005). Goodman (2004) highlighted that co-occurrence of depression in parents is likely high within families affected by mood disorders, which in turn leaves the child without a positive caregiver who could serve as a potential buffer against a less supportive parent. In brief, literature on maternal depression the over the past three decades have suggested that the mood disorder impacts the caregivers' direct interactions with the child and the overall family climate, both of which act as interactive stressors for the child.

**Neurocognition and Depressive Disorders**

Emotion regulation has a central role in the development of psychopathology (Cicchetti, Ackerman, & Izard, 1995) and has intimate associations with specific

cognitive abilities, such as decision-making (Mitchell, 2011); thus, adverse events that threaten one domain may compromise the other in parallel, increasing the relevance of cognitive investigations in psychiatric research. As such, it is essential to ascribe the developmental differences across cognitive domains in individuals under normative development, at-risk for depression, or clinically significant for depressive disorders. Neurocognition comprises of several broad cognitive domains, with executive function (problem-solving, strategy formulation, set-shifting; inhibition) and memory (working memory, short-term memory, recognition, recall) as prominent components. Neurocognitive measures have been reliably linked to neural substrates and circuitry and applied to assess cognitive functioning as an indicator of brain functioning in a wide-range of neurological and psychiatric disorders, offering an opportunity to evaluate the brain correlates with measured behaviors without the application of invasive or costly methods (e.g., magnetic resonance imaging; MRI)(Strauss, Sherman, & Spreen, 2006).

Empirical evidence to date pervasively implicates that neurocognitive processes are perturbed among individuals diagnosed with mood disorders with prominent evidence directed towards executive function and memory deficits (Harvey et al., 2004; Elderson-Thompson et al., 2003; Fossati et al., 1999; Fossati et al., 2002; Porter, Bourke, & Gallagher, 2007; Schatzburg et al., 2000). Impairments in executive function, which includes strategic planning, set-shifting, flexible organization, concept formation, and inhibitory control, are found across depressive disorders including major depressive disorder (Austin, Mitchell, & Goodwin, 2001; Porter, Bourke, & Gallagher, 2007; Stordal et al., 2004) and bipolar disorder (Murphy et al., 1999; Rossi et al., 2000), and considered to reflect functional abnormalities of the prefrontal cortex (PFC). Specifically, problem

solving (Naismith et al., 2003), mental flexibility (Austin et al., 2001; Naismith et al., 2003), decision-making (Chamberlain & Sahakian, 2006) and working memory -— all dedicated functions of the PFC — are reportedly deficient in those with major depressive disorder (Egeland et al., 2003; Landro, Stiles, Sletvold, 2002; Naismith et al., 2003; Rose & Edmeier, 2002). Depression symptom severity has been found to be associated to poorer executive functioning performance in those with major depression, particularly in cognitive flexibility and perseverative responses on neurocognitive tasks (e.g., Wisconsin Card Sort Test)(Grant, Thase, & Sweeney, 2001; Naismith et al., 2003). In a similar vein, Kessing et al. (1998) found that number of depressive episodes is associated with greater neurocognitive decline, implicating that both severity and chronicity of depression are linked to executive functioning skills. Notably, among those with major depression, those who showed greater deficit in executive functioning also yielded poorer treatment response (Grant et al., 2001).

Memory deficit, the main topic of this investigation, is another common cognitive characteristic of depression. Broadly, the right prefrontal cortex and medial temporal lobe (which includes the hippocampus, entorhinal cortex, and perirhinal cortex) are common areas involved in encoding, consolidating, storing, and retrieval of non-affective information such as words and designs (Squire, 1992; Tulving, Markowitsch, 1998; Wheeler, Stuss, Tulving, 1997). Notably, prefrontal cortical activation has been observed in encoding and cued retrieval tasks for episodic and non-episodic content (e.g., cued free recall, recognition memory tests)(Duzel et al., 1999; Rugg & Wilding, 2000). The hippocampus is also considered as a key substrate involved in the memory processing,

particularly in the consolidation of declarative memories (e.g., facts, events) from short term to long-term memory storage (Eichenbaum, 2004).

Among depressed patients, both the abilities to encode and retrieve are defective, reflected by inefficient storing and accessing of information (i.e., free recall and recognition)(Bearden et al., 2006; Brand, Jolles, & Gispen-de Wied, 1992; Bremner et al., 2004; Burt, Zembar, & Niederehe, 1995). It has been argued that memory dysfunction in those with depression pertains to deficits in the storing and retrieval of information rather than in the learning process (Bearden et al., 2006). Those with unipolar major depression, relative to non-depressed controls, showed no difference in learning curve of words or different strategies in memorizing non-affective verbal information (Bearden et al., 2006). Typically, memory difficulties appear to be most prominent during accessing of information. For example, greater depression severity has been linked to more impairment in recognition memory (Bearden et al., 2006; Burt et al., 2000) and free recall (Bearden et al., 2006; MacQueen et al., 2003; Porter, Gallagher, Thompson, & Young, 2003). Memory deficits are most prominent with recurrent depressive episodes (Basso & Bornstein, 1999; Fossati et al., 2004; Rapp et al., 2005) and earlier onset (Hickie et al., 2005), both subtypes that are typically associated with poorer prognostic outcome (i.e., treatment resistance, severity of depression; Reynolds et al., 1998; Solomon et al., 2000). Likewise, improvement in depressive symptoms across unipolar and bipolar patients from early admission to hospitalization to discharge has been linked to better verbal memory performance (Neu et al., 2001). Furthermore, in pre- and post-assessments of memory functioning in depressed patients with medication treatment (i.e., use of antidepressant and fluoxetine therapy), memory and attention functioning were improved

after 6 months of the intervention in addition to negative mood (Gallasi, Sarro, & Amore, 2006). Others similarly reported positive gains in memory performance with use of SSRI medication as intervention (Levkovitz et al., 2002).

In a similar vein, researchers using brain-imaging techniques have provided evidence of anatomical aberrations in prefrontal and temporal regions, and more specifically, the hippocampus. In a review by Drevets and colleagues (2008) and large meta-analytic study by Videbech and Ravnkilde (2015), gray matter volume of the dorsomedial and ventrolateral PFC regions and hippocampus are reduced in depressed patients compared to healthy controls. Other studies further suggest that the PFC and hippocampal gray matter differences begin early in the course of the illness (Botteron et al., 2002), are observed in individuals at risk for depressive disorders (i.e., at risk for major depression based on risk scores in genome-wide association analysis), implicating neurobiological risks linked of depressive disorders (Holmes et al., 2012), and are more extensive with recurrent episodes or longer duration of illness (MacQueen et al., 2003; McKinnon et al., 2009; Sheline, Sanghavi, Mintun, & Gado, 1999). It has been postulated that prolonged periods of depression may lead to PFC (particularly in the dorsolateral PFC), and hippocampal atrophy, which may augment risk of later episodes and treatment response (MacQueen et al., 2003; McKinnon, Yucel, Nazarov, & Macqueen, 2009; Sheline, Wang, Gado, Csernansky, & Vannier, 1996; Videbech & Ravnkilde, 2004).

Clinical improvement or remission has been linked to less gray matter atrophy in the PFC and hippocampus in addition to improved neurocognitive functioning (i.e., executive functioning, memory recall) as noted above, underscoring the prominent role of

these structures in the course of illness. In a cross sectional study, actively depressed patients with major depression evidence reduced PFC volume relative to health controls, whereas remitted patients do not (Salvadore et al., 2011). However, longitudinal research suggests that clinical remission is associated with *less* gray matter decline in PFC (Frodl et al., 2008). Similarly, reduction of gray area volume of the hippocampus is observed in patients with major depression and those who are remitted (Neumeister et al., 2005), albeit remitted individuals show less decline than non-remitted patients in a three year longitudinal investigation (Frodl et al., 2008). It should be noted that medication treatment (i.e., use of antidepressant medication) has been shown to have some protective value, as unmedicated patients with depression show greater hippocampal volume reduction with longer episode of depression whereas this association was not observed in medicated patients (Sheline et al., 2003). The protective effects of antidepressants against disruptions in morphometric development of PFC in depressed patients are less clear as most investigations apply cross-sectional designs with low sample sizes (for a review see Salvadore et al., 2011). It should be noted that investigators postulate that medication may protect further gray matter loss in the noted areas, but do not reverse existing gray matter reduction related to depression (prior to medication treatment)(Frodl et al., 2008), highlighting that the illness may be have long-lasting neurological outcomes. Collectively, emerging neurocognitive and imaging evidence suggest that onset of depression is associated with anatomical and functional alterations in the brain, particularly in the frontal and temporal regions, which in turn may introduce risk for dysfunctional cognition, more severe illness, and poorer prognosis.

While neuropsychological functioning has been widely assessed in individuals with depression, cognitive skills of children at risk of the illness through exposure to maternal depression remain unclear. While most investigations focus on patients diagnosed *with* depression, it is unclear whether specific cognitive deficits (e.g., memory functioning), a proxy for hippocampal functioning, may introduce developmental risks for the illness or result from the psychopathology. Research investigating neuropsychological functioning of children at risk for depressive disorders may offer more clarity regarding cognitive development as a vulnerability or resilience factor and correlate of emotional functioning.

**Stress, Hippocampal Functioning, and Memory: Neurobiological Risks for Depression**

Exposures to long-term or repeated stress are linked to hippocampal and prefrontal cortical dysfunction, emotion dysregulation, and memory impairment (McEwen, 1999; 2008). Stress in severe and chronic doses can lead to atrophy of the hippocampus (Lupien et al., 2005; Lupien et al., 2009), through multiple means including the reduction of neurotrophic factors such as brain-derived neurotrophic factor (BDNF) which in turn affects neurogenesis of limbic structures and hypercortisolemia (i.e., prolonged activation of the hypothalamus-pituitary-adrenal axis and elevated glucocorticoid levels) (Duman & Monteggia, 2006; Sheline et al., 2000). As reviewed by Sapolsky et al. (2000), chronic stress and elevated glucocortoid levels could result in reduced long-term-potentiation in the hippocampus (after frequent HPA activation), which neurobehaviorally manifests in poorer learning and memory. Others have begun to extend the glucocorticoid cascade hypothesis to account for the atypical development

of prefrontal cortex associated with early childhood adversity or trauma (Lupien et al., 2009). As reviewed by Lupien and colleagues (2009), stress in early and late-life have more toxic and potential long-term effects on neurodevelopment, as the HPA system is particularly sensitive during these periods. Low maternal sensitivity such as high intrusive or overstimulating behaviors during free play, as coded according to the sensitivity scale by Ainsworth et al. (1978), was related to greater cortisol increase after free play relative to pre-test conditions (Spanglar et al., 1994). Nine-month infants, but not three- or six-month infants, with mothers who show less sensitivity towards their social and affective cues also showed greater cortisol levels during initial pre-test conditions. The authors contended that results suggest longer exposure to less sensitive parenting may act as a stressor that could alter the HPA regulatory system; thereby, resulting with abnormal elevated baseline level of cortisol.

Maternal depression, which as noted above, often interferes with the parents' capacity to provide warm and sensitive care. Similarly, infants exposed to maternal depression prenatally and during postnatal period have higher baseline and average salivary cortisol level relative to those of healthy mothers (Ashman et al., 2002; Brennan et al., 2008), although no differences were observed across offspring exposed to depression during pregnancy only, postpartum only, or both (Brennan et al., 2008). Essex and colleagues (2002) observed atypical elevated salivary cortisol levels in 4.5-year-old offspring of depressed mothers, only when the parent reported persistent stress and depressive symptoms since the first 12 months, but not among children whose mothers had depression in during late toddlerhood or limited to early infancy. Furthermore, among the large sample of children (N=282), who provided salivary samples at 4.5 years,

those who yielded upper 25% on afternoon basal cortisol level exhibited more mental health symptoms based on parent and teacher-report inventories than youth in the 50% or lower 25%. Based on these findings, Essex et al. contended that their findings suggest exposure to repeated episodes or chronic maternal depression in early childhood, rather than single episode of the disorder, may result in prolonged activation of the stress system, which cascades into abnormal neurodevelopment. Subsequent research by Quas and authors (2004) examining the interaction of autonomic and cortisol reactivity and social support on memory functioning in 4- to 6-year-olds indeed found that children who demonstrated greater parasympathetic arousal (as measured by respiratory sinus arrthymia prior to task administration) and increased cortisol reactivity in response to laboratory stressor showed impaired free-recall memory when paired with low social support. These authors proffer that youth in high-stress environments may experience repeated HPA activation, which disrupts neurobehavioral functions associated with the hippocampus and prefrontal cortex. In brief, multiple investigators (e.g., Essex et al., 2002; McEwen, 2001; Sheline et al., 2000) examining the development of depression postulate that early exposure to adversity results in repeated activation of the HPA system (e.g., extended exposure to harsh environment or chronic experience of depression), triggering the desensitization of the stress system to release more of the steroid hormone cortisol to subsequent stressors and dysregulation of excitatory amino acids and metabolic processes that collectively damages hippocampal structure and function.

Indeed, MRI and behavioral evidence implicate the exposure to early childhood adversities impacts hippocampal and prefrontal cortical development. For example, among youth who experienced trauma (Carrion, Weems, & Reiss, 2007), higher salivary

cortisol and more self-reported perceived stress was related to reduced hippocampal volume approximately a year later, despite controlling for pubertal development and gender. Additionally, children from socially disadvantanged backgrounds (i.e., lower socioeconomic status; less parental education) without trauma also showed reduced hippocampal volume than same-age peers without the noted risks, highlighting that higher childhood adversities of different forms disrupt the typical maturation of this region. In an investigation examining neurodevelopment of depressed patients with a history of severe childhood stress (i.e., emotional of physical neglect), Frodl and authors (2010) found that depressed adult patients had reduced hippocampal and PFC volume relative to healthy patients, yet those with an added history of childhood stress (i.e., emotional or physical neglect) resulted with more pronounced anatomical changes than depressed patients without such history. Moreover, findings from this MRI study indicated that history of adversity in childhood and volumetric differences in noted brain regions were independently predictors of the severity and length of illness (Frodl et al., 2010), highlighting the long-term effects of early childhood stress on neurodevelopment and psychological health. It should be noted, however, some investigators contend the PFC and hippocampal structural/functional anomalies related to exposure to environmental stressors may manifest later in development rather than childhood (Lupien et al., 2011; Shonkoff & Garner, 2012; Woon & Hedges, 2008), as these perturbations reflect the continual build-up of neurotoxic effects of dysregulated stress system. To date, this hypothesis has not been fully clarified given the dearth of longitudinal and interdisciplinary research.

While compromised parenting may act as external stressors to young children, emerging evidence shows enriched home environment and supportive care may act as protective factors for a child's developing stress system (Lupien et al., 2009). For example, higher quality of maternal behavior, indexed by greater sensitivity to infants signals and cooperation (i.e., the degree mothers' initiation of interactions interfere/disrupt child's ongoing activity rather than support it), was associated to better recovery to baseline cortisol level after a mild stressor (Albers et al., 2008). In a study by Pendry and Adam (2007), stronger marital functioning (low conflict, high satisfaction among parents), but not maternal internalizing symptoms or maternal parenting quality (i.e., involvement and warmth), predicted lower average and morning basal cortisol levels in children. Blair and authors (2006) found that infants of mothers showing high maternal sensitivity showed lower basal cortisol levels, and a unique variation of cortisol reactivity and recovery to tasks that elicited negative affectivity. Infants of sensitive mothers showed greater immediate cortisol reactivity to the tasks, but also stronger recovery to baseline 40 minutes post-test; whereas, children of insensitive mothers showed greater basal cortisol levels, low reactivity and subsequent poor regulation of psychophysiological stress response. Finally, among children raised in higher stress home environments (i.e., low-income families) and greater maternal engagement (i.e., interaction, responsivity to child's cues) was associated with increased cortisol reactivity during infancy but lower average cortisol levels during toddlerhood (Blair et al., 2008). The investigators contended that their findings reflect the adaptive, developmental process, where the child's HPA system gradually improves in regulating the stress response better with repeated glucocorticoid production and negative feedback. In effect,

certain positive social influences could have significant bearing on the development of the stress system, and buffer against negative effects of existing stressors.

In brief, social adversities in early life, such as the experience of maternal depression, could potentially alter the course of hippocampal and PFC development and related behavioral functions through the accumulated neurotoxic effects of dysregulated stress system. It is possible that functional anomalies within these areas manifest in cognitive deficits that in turn augments risks of internalizing disorders.

**Neurocognitive Functioning of Children of Depressed Mothers**

Relative to the extant literature on adults with depression, the neuropsychological profile of children affected by maternal depression and the relationship between the cognitive functioning of the mother and the child remains unknown. Research evaluating offspring of depressed caregivers generally have used measures of intellectual functioning (e.g., full-scale intellectual quotients; FIQ), developmental assessments (e.g., Bayley Scales of Infant Development), or broad cognitive test batteries (e.g., Kaufman Assessment Battery for Children; KABC) as testing were conducted in early childhood. Majority of these investigations have similar findings depicting that at infancy these children underperform in these assessments relative to comparison peers, particularly when the depression occurs within the first year of the child's life (Cogill, Caplan, Alexandra, Robson, & Kumar, 1986; Hay et al., 2001). These at-risk children between 9- to 18-months old are delayed in an Object Concept task (Murray, 1992). Other research found discrepancies between offspring of depressed versus healthy mothers were observed in overall cognitive functioning on the Bayley Scales of Infant Development as early as 2 months of age (Sutter-Dallay et al., 2011; Whiffen & Gotlib, 1989),

independent of antenatal depression (Koutra et al., 2013). However, by approximately 20 months old, differences in overall cognitive performance between children of depressed versus comparison mothers largely dissipated. Numerous studies (e.g., Cicchetti, Rogosch, & Toth, 2000; Kurstjens & Wolke, 2001; Murray et al., 1996; Weissman et al., 1986) employing diverse assessment tools commonly report that general intellectual functioning of children of a depressed caregiver is comparable to that of control peers, although limited research continue to report cognitive disparities in elementary school age (Hay & Kumar, 1995; Hay et al., 2001). Hay et al. (2001) argued that the broad cognitive deficits in early childhood implicate that the stress and social experience of maternal depression may particularly affect learning and memory. However, it is possible that maternal depression exerts stronger effects on the cognitive competency of offspring in early childhood; yet, these children begin catching up with their peers beginning in late toddlerhood as they adapt to their environment.

Currently, despite the extensive research on overall cognitive functioning in youth at risk for internalizing disorders, there is a dearth of literature focusing on the specific neurocognitive abilities of children reared by depressed mothers, and majority of the existing studies emphasize on their executive functioning. Klimes-Dougan et al. (2006) examined neuropsychological functioning of adolescents, whose caregivers were diagnosed with bipolar disorder, major depressive disorder, or no psychiatric illness when the youth were toddler-age. As adolescents (approximately 15 years of age), the offspring that were raised by caregivers with major depressive disorder did not show neuropsychological deficits relative to comparison children; rather, only those reared by mothers with bipolar disorder were found to show impaired sustained attention, executive

function and perceptual memory. Likewise, in a study by Micco and colleagues (2009), 8- to 10-year-old children of mothers with major depressive disorder, panic disorder, and both types of disorders, showed no differences in their executive function and processing speed. Further, Wagner and colleagues (2015) examined executive function (selective, sustained, and divided attention; working memory; set shifting), among adolescents whose mother met diagnostic criteria for unipolar depression at the time of assessment compared to healthy counterparts, and found no group differences in the domain.

However, conflicting observations have been documented. An investigation by Belleau et al. (2013) showed that components of executive function, such as executive/complex attention, are slowed in youth (age 8 to 17 years) whose caregiver was diagnosed with a mood disorder (major depressive disorder, bipolar disorder). Additionally, Hughes et al. (2013) followed two to three-year-olds for four years and found that their mothers' depression symptom severity, measured by the Beck Depression Inventory (Beck et al., 1996), was predictive of the individual variance in their executive function (self-monitoring, strategy formation, planning) at six years of age. The authors contend that early exposure to family stressors such as maternal depression could result in long-term executive dysfunction given the protracted development of the PFC resulting in greater susceptibility to adverse environmental/parental influences. Additionally, a recent investigation by Perra et al. (2015) observed a link between postnatal maternal depression during the first 6 months with the offspring's development of imitation at approximately 12 months old, a form of learning that is associated with early memory development. Specifically, only 48% of infants of depressed mothers imitated a modeled behavior shown by an experimenter compared to 70% of healthy

infants who demonstrated this behavior. Given differences in the age of participants, age of child during caregiver's diagnosis, and breadth of cognitive testing (i.e., extensive neuropsychological battery or tasks specific to executive functioning), these heterogeneous results may stem from contrasts between research designs.

To extend the findings observed by Klimes-Dougan et al. (2006), Ng et al. (2015) examined neurocognitive functioning of 9- to 14-year-olds whose mother met diagnosis for major depressive disorder when the child was approximately 20 months old (N=41) compared to peers with mothers without a history of psychiatric illness (N=42), and the effect of chronicity of illness. Importantly, these researchers examined both the skills of the parent and the child, using the Cambridge Neuropsychological Test Automated Battery (CANTAB; Fray, Robbins, & Sahakian, 1997; Robbins et al. 1997) to better delineate specific areas that may be more vulnerable to psychopathology or social stressors. Generally, the CANTAB indexes frontal lobe functioning by testing problem-solving and planning abilities. Memory tests incorporated within the CANTAB also measures recognition memory for visuospatial information subserved by parietal and temporal lobe functions. These researchers found that depressed mothers and offspring showed more difficulty with a complex visual recognition memory test (i.e., four-choice forced recognition) than nondepressed caregivers and children, which somewhat echoed earlier findings by Cogill et al. (1986) that suggested memory functioning of 4-year-olds exposed to maternal depression is compromised relative to age-matched peers without parent psychopathology. However, no differences were observed by Ng et al. (2015) when the visual memory tests were simplified (i.e., two-choice forced recognition), or across executive function and working memory measures. Findings from this

investigation also revealed unique positive associations between memory performances (i.e., complex visual and working memory) of the parents and their children among the depression group. Therefore, the results underscored assertions from Klimes-Dougan et al. (2006) implicating executive function may be relatively preserved among children reared by mothers with depression. However, in contrast to the findings in Klimes-Dougan et al. (2006), Ng et al. (2015) observed some memory deficits specifically within the visual domain in the youth and their mothers in the depressed group only, which may reflect genetic influence (i.e., biological predisposition for hippocampal dysfunction) and/or social transmission of cognitive risk.

Notably, subsequent research investigating characteristics of early maternal depression (e.g., chronicity vs. single episode, severity of initial episode, number of episodes, duration of longest episode) have suggested that chronicity of exposure may introduce different risks to overall cognitive development (Grace, Evindar, & Stewart, 2003; Kurstjens & Wolke, 2001; for a review see Sohr-Preston & Scaramella, 2006). Specifically, recurrence of maternal depression (Cornish et al., 2005; Grace, Evindar, & Stewart, 2003; Kurstjens & Wolke, 2001) and additional exposure to low socio-economic status (Kurstjens & Wolke, 2001) were linked to poorer cognitive composite scores. As such, duration of exposure to maternal depression in addition to other adversities related to home environment are necessary to consider when assessing cognitive vulnerability of these youth. At present, based on the noted findings, it is unclear whether exposure to maternal depression may trigger alterations in the neurobiological stress system that cascade to memory dysfunction, despite the aforementioned literature suggesting that hippocampal dysfunction may act as risk for developing internalizing symptoms.

**The Current Study**

To address the gaps in the literature above, the proposed study will examine differences in memory functioning of children with depressed mothers (depressed caregivers; DC) versus nondepressed caregivers (NC). Additionally, this study will investigate whether mothers' memory functioning is associated with that of their children. The aims of this research will be to investigate the following questions after controlling for demographic variables (socioeconomic status, gender, age, child's overall intellectual functioning):

(1) Does memory functioning vary as a function of *exposure to chronic depression* (i.e., repeated and persistent episodes) or mother's current symptomatology?

(2) Given above noted literature suggesting hippocampal dysfunction may be associated with depression symptomatology, does internalizing symptomatology at 5 years of age predict later memory functioning at approximately 9 years of age?

(3) Is memory functioning of youth related to current internalizing symptomatology (self and parent-reported)? Does it act as a moderating variable between early exposure to maternal depression and current internalizing symptom presentation?

(4) Is memory functioning related to current internalizing symptomatology uniquely or to externalizing symptomatology alike?

(5) Do DC children differ from NC peers in their development of internalizing symptoms (i.e., yield different growth patterns for these symptoms)?

Based on prior research noted above, the following hypotheses were conjectured:

(1) DC children with mothers with chronic depression (i.e., mothers with depressive episodes across 5 timepoints) or recurrent depression (i.e., mothers who met diagnosic criteria for depressive episode other than the baseline session) would underperform on memory tests relative to youth whose mother experienced non-recurrent depression or NC parents, as repeated stress from episodes of parental psychopathology would exert more neurotoxic effect on hippocampal functioning. Additionally, mother's recent severity of depressive symptoms (indexed by the Beck Depression Inventory; Beck et al., 1961) was hypothesized to show weaker associations with the child's concurrent memory functioning, as previous literature implicate hippocampal dysfunction with cumulative or repeated exposure to adversities rather than acute stress. Should memory performance reflect as a neurobehavioral index of hippocampal functioning, youth exposed to more severe maternal depression (i.e., persistent forms of the ailment) are expected to struggle with memory functioning relative to those with isolated episodes.

(2) In a similar vein, higher internalizing symptoms at 5 years, reflective of more dysregulated stress reactivity, would likely be associated with poorer memory performance later at 9 years, should this cognitive domain reflect hippocampal functioning.

(3) Memory performance, as a measure of hippocampal functioning, is expected to moderate exposure to maternal depression with child internalizing symptomatology, as repeated experience of significant stressors have been shown

to desensitize stress regulatory system to subsequent adversities and heightening risk of psychopathology in the offspring.

(4) Similar pattern of memory functioning as a moderating role to externalizing symptom is hypothesized past literature have shown increased risk of externalizing disorders (e.g., disruptive and behavioral disorders) in youth exposed to maternal depression (Goodman & Gotlib, 1999; Marmorstein & Iacono, 2004). However, it is anticipated that the effect of memory as a moderating factor is stronger for internalizing symptomatology versus externalizing symptomatology given the greater genetic liability of maternal depression on the development of affective disorders in offspring (Halligan, Murray, Martins & Cooper, 2007).

(5) Children of DC mothers are anticipated to show increased internalizing symptomatology relative to NC youth given prior research of increased risk of depression (Downey & Coyne, 1990; Luoma et al., 2001). Specifically, NC youth are expected to show more stablility in reported internalizing symptomatology; whereas DC youth are hypothesized to show more elevated symptoms at baseline (i.e., approximately 18 months of age) followed by more instability or symptom changes. Notably, this prediction was made based on prior longitudinal investigations showing that DC youth have elevated but high fluctuations in total problem symptoms (i.e., including both internalizing and externalizing behaviors) from first year of life to around 8 to 9 years of age.

## Methods

### Participants

In the present study, the total participants included 100 children between 8 to 11 years of age (49F; *M*=9.49, *SD* = 0.59) and their mothers (*M*=39.63; *SD* = 4.78). These children were followed under a longitudinal project since their first participation in the study between 18 to 30 months. Table 1 outlines the demographic information of the participant groups. DC caregivers are mothers who had unipolar depression at some period of time since their child's birth; whereas, NC caregivers had no history of psychiatric illness.

The DC versus NC group yielded similar demographic characteristics (see Table 1). Independent t-tests indicated no significant difference in age of participant groups. However, a significant discrepancy in mothers' age was observed, with DC caregivers younger than the NC group ($t(98)=3.39$, $p=0.001$). No associations were observed between clinical groups (DC, NC) and child's gender, ethnic background, and family SES at baseline session. No difference in years of maternal education was found across groups. A higher proportion of NC mothers were married relative to DC mothers ($\chi^2(3)=11.11$, $p=0.01$). Of the DC mothers, six were separated or divorced and four were single parents who never married. Across the baseline and final experimental sessions, when the child was approximately 1.5 and 9 years of age respectively, DC mothers reported more severe depressive symptomatology based on the Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961)($ts>5.74$, $ps<0.001$).

**Table 1.** *Participant Characteristics of Mothers With and Without a History of Depression and Their Children.*

| | Depressed | | Nondepressed | |
|---|---|---|---|---|
| | *M or %* | *SD* | *M or %* | *SD* |
| **Child** | | | | |
| *N* | 50 | --- | 50 | --- |
| Gender | 26F | --- | 23F | --- |
| Age (years) | 9.52 | 0.51 | 9.47 | 0.67 |
| **Mother** | | | | |
| *N* | 50 | --- | 50 | --- |
| Age (years) | 38.12 | 5.26 | 41.14 | 3.72 |
| Maternal race (non-minority)* | 87.76% | --- | 94.00% | --- |
| Maternal education (years)* | 16.10 | 2.35 | 15.62 | 2.47 |
| Family SES (Hollinghead Scale)* | 3.90 | 0.90 | 4.12 | 0.84 |
| Percent married* | 80.00% | --- | 100.00% | --- |
| Beck Depression Inventory Total (baseline)* | 12.96 | 12.28 | 2.58 | 3.41 |
| Beck Depression Inventory Total (current) | 16.56 | 9.21 | 2.72 | 3.29 |

* *Note. Demographic information was reported at baseline.*

**Recruitment**

Participants for the present study were recruited as part of a longitudinal investigation of the effects of maternal depression on the development of their toddlers. Prior research indicated that socioeconomic status (SES) might pose as additional risk factor or stressor that coincides with maternal depression (Coyne & Downey, 1991) and is associated with lower neurocognitive functioning globally (Noble, Normal, & Farah, 2005); thus, our recruitment efforts focused on families that were not of low SES based on Hollinghead's standards (1975) to reduce possible confounding effects on our outcome measures. Additionally, we applied a criterion that excluded families with public assistance, and caregivers who did not minimally obtain a high school education. DC mothers were recruited through advertisements and fliers published in newspapers and local community notices, in medical offices and various bulletin boards across the

community. Local mental health professionals also provided our research team with referrals to mothers with depression interested in participating in the study. NC mothers and children were recruited within similar residential regions of the depressed caregivers.

All participating mothers initially completed the Diagnostic Interview Schedule (DIS-III-R; Robins et al., 1985) to determine depression status and other current/past major mental health disorder. Finally, to be included in the study, DC mothers had to meet the *Diagnostic and Statistical Manual of Mental Disorders (*3rd ed., revised; DSM-III-R; American Psychiatric Association, 1987) for major depression at some time after the birth of their child. Mothers who met criterion for bipolar disorder during or since the initial intake session were excluded. Furthermore, comparison mothers who were diagnosed with psychiatric conditions since the baseline evaluation of the investigation were omitted from the current study. This study and the reported procedures are approved by the Institutional Review Board of the University of Rochester.

**Procedures**

Initially, mothers enrolled in the study when their child was approximately 20 months of age. During this baseline session, these caregivers completed the Diagnostic Interview Schedule-III-R (DIS-III-R; Robins et al., 1985), a structured interview administered with trained experimenters to discern the presence of disorders associated with Axis I of the DSM-IIIR (American Psychiatric Association, 1987). The BDI was also administered to assess recent severity of depression. Results on the DIS-III-R and BDI (i.e., scoring in moderate to severe depression range in symptomatology) were used to distinguish the caregivers with depressive disorders in the first 30 months of their child's life relative to those who did not demonstrate any psychiatric etiology.

Subsequently, DIS-III-R and BDI was used to monitor caregivers' diagnostic status during four follow-up appointments: when the child was approximately 3, 4, 5, and finally between 8 to 11 years of age (i.e., on average 9 years of age). Similarly, the caregivers completed the Child Behavior Checklist (CBCL; Achenbach & Edelbrock, 1983) as a measure of their behavioral and emotional functioning during the baseline appointment and follow-up sessions when the child was 5 years old and again at 8 to 11 years of age.

At the final session, both mothers and their offspring were independently administered the California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1987; Delis, Kramer, Kaplan, & Ober, 1994) by trained research assistants. Additionally, the child participants completed three visual memory subtests from the Wide Range Assessment of Memory and Learning (WRAML; Sheslow & Adams, 1990), and completed a self-report inventory of depression symptoms (Children's Depression Inventory, Kovacs, 1985).

**Materials**

**Diagnostic Interview Schedule-III-R (DIS-III-R).** The DIS-III-R (Robins et al., 1985) included forced choice questions that are given in modules to investigate the endorsement of symptoms across Axis I disorders based on DSM-IIIR (American Psychiatric Association, 1987). The DIS-III-R is a highly structured interview with a set sequence of questions. Items were answered with "Yes" or "No". Responses are entered in a computer program that yields the resulting diagnoses (out of a possible 49 diagnoses from Axis I), based on algorithms on normed data. Interviewers were trained in the administration of the DIS-III-R to criterion reliability prior to assessing mothers in the

current study. Validity and reliability in the application of DIS-III-R for psychiatric research has been supported in early investigations with typically developing and clinical populations (Robins, Helzer, Croughan, & Ratcliff, 1981; Robins, Helzer, Ratcliff, & Seyfried, 1982).

**Beck Depression Inventory (BDI).** The BDI (Beck et al., 1961) is a self-report inventory consisting of 21 items. This inventory was used to assess current depressive symptomatology between groups. Questions assessed physiological, emotional, cognitive, perceptual, and somatic symptoms during the past two weeks based on a 0 to 3 scale, with 0 reflecting the absence of the symptom and 3 indicating severe endorsement of the symptom. Responses across the 21 items are summed to yield a total score indicate the severity of depressive symptomatology: none to minimal depression (<10), mild to moderate depression (10-18), moderate to severe depression (19-29), and severe depressive symptomatology (30-63)(Beck, Steer, & Garbin, 1988). The test retest stability estimates for psychiatric population range from 0.48 to 0.86, and 0.60 to 0.83 for nonpsychiatric samples (Beck et al., 1988). Past research examining adults with and without psychiatric conditions have shown that the BDI has high internal consistency, content validity, and discriminant validity against non-depressed, normal development (Beck et al., 1988; Richter, Werner, Heerlein, Kraus, & Sauer, 1998). Thus, the same measure was used in conjunction with DIS-III-R across timepoints to assess depressive symptomatology of mothers.

**Child Behavior Check List (CBCL).** Mothers completed the caregiver version of the Child Behavior Checklist at baseline and subsequent assessment sessions (when the child was approximately 5 years and finally around 8 to 11 years of age) as a measure of

behavioral and emotional adjustment at the time. Two versions of the CBCL were used as one was normed with school-age youth (4-16 years; CBCL; Achenbach & Edelbrock, 1983) and consisted of 118 items, while another was created for younger children (2-3 years; Achenbach, Edelbrock, & Howell, 1987) and consisted of 99 items. Across both versions of the inventory, caregivers were instructed to rate how true per description reflects their child in the past 6 months (0 = not true, 1 = sometimes true, 2 = very true). Responses were summed to yield raw scores and transformed to T-scores, based on the inventory manual. The CBCL yield multiple content scales including Anxious/Depressed, Withdrawn, Somatic Complaints, Hyperactivity, Attention Problems, and more, and yielded Internalizing and Externalizing scales. This study focuses on the association between memory functioning and depression; therefore, the T-scores for Internalizing symptoms would be used in data analysis. All caregivers completed the CBCL at baseline. Of note, there were 16 incomplete CBCL forms at the 5-year appointment, and two at the final session. Additionally, across the three baseline and follow-up appointments, majority of the CBCL were completed by mothers (i.e., over 95% of sample per timepoint). Discriminative validity and reliability of these measures have been documented (Achenbach, 1991, 1992).

**Children's Depression Inventory (CDI).** Children completed a self-report version of the CDI (Kovacs, 1985) at the final experimental session to determine their current depressive symptoms. The CDI comprises of 27 items and is normed against youth between 7 to 17 years of age. For each item, participants were asked to indicate one of three descriptions that depicts how they felt emotionally, physically or cognitively the past two weeks. This inventory yields five subscales (Negative Mood, Ineffectiveness,

Interpersonal Problems, Anhedonia, and Negative Self-Esteem), and a Total CDI composite. Raw scores were converted to T-scores in accordance with the CDI manual. All but one child participant completed the CDI. Reliability for the CDI has been supported in prior studies (alphas 0.74 to 0.89 across gender and age)(Smucker, Craighead, & Green, 1986). It should be noted that while CDI has been shown to measure depressive symptoms adequately, it is not a diagnostic tool (see Fristad, Emery, & Beck, 1997).

**California Verbal Learning Test, Children's Version (CVLT-C).** The CVLT-C (Delis et al., 1994) was administered to children in their final follow-up appointment (when they were between age 8 to 11 years of age) to assess their verbal learning and memory abilities. CVLT-C is an established test used for neuropsychological evaluation of neurological and psychiatric disorders (see Strauss et al., 2006). The test included an oral presentation of a list of 15 words to the participant, and an immediate recall of the items. The list presentation and recall were repeated four additional times to assess the learning curve over a total of five trials. Subsequently, a second list of 15 words is presented once and immediately recalled as interference stimuli. After the recall of these items, participants were instructed to recall the original word list without cues given. Finally, categorical cues (e.g., *What words from the list are fruits?*) are offered to facilitate word recall by organizing the retrieval process. After a 20-minute delay, participants are asked to spontaneously recall words from the original list, and subsequently offered categorical cues to determine whether added structure will assist in delayed memory recall of verbal information. The raw scores are converted to T-scores using age-match norms, according to the manual. Altogether, CVLT provided index of short delay free recall, short-delay

cued recall, long-delay free recall (i.e., 20-minute delay), and long-delay cued recall. CVLT verbal learning and recognition has been linked to hippocampal and frontal functioning (Johnson et al., 2001). In line with prior research Delis et al. (1988) and Wiens, Tindall, & Crossen (1994), a composite score was obtained using these four indices of verbal memory recall. Exploratory factor analysis using maximum likelihood estimation was applied to determine whether the four subscales loads into one factor, given the strong correlations between variables (rs > 0.77). The four unrotated variables yielded a single factor with a total eigenvalue of 3.39 and explained 84.83% of the variance. The extraction sum of squared loadings yielded a total of 3.20 with 79.87% of variance explained. All factor loadings ranged between than 0.85 to 0.95 reflecting similar variance explained across variables. As such, the four subscales were converted to standard scores and averaged to yield a single Verbal Memory composite score.

**Wide-Range Assessment of Memory and Learning (WRAML).** Three subtests of visual learning and memory from WRAML (Sheslow & Adams, 1990) were administered to child participants. Given WRAML is normed on children, caregivers did not complete the test. The design memory subtest required participants examining five cards of geometric forms individually for 5 seconds. Participants were given a 10 second delay and instructed to draw the card's content. For the picture memory subtest, detailed scenic pictures are shown for 10 seconds, removed, and replaced with a second scenic illustration. Participants were asked to identify parts of the picture that are added/new, modified, or moved. Finally, a measure of visual learning required participants to closely attend to the researcher placing her finger in a series of holes on a board and immediately recalling the exact order of finger placement. With each additional trial, number of

placements and spatial order increased in difficulty to determine participants learning of visual sequences. After converting the subtest raw scores to standard scores, these are summed and transformed to a Visual Memory Index score in accordance to the assessment manual against age-matched norms (Sheslow & Adam, 1990). WRAML has been used to examine non-verbal learning and memory functioning in pediatric population for neurological insult and ailment, learning disabilities, and characterization of children at risk of psychiatric illness (Lajiness-O'Neill, Erdodi, & Bigler, 2010; Pham & Hasson, 2014; Vasa et al., 2007; for a review see Strauss et al. 2006). Visual and spatial long-term memory has been linked to be hippocampal functioning; however, short-term visual memory has also been associated with functioning within the parietal and occipital cortices (Slotnick, Thompson, & Kosslyn, 2012; Todd & Marois, 2004; Xu & Chun, 2006). Animal and human research on neurological lesions further underscore these observed brain-behavioral associations (Squire, Stark, & Clark, 2004).

Of note, given the relatively weak correlation strength between Verbal Memory and Visual Memory indices ($r=0.24$, $p=0.02$), these measures were examined separately rather than averaged into a composite memory score.

**Wechsler Intelligence Scale for Children – Third Edition (WISC-III).** The WISC-III (Wechsler, 1991) was administered at the final session to assess for overall cognitive functioning and used as a covariate in the moderation regression analyses. The WISC-III is a standardized assessment battery that assesses intelligence in youth age 6 to 16 years. Eight subtests named Picture Completion, Picture Arrangement, Block Design, Object Assembly, Information, Similarities, Vocabulary and Comprehension were administered. Raw scores are transformed into standard scaled scores based on age-matched norms in

accordance with the assessment manual. The scaled scores across subtests are summed and converted into two standard scores, Performance Intelligence Quotient (PIQ) and Verbal Intelligence Quotient (VIQ), and an overall index, Full-scale Intelligence Quotient (FIQ).

**Data Analysis**

Mothers' DIS-III-R assessment results and BDI symptoms (total score > 19) across five timepoints (i.e., child at baseline; approximately 3, 4, and 5 years of age; and finally between 8 to 11 years of age) were used to classify them as nondepressed, depressed recurrent, depressed non-recurrent, and depressed chronic to determine effects of chronic maternal depression on memory development of offspring. Depressed mothers with non-recurrent depression are caregivers who met diagnostic criteria for a unipolar depressive disorder during baseline solely, whereas those with recurrent specifier are those who met the classification more than the initial session. Those classified as chronically depressed met diagnostic criteria for depression across all timepoints. Importantly, six NC mothers experienced depression in a follow-up session; therefore, statistical analyses examining the effects of chronic maternal depression did not include data from these mothers and offspring. In total, 26 mothers were classified as chronically depressed, 10 with recurrent depression, 14 with non-recurrent depression, and 44 with no episode of depression.

Exposure to maternal depression at baseline was dummy-coded (0=no depression, 1= met diagnostic criteria for depression), and chronicity of maternal depression was coded into 0 (no depression), 1 (non-recurrent depression), 2 (recurrent depression), and 3 (chronic depression) to reflect greater exposure with higher values. Continuous

variables were mean centered to reduce multicollinearity and aid in the interpretation of the resulting betas in the following analyses. Variance inflation factors (VIFs) were monitored (VIF < 3) across regressions to detect severity of multicollinearity. To answer Research Questions 1 and 2, hierarchical multiple regressions were employed to examine whether chronicity of maternal depression, mother's current symptomatology (indexed by current BDI Total score), or earlier internalizing symptomatology at 5 years independently predicts children's verbal and visual memory performances at 9 years of age, after controlling for demographic variables (child's age, child's gender, family SES level and child's overall cognitive functioning or FIQ). These analyses were repeated employing total CDI score and T-scores for internalizing and externalizing symptomatology on the CBCL as dependent variables. Importantly, CDI total score and CBCL internalizing/externalizing t-scores were used as dependent factors to determine whether these relationships differ as a function of the reporter (self versus caregiver) or type of symptom (internalizing versus externalizing).

Subsequently, to address Research Question 3 and 4, hierachical multiple regressions were used to examine whether children's verbal memory or visual memory composites predict their total depressive symptoms (i.e., CDI total score) and internalizing/externalizing symptomatology (i.e., CBCL subscale T-scores). As noted above, the regressions examining associations between symptomatology and memory were conducted separately for visual memory and verbal memory given their weak correlation. Finally, the interaction term between chronicity of maternal depression and visual/verbal memory was included as a predictor to determine the moderating effect of memory on symptom outcome.

To address Research Question 5, T-scores for internalizing symptoms based on CBCL from 1.5 years, 5 years, and approximately 9 years of age were plotted on a loess curve to determine whether linear, non-linear, or quadratic growth curve analyses would be appropriate based on the data pattern. As illustrated in Figure 12, internalizing symptoms across time and group presented as a non-linear pattern. A linear fixed effects model was conducted to confirm the observation. Of note, a quadratic model was not an appropriate fit due to the number of timepoints of the data-collection. Thus, to examine the group differences in the growth of internalizing symptoms after the baseline appointment, repeated measures analysis of covariance (ANCOVA) was applied with similar covariates as noted above (child's gender, family SES level, and internalizing symptom t-score at baseline). A repeated measures ANCOVA was conducted with internalizing symptomatology t-scores at 5 and 9 years of age as the dependent variable, and the T-score for internalizing symptoms at baseline as a covariate in addition to gender and family SES.

## Results

### Chronic Maternal Depression as an Independent Predictor of Current Memory Functioning and Psychological Symptoms in Offspring

Table 2 provides descriptive information of the memory composites, depression symptoms, internalizing symptomatology across the three timepoints, and externalizing symptoms across clinical groups (DC, NC). Figure 1 illustrates the independent associations between verbal memory, exposure to chronic forms of maternal depression, and current symptoms, and Figure 2 represents similar associations with visual memory index. Of note, gender ($\beta$=0.26, t=2.57, p=0.01), age ($\beta$=0.24, t=2.42, p=0.02), and FIQ

(β=0.23, t=2.17, p=0.03) were significant covariates when combined with exposure to chronic maternal depression to predict verbal memory composite. These findings indicated that youth who are female, older in age, and stronger intellectual functioning are associated with demonstrating better verbal memory performance on the CVLT-C. Similarly, for visual memory index, FIQ was a significant covariate (β=0.37, t=3.51, p=0.001) when combined with exposure to chronic maternal depression, reflecting that stronger overall cognitive functioning is associated with better visual memory functioning.

**Table 2.** Descriptive Statistics of Children's Memory and Psychological Functioning as a Function of Exposure to Maternal Depression.

| | Maternal Depression | Typical Development |
|---|---|---|
| ***Baseline*** | | |
| Internalizing Symptoms (T-score) | 51.10(8.09) | 46.24(8.16) |
| ***5 years*** | | |
| Internalizing Symptoms (T-Score) | 47.48(8.51) | 40.87(6.88) |
| ***9 years of age*** | | |
| Visual Memory Index (Standard Score) | 102.50(14.22) | 105.60(16.00) |
| Verbal Memory Composite (Standard Score) | 97.95(2.14) | 102.06(2.07) |
| Externalizing Symptoms (T-Score) | 51.23(12.42) | 44.51(9.29) |
| Internalizing Symptoms (T-Score) | 54.02(9.91) | 46.16(9.33) |
| Child Depression Inventory (CDI) Total | 5.74(4.43) | 4.94(3.96) |

Note. Average scores and standard deviations (within parentheses) are reported. CDI total score is a sum of ratings across 27 items and is not under a normal distribution.

Hierarchical multiple regressions with the noted covariates (gender, age, family SES, and child's FIQ) showed that children's exposure to chronic maternal depression is not associated with their visual memory functioning, but is predictive of their verbal memory functioning (β=-0.23, t=-2.27, p=0.03). Notably, repeated exposure to maternal depression was associated with poorer performance on the CVLT-C. Group differences in

verbal memory functioning were underscored with a post-hoc Tukey's HSD test, which showed youth with chronic exposure underperformed relative to those with no exposure ($p=0.045$)(see Figure 3). Additionally, exposure to chronic maternal depression was associated with increased internalizing and externalizing symptoms as reported by mothers ($\beta s>0.31$, $ts>3.08$, $ps<0.01$), but not self-reported depressive symptoms. Posthoc Tukey's tests indicated youth with exposure to any duration of depression (chronic, recurrent, or non-recurrent) yielded greater internalizing symptoms than NC youth ($ps<0.03$); whereas, solely children exposed to chronic exposure showed more externalizing behaviors than NC peers ($p=0.02$)(see Figures 4 and 5). Contrary to our hypotheses, verbal and visual memory at approximately 9 years of age were not significant predictors of self-reported depressive symptoms or internalizing and externalizing symptoms as rated by mothers.

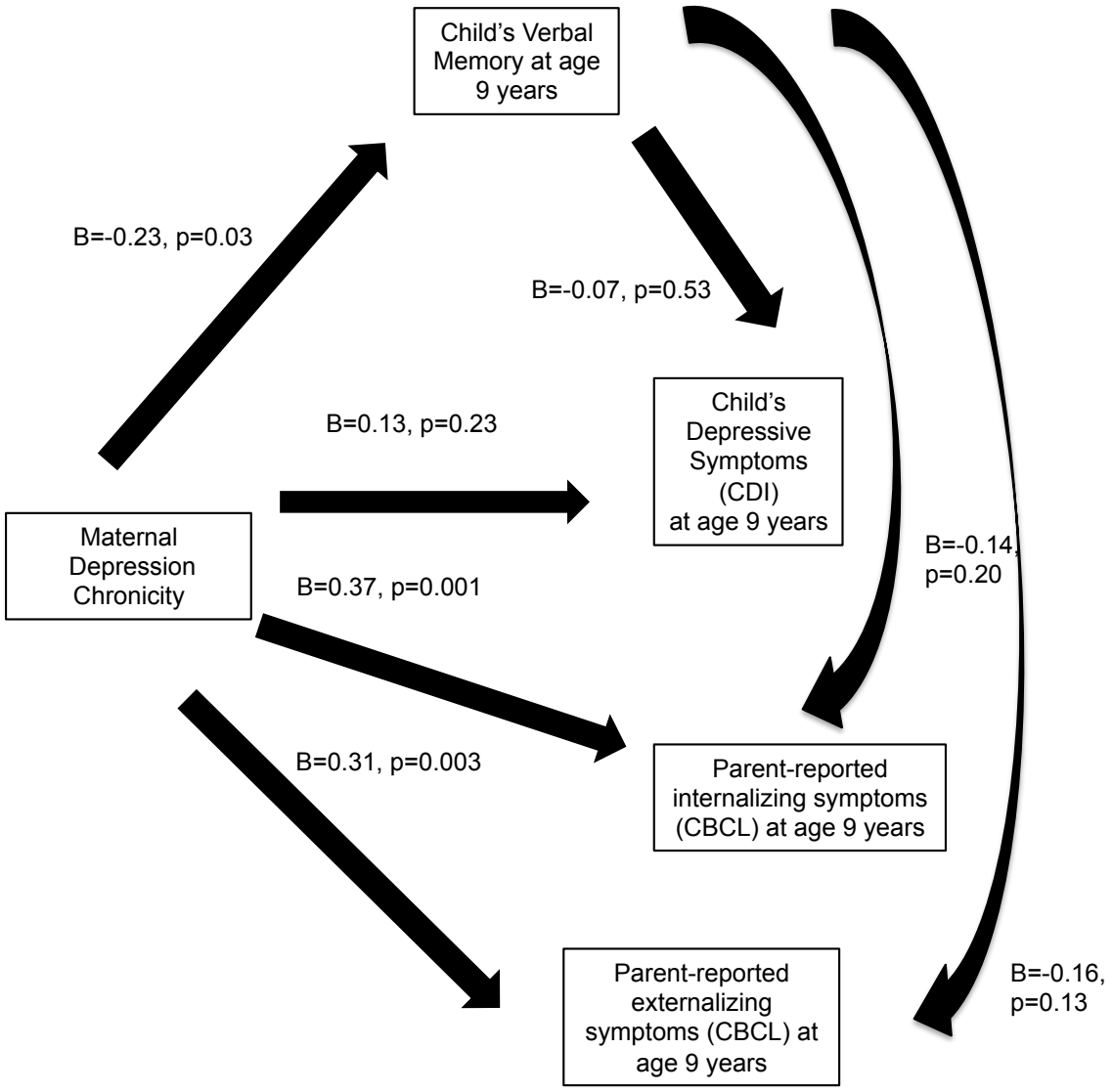


**Figure 1.** Associations between chronicity of maternal depression, and verbal memory performance and self- and parent-reported psychological symptoms of offspring at 9 years of age, after controlling for age of memory testing, gender, family socioeconomic status and child's overall cognitive functioning. Standardized betas and p-values for independent multiple linear regressions are presented.

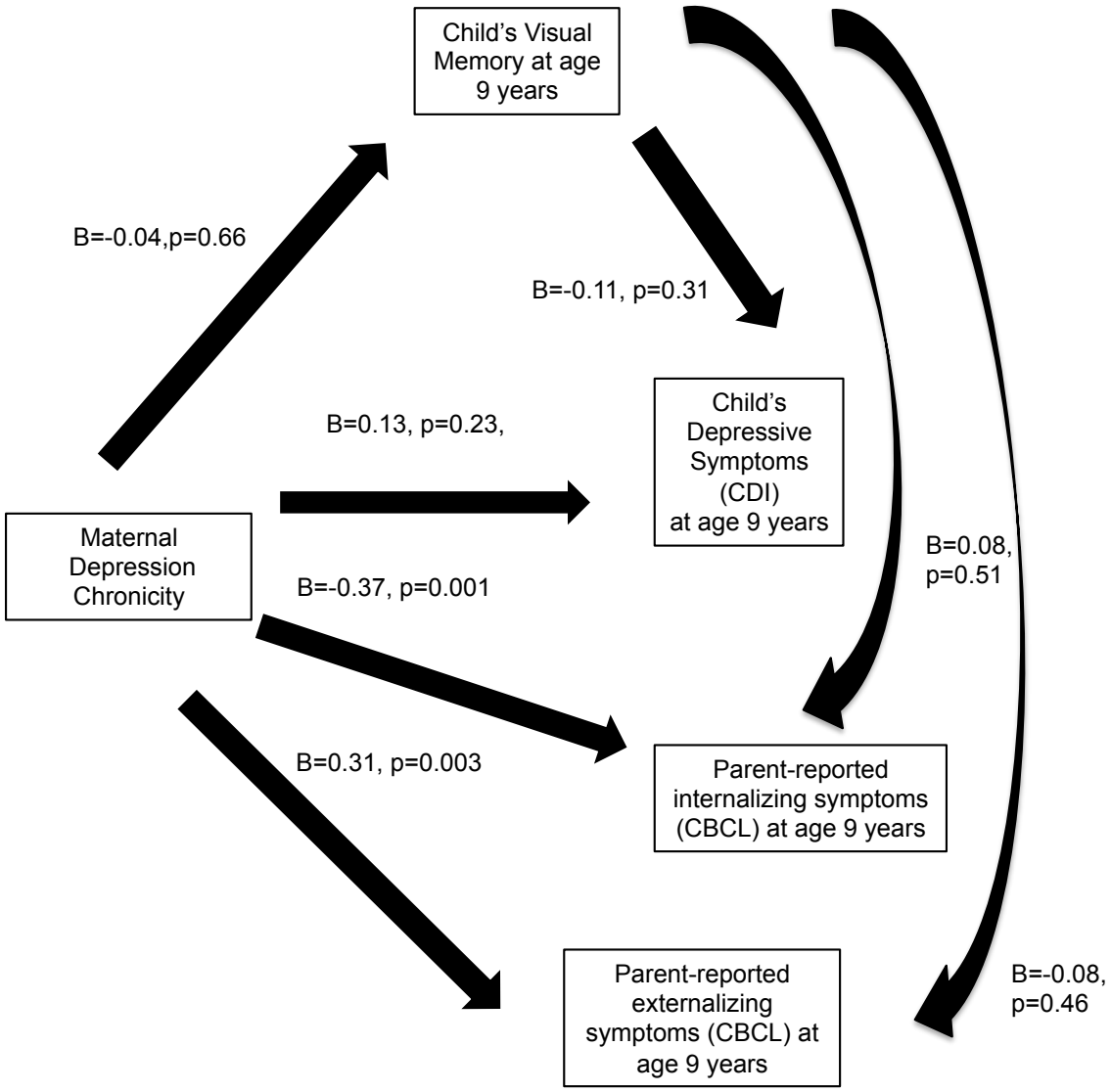


**Figure 2.** Associations between chronicity of maternal depression, and visual memory performance and self- and parent-reported psychological symptoms of offspring at 9 years of age, after controlling for age of memory testing, gender, family socioeconomic status and child's overall cognitive functioning. Standardized betas and p-values for independent multiple linear regressions are presented.

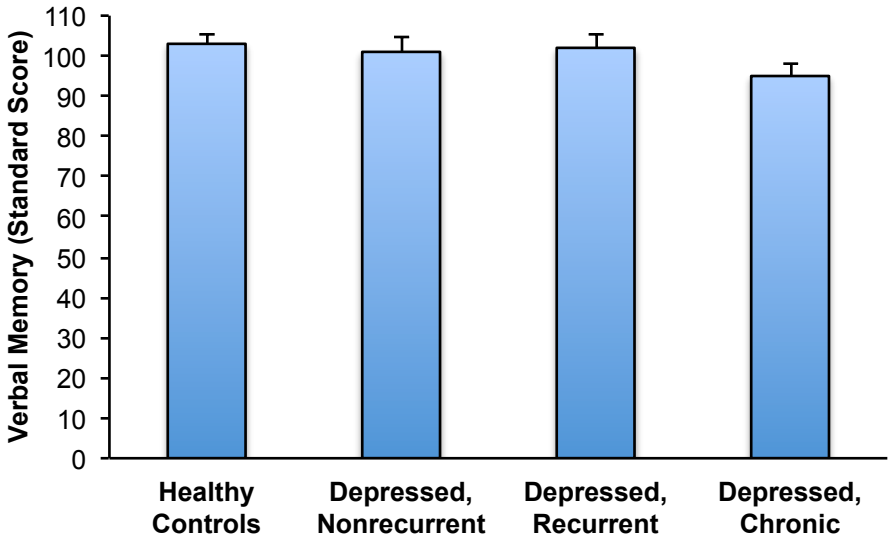


**Figure 3.** Average verbal memory performance on the CVLT-C (and standard error) as a function of exposure to chronic maternal depression (N=94).

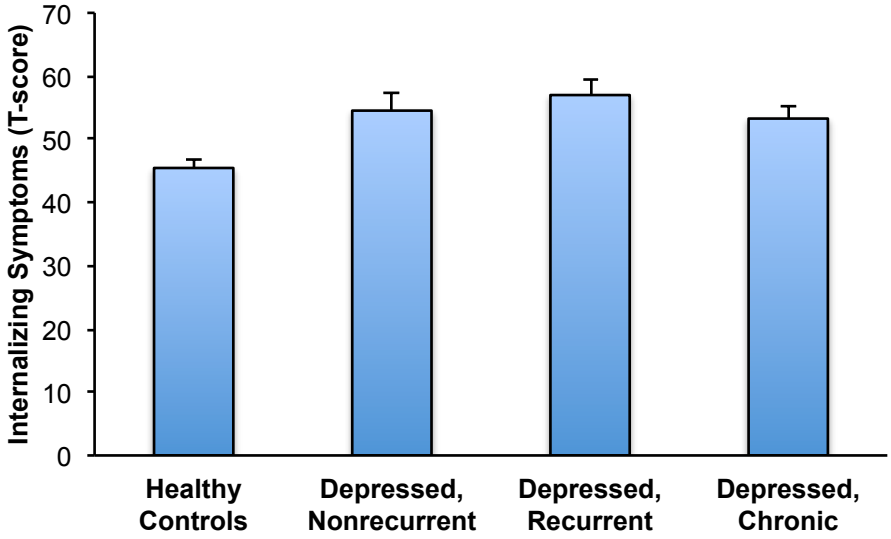


**Figure 4.** Average internalizing symptoms (t-score) as a function of exposure to chronic maternal depression (N=92).

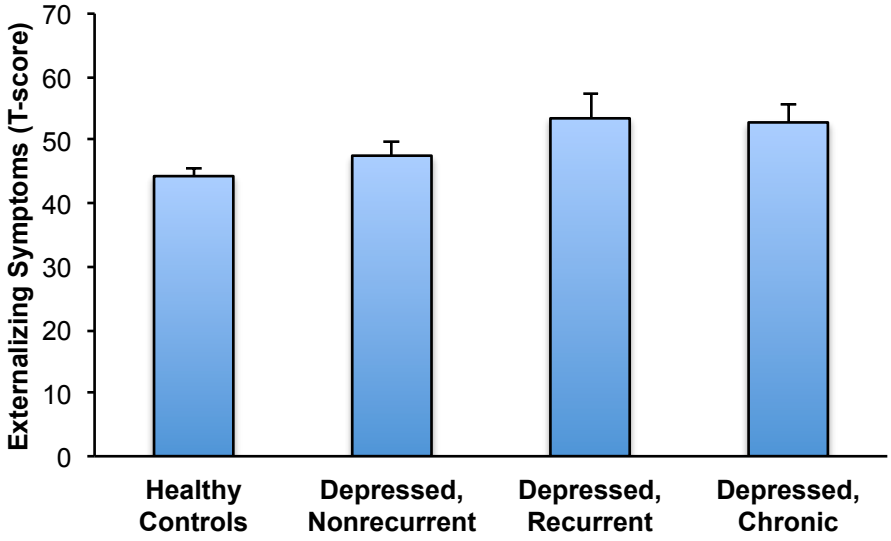


**Figure 5.** Average externalizing symptoms (t-score) as a function of exposure to chronic maternal depression (N=92).

**Recent Maternal Depression Severity as Independent Predictor of Current Memory Functioning and Psychological Symptoms in Offspring**

Figure 6 illustrates the independent associations between recent depression severity of mothers as indexed by BDI, and verbal memory performance and current symptoms in offspring. Similarly, Figure 7 represents these associations with the visual memory index. Gender ($\beta$=0.22, t=2.15, p=0.04) and FIQ of children ($\beta$=0.27, t=2.48, p=0.02) were significant covariates when combined with current maternal depression severity (i.e, when offspring were approximately 9 years of age) to predict their concurrent verbal memory performance, whereas, only FIQ ($\beta$=0.38, t=3.74, p<0.001) was related to their visual memory performance. No significant associations were observed between the recent severity of maternal depression with the child's current memory or psychological functioning at 9 years of age. These results in conjunction with those above suggest that *cumulative and repeated* experiences rather than recent/acute exposure of parent psychopathology may be linked to neurobehavioral difficulties such as memory decline.

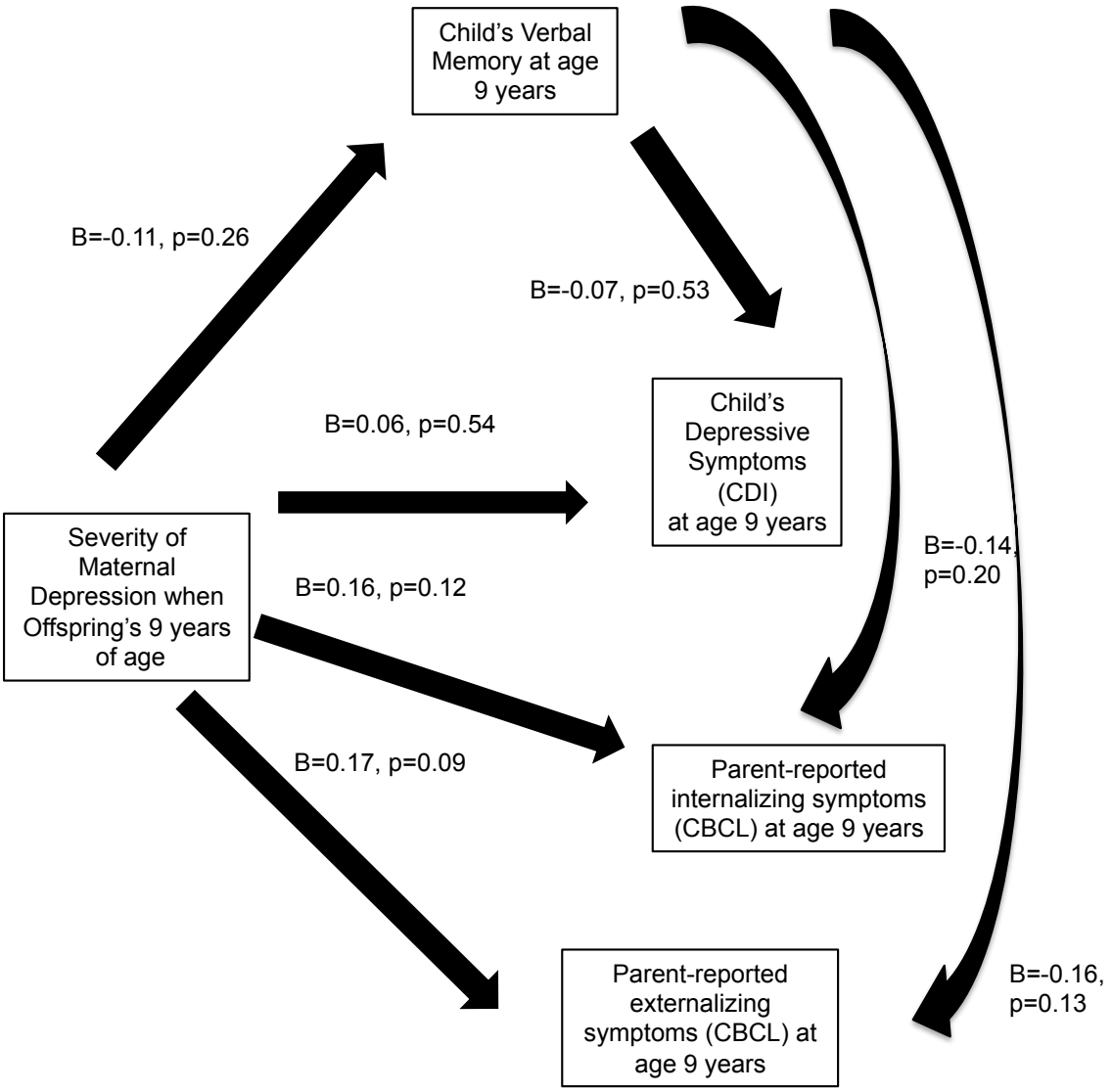


**Figure 6.** Associations between recent severity of mother's depressive symptomatology, and verbal memory performance and self- and parent-reported psychological symptoms of offspring, after controlling for age of memory testing, gender, family socioeconomic status and child's overall cognitive functioning. Standardized betas and p-values for independent multiple linear regressions are presented.

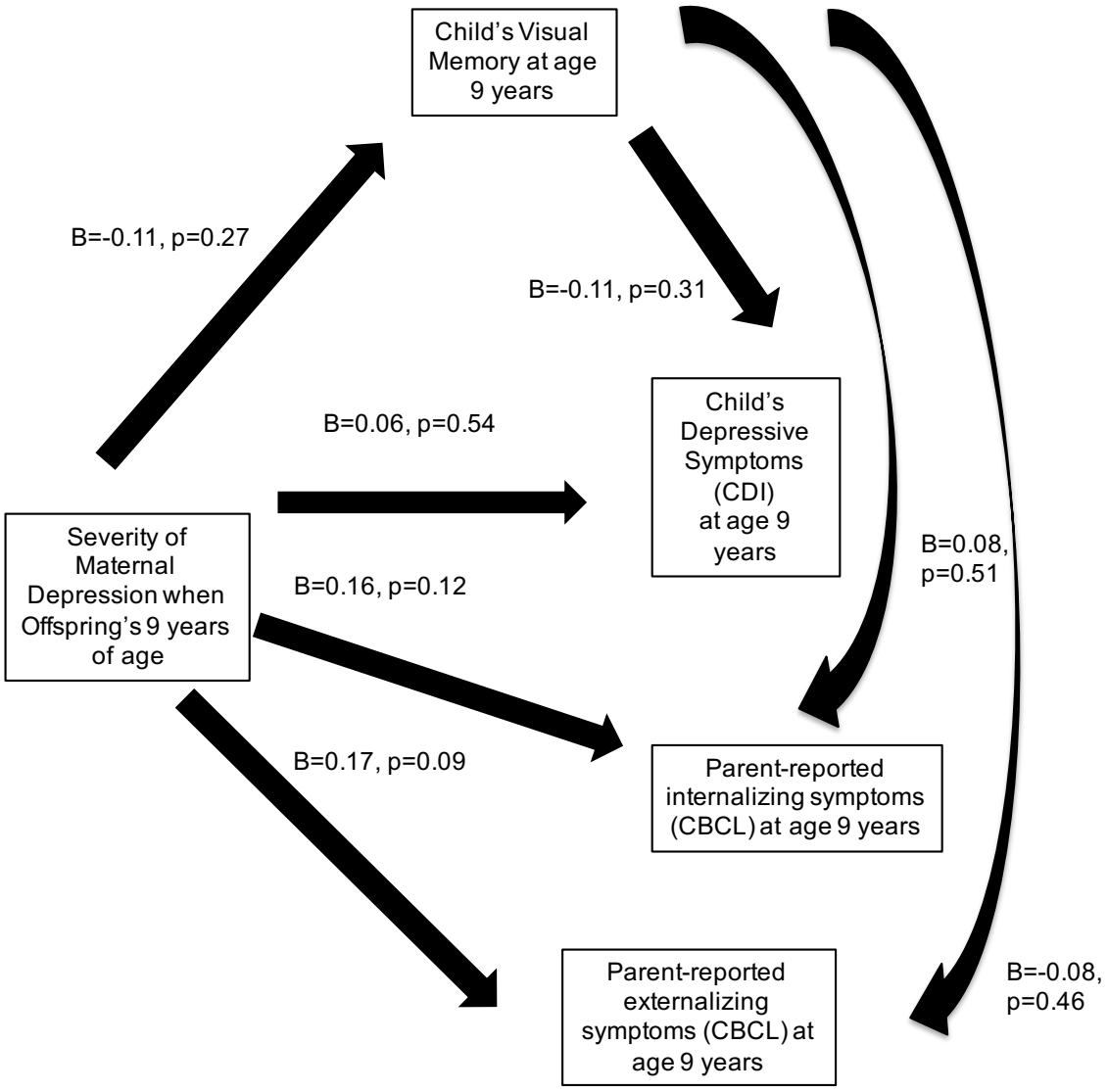


**Figure 7.** Associations between recent severity of mother's depressive symptomatology, and visual memory performance and self- and parent-reported psychological symptoms of offspring, after controlling for age of memory testing, gender, family socioeconomic status and child's overall cognitive functioning. Standardized betas and p-values for independent multiple linear regressions are presented.

**Early Internalizing Symptomatology as Independent Predictors of Later Memory Functioning and Psychological Functioning in Youth**

Figure 8 shows the independent associations between earlier internalizing symptomatology at 5 years, and later verbal memory performance and psychological symptoms at 9 years. Figure 9 illustrates similar relationships but with visual memory performance. Of note, gender ($\beta$=0.30, t=2.83, p=0.006) and FIQ ($\beta$=0.28, t=2.31, p=0.02) were significant covariates when combined with earlier internalizing symptom t-scores to predict verbal memory composite scores of 9-year youth. For visual memory, age ($\beta$=0.25, t=2.59, p=0.01) and FIQ ($\beta$=0.51, t=4.63, p<0.001) were significant covariates. Lower FIQ ($\beta$=-0.24, t=2.15, p=0.04) was also associated with greater externalizing symptoms.

Hierarchical multiple regressions yielded no significant effect of earlier internalizing symptomatology on visual or verbal memory performances. Internalizing symptoms at 5 years were not related to self-reported depressive symptoms at 9 years, but were predictive of caregiver-ratings of internalizing ($\beta$=0.60, t=6.64, p<0.001) and externalizing symptoms ($\beta$=0.39, t=3.92, p<0.001). All illustrated in Figures 10 and 11, these results suggest that the severity of early internalizing symptoms of children at 5 years is associated with greater psychological difficulties later at 9 years, based on caregiver-ratings.

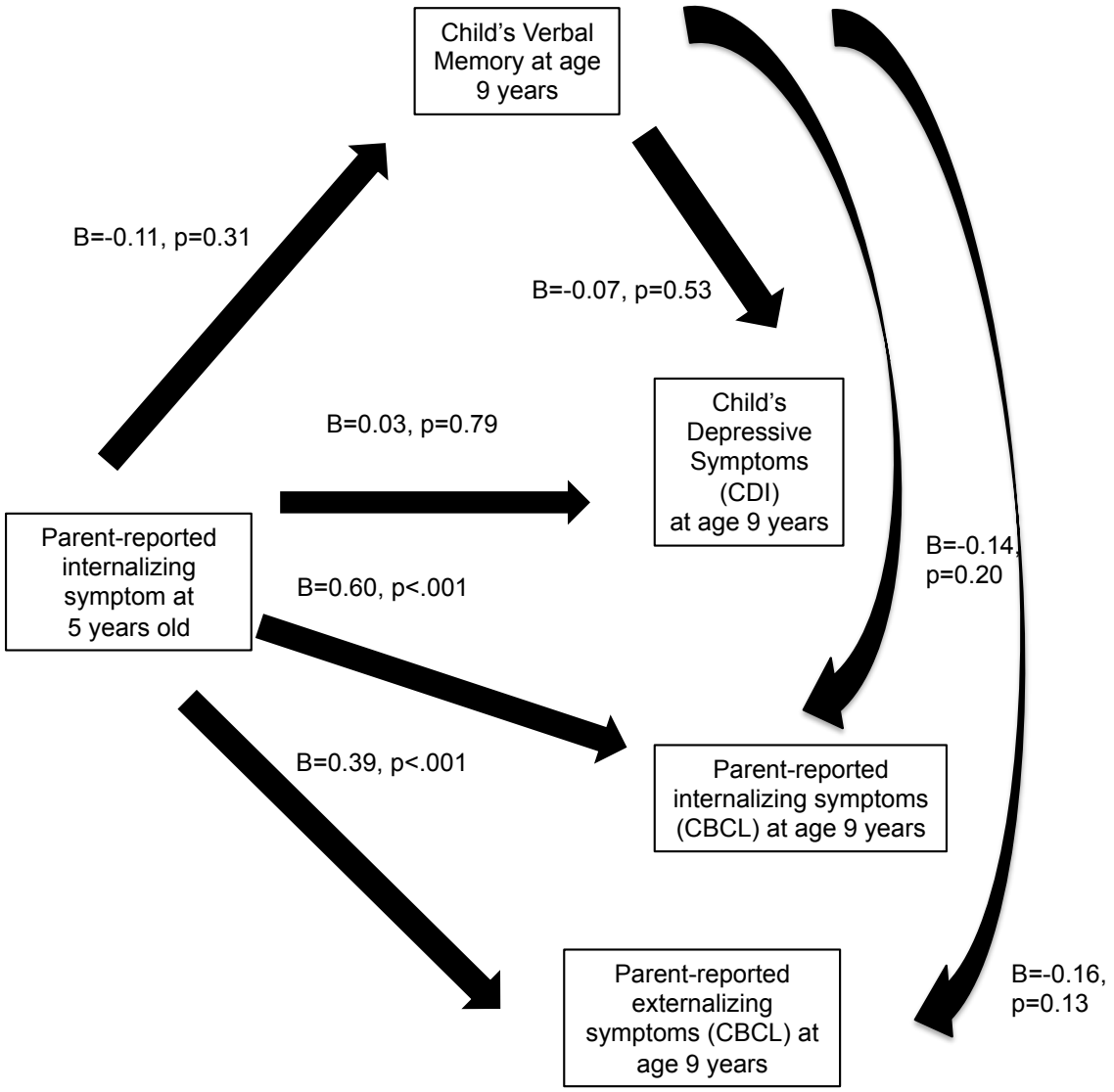


**Figure 8.** Associations between earlier internalizing symptomatology at 5 years, and later verbal memory performance and self- and parent-reported psychological symptoms of children at 9 years, after controlling for age of memory testing, gender, family socioeconomic status and child's overall cognitive functioning. Standardized betas and p-values for independent multiple linear regressions are presented.

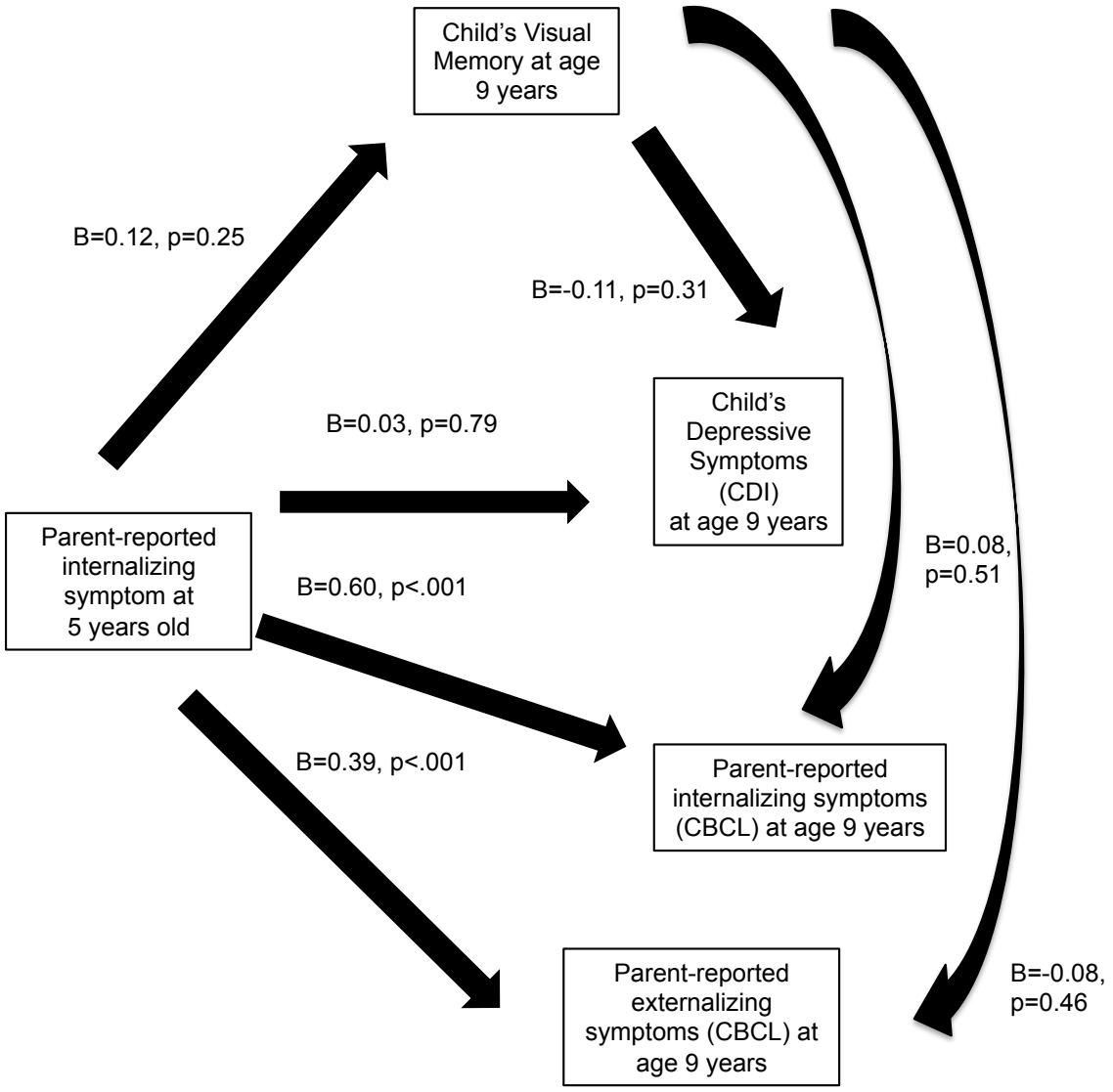


**Figure 9.** Associations between earlier internalizing symptomatology at 5 years, and later visual memory performance and self- and parent-reported psychological symptoms of children at 9 years, after controlling for age of memory testing, gender, family socioeconomic status and child's overall cognitive functioning. Standardized betas and p-values for independent multiple linear regressions are presented.

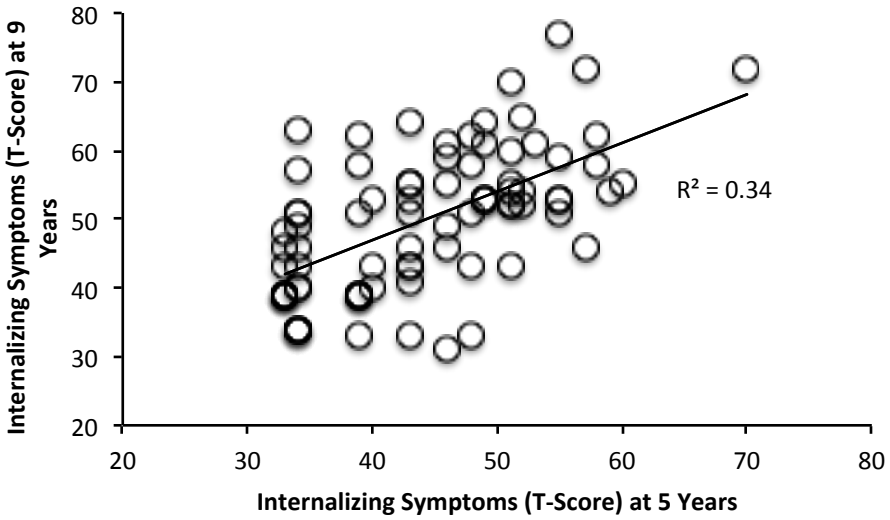


**Figure 10.** Average internalizing symptomatology (t-score) at 9 years as a function of earlier symptoms at 5 years.

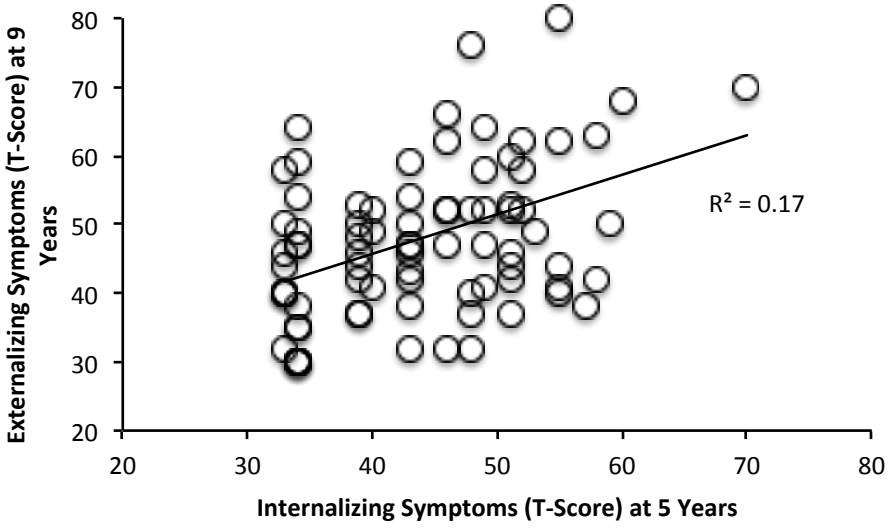


**Figure 11.** Average externalizing symptomatology (t-score) at 9 years as a function of earlier symptoms at 5 years.

**Moderating Effect of Memory Functioning on Chronic Maternal Depression and Current Symptoms**

Table 3 and 4 outlines the associations between chronic maternal depression, child's visual/verbal memory, and the interaction between the two variables with the offspring's psychological functioning (self-reported depression symptoms, parent reported internalizing symptoms, and parent-reported externalizing symptoms). Covariates were not significant across regression analyses. Chronicity of maternal depression was significantly predictive of the offspring's internalizing and externalizing symptoms when considered jointly with verbal memory performance ($\beta s>0.30$, $ts>2.83$, $ps<0.005$). Similar effects were observed when chronic maternal depression was considered jointly in a regression model with visual memory index scores ($\beta s>0.31$, $ts>3.04$, $p<0.005$).

The effect of the interaction between chronic exposure to maternal depression and the child's verbal memory performance was marginally significant ($\beta=-0.28$, $t=-1.90$, $p=0.06$) in predicting child's externalizing symptomatology. Follow-up multiple linear regressions were conducted to examine the associations between verbal memory performance and externalizing symptoms across participant groups (i.e., children exposed to chronic, recurrent, non-recurrent, or no maternal depression). No relationship between child's performance on the CVLT and their externalizing symptoms was found among comparison participants or offspring of mothers with chronic or non-recurrent depression. However, among children of mothers with recurrent depression, a significant association between these variables was observed ($\beta=-0.52$, $t=-3.85$, $p=0.03$), suggesting poorer verbal memory performance was related to greater externalizing symptoms in these at-risk youth. However, this subpool of participants is extremely limited (N=10), thus, this

association should be considered with caution given concerns of statistical power. Furthermore, no other significant interaction effects were observed, implicating that memory functioning has a weak moderating effect on *concurrent* psychological functioning.

**Table 3.** Multiple Regression Analyses Showing the Associations between Exposure to Chronic Maternal Depression and Verbal Memory on Child's Symptomatology (N=100).

| | Self-Report CDI Total | Parent-Report CBCL Internalizing Symptoms | Parent-Report CBCL Externalizing Symptoms |
|---|---|---|---|
| **Step 1** | | | |
| Gender | -0.05(-0.47) | -0.13(-1.14) | -0.04(-0.37) |
| Age of Cognitive Testing | -0.15(-1.43) | 0.01(0.12) | -0.15(-1.39) |
| Family SES | -0.07(-0.59) | -0.11(-0.92) | -0.16(-1.40) |
| IQ | -0.09(-0.76) | 0.03(0.28) | -0.12(-1.04) |
| $R^2$(F-statistic) | 0.04(0.94) | 0.03(0.62) | 0.08(1.73) |
| **Step 2** | | | |
| Chronicity of Maternal Depression (CMD) | 0.11(0.98) | 0.33(3.03)** | 0.30(2.83)** |
| Verbal Memory Index (VRM) | -0.08(-0.50) | 0.08(0.54) | 0.14(0.91) |
| CMD x VRM | 0.09(0.54) | -0.22(-1.43) | -0.28(1.90)+ |
| $R^2$(F-statistic) | 0.06(0.72) | 0.18(2.46) * | 0.22(3.24)** |
| $R^2$-Change(F-Change) | 0.02(0.45) | 0.15(4.81)** | 0.14(4.92)** |

*** $p < .001$ ** $p < .01$ * $p < .05$ +$p<0.10$

Note. Standardized betas and t-statistics (within parentheses) are reported.

**Table 4.** Multiple Regression Analyses Showing the Associations between Exposure to Chronic Maternal Depression and Visual Memory on Child's Symptomatology (N=100).

| | Self-Report CDI Total | Parent-Report CBCL Internalizing Symptoms | Parent-Report CBCL Externalizing Symptoms |
|---|---|---|---|
| **Step 1** | | | |
| Gender | -0.07(-0.66) | -0.14(-1.32) | -0.03(-0.29) |
| Age of Cognitive Testing | -0.14(-1.36) | 0.02(0.18) | -0.15(-1.43) |
| Family SES | -0.07(-0.60) | -0.10(-0.87) | -0.15(-1.31) |
| IQ | -0.09(-0.80) | 0.03(0.28) | -0.11(-0.93) |
| $R^2$(F-statistic) | 0.04(0.96) | 0.03(0.74) | 0.07(1.59) |
| **Step 2** | | | |
| Chronicity of Maternal Depression (CMD) | 0.12(1.12) | 0.37(3.56)*** | 0.31(3.04)** |
| Visual Memory Index (VM) | -0.03(-0.22) | 0.11(0.83) | -0.11(-0.81) |
| CMD x VSM | -0.15(-1.06) | -0.06(-0.45) | 0.06(0.39) |
| $R^2$(F-statistic) | 0.08(1.05) | 0.17(2.40)* | 0.17(2.42)* |
| $R^2$-Change(F-Change) | 0.04(1.17) | 0.14(4.50)** | 0.10 (3.34)* |

*** $p < .001$ ** $p < .01$ * $p < .05$ +$p<0.10$

Note. Standardized betas and t-statistics (within parentheses) are reported.

**Growth Pattern of Internalizing Symptoms**

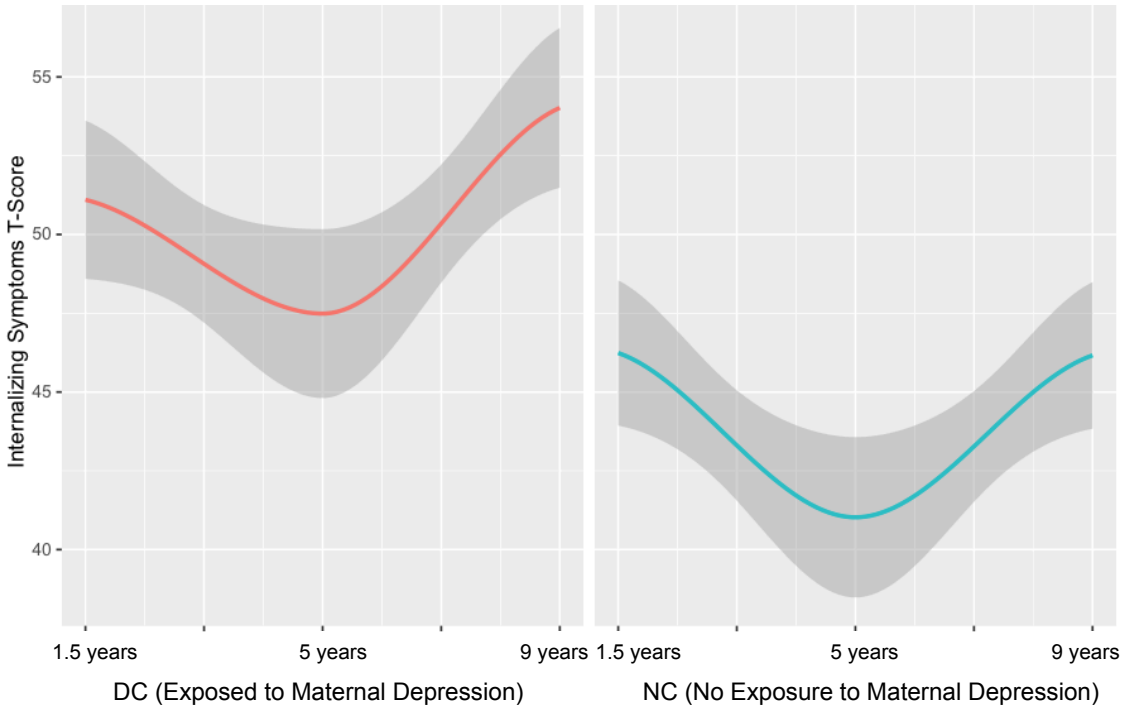


Figure 12. Pattern of internalizing symptoms at 1.5 years, 5 years, and 9 years as a function of exposure to maternal depression.

As shown in Figure 12, the growth of internalizing symptoms in both DC and NC groups was non-linear and yielded a quadratic trend. Linear mixed effects regression model showed no effect of Group or interaction of Group and Time (ts <1.94, ps ≥ 0.06). However, a significant effect of time (t(188)=2.02, p=0.04) and an intercept (t(188)=32.58) were found, reflecting greater internalizing symptoms by DC over NC children at baseline. As noted above in Data Analysis, repeated measure ANCOVAs were conducted to follow up the group differences in internalizing symptoms at age 5 and 9 after controlling for baseline symptoms respectively. Further, a quadratic polynomial regression would not be appropriate for the number of timepoints and the difference in the time between sessions (i.e., the average time between the baseline to the 5 year session is approximately 3.5 years, whereas the time between 5 year to 9 year session was

approximately 4 years). Notably, across the ANCOVA analyses below, baseline internalizing symptoms was a significant covariate implicating a relationship between earlier symptoms with later development of internalizing behaviors. After controlling for the baseline internalizing symptoms and demographic variables, ANCOVA analyses indicated marginally significant effect of time ($F(1,75)=3.47$, $p=0.06$), reflecting mildly greater symptoms at age 9 ($M=49.94$; $SD=0.98$) over age 5 ($M=44.26$; $SD=0.88$). Additionally, a main effect of group was observed with DC youth ($M=51.34$, $SD=1.14$) showing more severe internalizing symptoms than NC children ($M=42.86$, $SD=1.16$)($F(1,75)=19.68$, $p<.001$). An interaction of group and time reached marginal significance ($F(1,75)=3.06$, $p=0.08$).

Specifically, follow-up ANCOVAs separately conducted for DC and NC children indicated that NC children showed no significant difference between 5 and 9 years ($M_5 = 40.82$; $S_5 = 6.96$; $M_9 = 44.67$, $SD_9 = 8.17$); whereas, DC children showed moderately more symptoms at 9 years relative to 5 years ($M_5 = 47.75$; $S_5 = 8.77$; $M_9 = 55.42$. $SD_9 = 9.68$)($F(1, 36)=3.86$, $p=0.057$). Furthermore, although baseline symptoms was a significant covariate for the NC group ($F(1,36)=10.97$, $p=0.002$), this covariate showed no effect on the DC group, suggesting the differential impact of early childhood internalizing symptoms on later development of these characteristics.

## Discussion

The current study aimed to examine the effect of exposure to maternal depression on memory functioning, a neurobehavioral measure of hippocampal functioning, and the associations between this cognitive index with internalizing symptoms. Given past literature implicating increased risk of depression and anxiety in youth exposed to

maternal depression (Goodman & Tully, 2008; Hammen & Brennan, 2003), this investigation aims to better elucidate whether chronic exposure to such environment may have more significant impact on memory as prolonged exposure to stress has been postulated to trigger long-term alterations in hippocampal structure and function (Conrad, 2008; McEwen, 1999; 2008). In turn, such maladaptation of the neurobiological stress system could result in greater vulnerability for internalizing disorders (MacQueen et al., 2003).

In brief, five main findings were observed in the current study. First, chronic exposure to maternal depression was associated with lower verbal memory functioning and greater parent-reported symptoms of internalizing and externalizing symptoms at 9 years, but not self-reported depressive symptoms or visual memory. Second, acute depression severity, as indexed by current maternal depressive symptoms, was not related to the offspring's concurrent memory or psychological functioning. Third, earlier internalizing symptoms at 5 years were associated with higher internalizing and externalizing behaviors later at 9 years based on parent-report inventories, but not to self-reported depressive symptoms and memory functioning. Fourth, memory functioning at 9 years was not a significant moderating variable between earlier chronic exposure to maternal depression and psychological symptoms at 9 years (across self and parent-reporting inventories and internalizing versus externalizing symptoms). Finally, across children exposed to maternal depression and typical home environments, internalizing symptoms similarly developed in a non-linear pattern from 18 months to 9 years. Importantly, DC youth showing generally elevated symptoms relative to NC counterparts across timepoints but most prominently at age 9.

Altogether, consistent with our hypothesis, chronic exposure to parent psychopathology is linked to greater risk of later memory dysfunction and psychological symptoms, whereas acute/recent maternal depressive severity did not yield such relationships. Contrary to our predictions, memory functioning at 9 years was unrelated to concurrent psychological functioning. Further, the development of internalizing symptoms shows a similar maturational pattern as in those without parental risk. However, these offspring of depressed mothers present with more severe internalizing behaviors at an early age relative to those without the risk, and continue to show more elevated symptoms across time.

**Chronic Exposure to Maternal Depression, Later Memory Functioning, and Psychological Symptoms**

Consistent with McEwen (1999; 2008), chronic exposure to stress, such as parent depression, was associated with poorer memory performance, specifically of the verbal domain. Unexpectedly, however, this association was not observed with visual memory functioning. Although memory functioning is broadly attributed to hippocampal functioning, visual and verbal memory are also subserved by differential neural regions. Verbal memory is undergirded by the left prefrontal and left medial temporal lobe, and is mediated by the hippocampus (Fernandez et al., 1998; Fernandez et al., 2002; Grunwald et al., 1999; Wagner et al., 1998). In contrast, visual memory functioning is attributed to the posterior parietal, occipital region, and inferior temporal region, depending on memory related to visuospatial information or object recognition (Kesner, Bolland, & Dakis, 1993). Consequently, it is possible that the differential associations reflect greater sensitivity of left temporal lobe to chronic experiences of adversity or suboptimal

caregiving environment. Moreover, given our visual memory index score was comprised of memory recall of visuospatial (e.g., finger tapping) and visual object information, the diffused neural representation related to this broad construct may explain why visual memory was not associated with adverse early caregiving environments. In effect, it is possible that the various substrates related to visual memory broadly are more resistant to environmental stressors or are more adaptive to such circumstances.

However, it should be noted that despite the observed relationship found between chronic exposure to maternal depression and verbal memory, on average youth with chronic depression broadly scored within the average range of functioning on the standardized memory tests. Thus, while chronic exposure to adversities or cumulative stress may be related to decrements in hippocampal functioning, neurobehavioral measures suggest that the degree these substrates' functioning has been affected is relatively low. It is plausible that different functions of the hippocampus (e.g., stress regulation, memory, learning, spatial navigation) may be more sensitive to cumulative stress and likewise others may be more susceptible to ongoing adversity. For example, stress regulation may be more sensitive to persistent exposure to adversities due to neurochemical alterations; whereas, stressors may have less robust effect on memory functioning. Additionally, both visual and verbal memory composites in this study were comprised of different stages in memory retrieval (e.g., immediate recall, delayed recall, recognition), which may involve distinct neural substrates in conjunction with the temporal lobe (Rugg et al., 1998; Staresina & Davachi, 2008; Squire, Wixted, & Clark, 2007). As such, specific stages of memory recall (e.g., consolidation, delayed recall) may be better functional indices of the hippocampus. In effect, repeated stress may not

adversely impact all facets of memory functioning equally. Further longitudinal research examining specific memory faculties (e.g., recognition, recall, encoding), in conjunction with other neurophysiological measures (e.g., cortisol production) related to this substrate will be necessary to better understand how repeated stressors may impact hippocampal functioning, and predispose youth to mood disorders.

**Current Maternal Depression Severity and Earlier Internalizing Symptoms: Associations with Later Memory Functioning and Psychological Symptoms**

In line with Hammen and Brennan (2003), results indicated that chronic exposure to maternal depression yields more elevated risk of internalizing symptoms than severity of the current episode. Cumulative stress has been suggested to trigger long-term changes in neurodevelopment, physical health, and subsequently mental health, coined allostatic load (Ewen, 2004). Researchers have postulated that chronic stressors elicit different adaptive processes, which require varying degree of social, emotional and cognitive resources (Hammen, Brennan, Keenan-Miller, Hazel, & Najman, 2010). For example, Hammen and colleagues (2010) found that although both cumulative and acute family stressors are associated with greater depressive symptoms in youth, those with chronic stressors and genetic risks showed most severe symptomatology. In turn, no gene-environment interactions on depressive symptoms were found for youth exposed to acute stressors. In addition, Essex et al. (2002) observed that 4.5-year-old offspring of mothers with depression produced elevated cortisol levels when exposed to maternal stress since early infancy, but not when exposed to concurrent or early stress solely. Results of the current investigation and those of Essel et al., (2002 and Hammen et al. (2010) implicate

that chronic stress may activate different adaptive mechanisms and interact with other psychosocial or biological factors, increasing the child's susceptibility to depression.

However, it should be noted that chronic and acute or recent stress is often challenging to dissociate. Individuals exposed to chronic stress typically are more likely to experience additional acute stressors or episodic stressful life events (e.g., recent change in a close relationship, academic performance, or social life)(Hazel, Hammen, Brennan, & Najman, 2008). As such, there are clear problems in operationalizing chronic versus acute or recent stress, as the recent stressor may be a related event to the original source (Hazel et al., 2008). For example, maternal depression is associated with greater marital discord and disruptions in family relationships, which may present as an acute stressor when father and child engage in recent conflict. Subsequent investigations should consider examining more isolated stressful events to better delineate differential effects of chronic versus recent/acute stress on internalizing symptoms in vulnerable youth. For instance, individual stressful events that are confined within a time period (e.g., natural disaster, transition in residence/school) versus long-term stressful events (e.g., parent psychopathology, substance dependency by parents, parents' functional impairment due to medical ailment) may elicit different adaptive mechanisms that impact psychological health. Likewise, considerations of the intensity of stress experienced (i.e., *how stressful the event is felt*), and repetition of stressors versus continued exposure to a stressor should also be considered, as each of these characteristics may constitute chronic stress but also contribute to adaptation or maladaptation in varying ways.

Interestingly, internalizing symptoms at 5 years were not associated with memory functioning at 9 years. As indicated in Table 2, internalizing behaviors in DC and NC

youth were relatively low, as both groups broadly scored within the normal developmental range. As such, it is possible that the DC and NC youth experienced less internalizing symptoms at 5 years (Table 2 and Figure 12); thus, neural substrates related to stress regulation such as the hippocampus were less adversely affected. These findings are somewhat contrary to the stress generation model endorsed by Hammen (2006). Hammen contended that children are active agents in the environment, and those at risk for depression through harmful environments could burden themselves with even more stress by the way they interact with their surroundings. Our finding, i.e., the lack of association between internalizing symptomatology at 5 and 9 years old with memory indices in youth, may be due to the children's' relatively low internalizing features. As such, these youth might not elicit negative interactions with their environment (e.g., fathers, siblings, etc.) or create additional environmental stressors for themselves; thus, their stress regulatory system and related neural substrates such as the hippocampus are not significantly affected. Consequently, it should be emphasized that although our findings show some support that chronic exposure to depression specifically affects memory functioning in offspring, these youth generally showed relatively preserved memory capacity, as indicated by their strong performance, reflecting somewhat resilient hippocampal functioning.

**Memory Functioning as Moderating Predictor of Psychological Functioning and Early Maternal Depression**

Contrary to our hypotheses, memory functioning was not a strong moderating factor between chronic exposure to maternal depression and internalizing or externalizing behaviors. In the current study, measures of memory and psychological functioning in

children were collected at the same sessions at 9 years. It is possible that memory dysfunction, a neurobehavioral index of hippocampal functioning, is predictive of *future* internalizing symptoms but not of *current* status, as abnormal functional development of the substrate may impede later capacity to cope with additional stressors or regulate negative emotions.

Moreover, in the current study, DC and NC youth, on average, scored within age-expectations across cognitive and internalizing symptom measures, suggesting that these youth showed relatively positive adaptation to the stressful caregiving environment. It is also possible that psychological symptomatology and memory functioning are not dissociable when these areas of functioning are within "normal" limits. For example, memory dysfunction, or irregularities in hippocampal functioning, may be associated with concurrently greater internalizing symptoms solely when the child is of clinical status (i.e., afflicted with severe emotion dysregulation or mental health ailment) but not more typically developing. Given the recruitment standards applied in the study, it is also plausible that DC participants received some environmental supports that buffer the stress associated with maternal depression. For example, both DC and NC youth had parents with relatively high degree of education and are of middle to upper socioeconomic status. Furthermore, most of the children had parents who were married and thus may have received socioemotional support from fathers that protect them from the negative effects of maternal depression. In brief, DC youth in our study may have protective factors in their social environment that contribute to their capacity to cope with adversity and emotion regulation.

**Maternal Depression and Externalizing Symptoms in Offspring**

Although children's performance on memory assessments was not associated with psychological functioning broadly, chronic exposure to maternal depression predicted greater externalizing behaviors, similar to associations observed in internalizing symptoms. These findings are in line with those reported by Ewell Foster et al. (2008). The investigators found that chronicity and severity of maternal depression are associated with both child's internalizing and externalizing symptoms. Other research has also shown that youth of depressed mothers show more disruptive behaviors (Kim-Cohen et al., 2005).

In addition, specific to those with recurrent depression alone, poorer verbal memory functioning was associated with greater externalizing symptoms. This association was not observed among children of mothers with non-recurrent or chronic depression. The specificity of this association in caregivers with recurrent episodes of depression could potentially stem from the unpredictability of mothers' mental health functioning in this group relative to others. For example, mothers with non-recurrent depression may have had the disorder at the baseline session but showed relative stability in low symptomatology in subsequent sessions at 3, 4, 5 and 9 years. Likewise, those with chronically depressed mothers may have adapted to the expectations of high depressive symptoms given the persistent illness. However, youth with mothers with recurrent depression might struggle to adjust and reorganize their cognitive, biological, and social systems given the inconsistent changes in parents' behaviors. Mothers diagnosed with depression typically criticize and engage in conflict with offspring more than healthy caregivers (Low & Stocker, 2005; Marmorstein & Iacono, 2004; Rogosch, Cicchetti, & Toth, 2004). As such, children of mothers with recurrent

depression may struggle with the unpredictable parent-child interactions and relations, which in turn results in poor emotional adjustment, greater hippocampal and memory dysfunction, and greater risk of externalizing symptoms over time. Externalizing behaviors and parent-child conflict also shows a bidirectional effect (Burt, McGue, Kruger, & Iacono, 2005); thus, youth showing more disruptive behaviors as a function of maternal depression may interact with parents in a manner that would escalate conflict and caregivers' symptomatology. As such, these results highlight the need for early treatment for mothers with depression and parent-child relational intervention to aide mothers in providing more positive interactions with offspring and increasing their sensitivity to their child's emotional and social cues. Emerging but limited investigations have begun to show the efficacy of interventions such as toddler-parent psychotherapy in increasing attachment security and promoting cognitive development in offspring with depressed mothers (Cicchetti et al., 2000; Cicchetti, Toth, & Rogosch, 1999; Toth, Rogosch, Manly, & Cicchetti, 2006), which in turn reduces risks for developing mental health ailments. However, as noted in Results, this association observed among mothers with recurrent depression should be considered with caution given the low sample size (N=10). All in all, the observed findings above highlight the importance of early introduction of interventions for mothers with depression, as prolonged exposure of maternal depression may have widespread adverse impact on offspring's mental health.

**Growth Patterns of Internalizing Symptoms**

Although both DC and NC showed a non-linear pattern of development of internalizing behaviors, symptomatology at baseline was a significant covariate for subsequent behaviors at 5 and 9 years old in typically developing children, whereby this

variable was not a prominent covariate in the clinically at-risk group. Moreover, DC youth showed greater disparity in symptoms than NC children at 18 months and at 9 years old relative to 5 years of age, despite showing similar growth pattern. The differential association of early baseline functioning on subsequent behaviors, varying elevation in symptoms across timepoints in DC youth, and the lack of association between earlier symptoms with later memory functioning provide some support that disorganization of psychological, biological, and cognitive systems in children at risk for depression. Cicchetti and Toth (1998) proffered that children of depressed mothers who are at greater risk of developing the mood disorder may form incoherent organization of internal systems, resulting with greater vulnerability to developing depression. These researchers contended that each developmental stage is associated with unique challenges, which elicit adaptive processes. Children who are at greater risk for depression, such as those exposed to parents' with mental ailments genetically or environmentally, may show increasingly insufficient or poor adaptation across developmental stages.

Given the lack of association between baseline and subsequent symptoms in DC versus NC youth, it is also likely that the effect earlier symptoms play on subsequent development of psychopathology modifies over time as additional risks or protective factors occur. Notably, due to limitations with statistical power and sample size and the number of covariates used, the current study did not control for possible buffers to stress (e.g., additional guardian or father involvement) or risks (e.g., fathers' with depression or other mental health ailments), although the latter is often common in youth with depressed mothers (Paulson et al., 2010). As such, it is possible that additional

environmental stress associated with maternal depression may increasingly influence self-organization in youth, such that risks for depressive disorders intensify with age. Indeed, research has reported greater prevalence of depression in adolescence relative to earlier childhood (Andersen & Teicher, 2008), and that psychosocial and biological correlates with depressive symptoms during this stage differ from other developmental periods (Rice, Harold, & Thapar, 2002). Further longitudinal investigations are necessary to better understand the ontogeny of depression in youth exposed to maternal depression, and the potential role of other family members in the positive or negative adaptation processes.

**Limitations**

Despite the novel contributions to the current investigation, several limitations should be considered in subsequent research, in addition to those noted above. Given the strong genetic influence on major depression (Sullivan et al., 2000), further investigation examining the familial history of the psychopathology would be important to consider, as it would allow better delineation of youth whose parents developed depression from environmental factors alone from those with familial history of the disorder. In a similar vein, the current study did not control for the mothers who had depression and were treated with medication during pregnancy, which has been found to impact cognitive development (Casper et al., 2003; Davalos et al., 2012). Additionally, given the relatively low sample size and number of statistical tests necessary to address research questions, selected demographic and cognitive factors were applied as covariates. As such, mothers' cognitive abilities, such as overall IQ, verbal or visual memory functioning, or executive functioning, were not included as covariates. Subsequent studies investigating the

association between early exposure to maternal depression and later memory development should also control for mother's overall intellectual development and memory functioning. For example, it is unclear whether the memory performance of youth would be more strongly contributed by genetic influences to cognitive development (e.g., verbal skills, speed of processing, visual or verbal memory) as specific facets have been shown to have higher heritability (Plomin, Fuler, Corley & DeFries, 1997). Moreover, socioeconomic status has been found to moderate heritability and environmental influences on IQ and verbal skills in children (Rowe, Jacobson, & Van den Oord, 1999; Turkheimer, Haley, Waldron, D'Onofrio, & Gottesman, 2003), such that among families from disadvantaged backgrounds, genetic influences contributed to less variance of cognitive skills in offspring than those with from families of high socioeconomic status or greater education.

The current study also examined early exposure to parental psycopathology as a risk factor for hippocampal dysfunction. However, future investigations should also examine possible protective factors that could buffer the stress of maternal depression. For example, past research has suggested that the involvement of the father moderates exposure to maternal depression and later presentation of internalizing symptoms in offspring (Mezulis, Hyde, & Clark, 2004). However, likewise, the diagnosis of paternal depression in addition to maternal depression exacerbated risks for problems with internalizing and externalizing behaviors (Mezulis et al., 2004). Moreover, meta-analytic studies have suggested rates of depression across both parents may be particularly augmented within the first year after child's birth (Paulson & Bazemore, 2010), which reportedly reduces parents' engagement in enrichment or academic activities with their

children (Paulson, Dauber, & Leiferman, 2006) potentially impacting their cognitive and emotional development early in life.

It should be noted that several inventories were used to assess psychological development in youth; however, differential results observed between self versus caregiver ratings raises concern regarding reporter biases. In particular, given that over 90% of the parent-report inventories were completed by the mothers, of which approximately half were suffering from depression, it is possible that these parents were biased in their assessment of their child. Indeed, several research have suggested that parents with psychopathology may be biased in their symptom endorsement for their offspring, as their own internalizing symptoms cloud their perception and standards of "normal" behavior in their children (Briggs-Gowan, Carter, & Schwab-Stone, 1996; Chilcoat & Breslau, 1997; De Los Reyes & Kazdin, 2005). Similarly, teachers of children who are diagnosed with psychiatric disorder often perceive their behaviors in a biased manner, consistent with their preconceived notion of the child's psychopathology (Briggs-Gowan, Carter, & Schwab-Stone, 1996; Chilcoat & Breslau, 1997; De Los Reyes & Kazdin, 2005; Kroes, Veerman, & De Bruyn, 2003). Therefore, in subsequent research, the use of multiple informants would be important to provide greater insight whether the reporters may be biased or if the behaviors are consistently displayed across contexts or are limited to specific triggers. Importantly, the use of the same inventory with multiple reporters (e.g., Behavior Assessment System of Children; Parent, Teacher, and Self Report versions) would aide in the interpretation of findings rather than use of various inventories with different norms.

## Conclusion

In summary, chronic exposure to maternal depression but not acute or recent severity of the illness was predictive of verbal memory functioning in offspring; however, memory generally did not moderate the association between early exposure to maternal depression and concurrent internalizing symptoms. Most significantly, despite similar pattern of development of internalizing behaviors, children with depressed mothers show elevated symptoms across timepoints from 18 months to 9 years with greater disparity from typically developing youth with greater age. The present findings highlight the need for further longitudinal investigations to better understand the intersection of affective and neurocognitive sequelae of maternal depression in offspring.

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