## NEUROPSYCHOLOGICAL AND HEALTH PREDICTORS OF THEORY OF MIND IN OLDER ADULTS

by

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### ABSTRACT

The ability to reason about mental states, or theory of mind (ToM), is a defining human capacity with implications for late-life social understanding. Current aging research suggests that ToM draws heavily from traditional neurocognitive resources; however, to our knowledge, no published studies have explored potential modifiers of these links. We examined associations between ToM, neurocognitive ability and blood pressure in N = 66 cognitively intact community-dwelling older adults (65–92 years). While increased age, high blood pressure, and neuropsychological ability emerged as important independent predictors of older adults' ToM, relationships are not straightforward. Important interactions between poor neurocognitive scores and reduced ToM may be more salient in certain groups of older adults with elevated blood pressure. Findings suggest that previous models of cognitive involvement in ToM may be necessary, but not sufficient to explain age-related changes in mental state reasoning.

**Keywords**: theory of mind; aging; neuropsychological ability; health; blood pressure

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To my parents and siblings, whose unconditional love and support have brought me through

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And to Chris, for his strength, patience and unwavering belief in my abilities.

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### INTRODUCTION

Humans rely on a wide range of evidence to be able to predict and understand the social world. Increased interest in the mechanisms underlying social reasoning has led to an appreciation of the importance of theory of mind (ToM). ToM refers to the ability to make introspective judgments about one's own or another person's mental states-including thoughts, desires, hopes, emotions and intentions (Happé, Winner, & Brownell, 1998; Premack and Woodruff, 1978). It is an evolved capacity of higher-level cognition, or metacognition, which is both functionally important and evolutionarily adaptive. Arguably, ToM is an exemplary capacity unique to human beings (Saxe, 2006; Wellman & Lagattuta, 2000). Navigation through the social world requires individuals to be able to reflect on the contents of a variety of mental states. In this sense, being able to interpret cues that signal mental states may be related to the maintenance of successful relationships, healthy mental functioning, and overall life satisfaction (Carton, Kessler & Pape, 1999). We have adopted the convention of recent literature in this field and use the terms 'ToM' and 'mental state reasoning' interchangeably to denote the ability to attribute and reason about a variety of unobservable mental states (e.g., Abraham, Rakoczy, Werning, von Cramon, & Schubotz, 2010; Bernstein, Sommerville, & Thornton, in press, Saxe & Powell, 2006; Young, Dodell-Feder, & Saxe, 2010).

Investigations of ToM in aging indicate that mental state reasoning may be vulnerable to age-related decline among older individuals (Maylor, Moulson, Muncer, & Taylor, 2002; Sullivan & Ruffman, 2004). Authors suggest that these reductions begin to emerge in mid-life and continue throughout older adulthood (Bernstein et al., in press; Pardini & Nichelli, 2009). Further, a number of studies have examined the links between reductions in mental state reasoning and traditional neuropsychological abilities known to decline with advancing age. This line of research generally suggests that among older adults, the ability to reason about mental states draws heavily upon neuropsychological resources such as executive function, speed, and language (e.g., German & Hehman, 2006; McKinnon & Moscovitch, 2007; Newton & de Villiers, 2007).

Notably, empirical evidence supports the role of medical health as an important predictor of age-related cognitive change (Spiro & Brady, 2008; Wahlin, MacDonald, de Frias, Nilsson, & Dixon, 2006). In particular, well-described vulnerability factors for cardiovascular disease are associated with late-life cognitive change and have been identified as major risk factors for Alzheimer's disease and other dementia (Whitmer, Sidney, Selby, Johnston & Yaffe, 2005). One potential modifier that has demonstrated reliable cognitive effects in late life is uncontrolled blood pressure. Blood pressure is an important marker of vascular aging, and high blood pressure in particular may exert negative effects on specific areas of neuropsychological function (e.g., Elias, D'Agostino, Elias, & Wolf, 1995; Saxby, Harrington, McKeith, Wesnes, & Ford, 2003; Waldstein, Brown, Maier & Katzel, 2005). Importantly, many of the

neurocognitive domains preferentially affected by blood pressure overlap with those hypothesized to support ToM. Thus, individual differences in blood pressure may be important predictors of neurocognitive decline in abilities suggested to support mental state reasoning, and therefore may have an adverse effect on ToM in older individuals.

#### Models of Theory of Mind

ToM has been studied extensively over the last 20 years, most prolifically from an early developmental perspective (see Flavell, 2004; Wellman & Lagattuta, 2000 for reviews). Evidence cites marked shifts in children's mental state reasoning during the pre-school years, where children come to appreciate that they (and others) may hold beliefs about reality that are false (Wimmer & Perner, 1983). Engrained within this literature is a debate surrounding the nature and extent to which traditional neuropsychological abilities may be crucial components underlying the early development of ToM and its maintenance in adults. Two competing models of ToM are prominent throughout the literature: Modularity and non-modularity. Specifically, competing lines of evidence exist regarding whether mental state inferences are generated by a cognitive mechanism specialized for that purpose (modularity), or rather; rely heavily on recruitment from traditional neuropsychological resources such as executive function, processing speed and language (non-modularity) (Scholl & Leslie, 1999; Streck & Begeer, 2010).

The first model advances ToM as a 'modular' cognitive construct. Theoretically, this viewpoint assumes that ToM is a specialized capacity that possesses a dedicated cognitive mechanism. This conception features ToM as innate, domain-specific, and implies a static and inflexible developmental trajectory (Brüne & Brüne-Cohrs, 2006). Initially, strong theoretical arguments from developmental dissociation studies endorsed the modularity of ToM; these arguments stemmed from observations that children with autism were fundamentally impaired in their ability to understand the thoughts and feelings of others, but displayed preserved performance on tasks that did not required mental state inferences (Gopnik, Capps, & Meltzoff, 2000). Since autism is a neurologically innate disorder that presents with marked impairments in ToM, proponents of modularity contend that ToM must itself be innate (Gopnik et al., 2000). Other arguments for modularity include: fast, involuntary processing (e.g., Cohen & German, 2010), implementation in specific neural architecture (e.g., medial prefrontal cortex, Frith & Frith, 2006; Saxe, 2006), and susceptibility to selective impairments following brain damage in frontal regions (cf. brain injury: Apperly, Samson, Chiavarino, Bickerton, & Humphreys, 2007; Geraci, Surian, Ferraro, & Cantagallo, 2010; Stone, Baron-Cohen, Calder, Keane, & Young, 2003; stroke: Happé, Brownell, & Winner, 1999). A full discussion of modularity is presented in Scholl and Leslie (1999).

In contrast, the view of ToM as a developing (as opposed to innate) cognitive capacity provides a framework to examine the role of contributions from other cognitive resources. This second, 'non-modularity' model proposes that

ToM draws heavily on support from traditional neuropsychological domains – most notably executive function (inhibitory control, working memory) and language (grammar, semantics, vocabulary; Streck & Begeer, 2010). Within this model, ToM is thought to emerge gradually in early childhood as supporting neuropsychological resources emerge (Leslie, Friedman, & German, 2004; Streck & Begeer, 2010). Such resources will remain involved throughout the lifespan, insofar as task demands are such that they are required (Leslie et al., 2004). In contrast to modular models, the non-modular approach proposes that reductions in mental state reasoning will occur when age-related impairments are observed in neuropsychological resources from which ToM may draw (Streck & Begeer, 2010). Converging lines of research from both child-development and aging research provide evidence that effective ToM appears to depend upon intact functioning of its supporting neuropsychological resources (Apperly, Samson, & Humphreys, 2009; Carlson & Moses, 2001; Streck & Begeer, 2010). As such, a key topic of research has focussed on delineating whether these supporting neuropsychological resources are necessary only for the emergence of ToM, or if they display continued maintenance in its functioning (Apperly et al., 2009).<sup>1</sup>

<sup>&</sup>lt;sup>1</sup> It should be noted that early developmental literature provides theories supporting the role of neuropsychological resources in both the emergence (i.e., neuropsychological resources are involved strictly in the development of ToM as a construct) and continued competence (i.e., neuropsychological resources continue to support mature ToM capacity) of mental state reasoning (Moses, 2001; Streck & Begeer, 2010). However, the majority of research on mental state reasoning in adults reliably supports the continued involvement of supporting neuropsychological resources in mature ToM (Apperly et al., 2009; Streck & Begeer, 2010).

Contemporary findings are largely consistent with non-modular models of ToM, suggesting that mental state reasoning continues to rely upon traditional neuropsychological resources in adulthood (Apperly et al., 2009; Streck & Begeer, 2010). Early developmental literature lends greatest support for the role of executive function (particularly inhibitory control and working memory) and language in early ToM (e.g., Carlson & Moses, 2001; Carlson, Moses, & Breton, 2002; de Villers, 2000; Milligan, Astington, & Dack, 2007). It has also been suggested that ToM may place high demands on processing resources, as these tasks often require multiple cognitive actions such as holding beliefs in mind, manipulating, and comparing information (Apperly et al., 2009; see also German & Hehman, 2006). Individual differences in the expression, timing, and utilization of ToM observed in early development are also relevant to aging populations (Wellman & Lagattuta, 2000). Older age is associated with greater variability in neuropsychological performance (Morse, 1993), in addition to a higher prevalence of factors that may negatively influence cognition (e.g., declining health; Spiro & Brady, 2008). Indeed, cognitive aging may be an ideal field in which to study how traditional cognitive abilities are involved in ToM, in that declines in several neuropsychological domains that may play a supporting role are often reported in late life (e.g., executive abilities, speed; Hasher & Zacks, 1988; Salthouse, 2010).

#### Neurocognitive Involvement in Late Life Theory of Mind

Studies of ToM in aging yield somewhat mixed evidence regarding the extent to which age-related declines in mental state reasoning reliably occur. Multiple factors may contribute to mixed findings, many of which include methodological determinants such as variability in the number and types of tasks used to index ToM and inconsistent sampling of older age ranges. While some studies have found no differences in mental state reasoning between younger (university undergraduate students) and older adults (e.g., MacPherson, Phillips, & Della Sala, 2002; Slessor, Phillips, & Bull, 2007), others have suggested that older adults may outperform their younger peers on tasks with mental state content (i.e., requiring participants to reflect on the mental states of another person, such as thoughts, beliefs, hopes, and intentions; Happé et al., 1998). For example, the first study to investigate ToM in older adults (ages 61-80 years) used a series of short stories requiring first- and second-order mental state inferences<sup>2</sup> (Strange Stories task, Happé, 1994; Happé et al., 1998). The authors found that older adults outperformed their younger peers on the Strange Stories task, and concluded that accrued life experiences and 'increased wisdom' were driving forces behind older adults' superior mental reasoning (Happé et al., 1998).

<sup>&</sup>lt;sup>2</sup> ToM is typically measured using first- and second-order tasks. First-order tasks require inferences about a single person's mental state (Baron-Cohen, 2000), whereas second-order tasks require inferences about multiple viewpoints, and are thought to involve greater neuropsychological demands than first-order tasks (i.e., considering one person's perspective about another person's mental state; see Baron-Cohen, 2000; McKinnon & Moscovitch, 2007). A selection factor in our use of Happé's (1994) *Strange Stories* task as our dependent measure was its incorporation of both first and second-order ToM questions, and its prominent use in the cognitive aging literature examining mental state reasoning (e.g., Charlton et al., 2009; Happé et al., 1998; Maylor et al., 2002; Sullivan & Ruffman, 2004).

Nonetheless, the majority of literature supports the existence of reliable, age-related *reductions* in mental state reasoning in individuals over the age of 60 (Bailey & Henry, 2008; Bernstein et al., in press; Charlton, Barrick, Markus, & Morris, 2009; Maylor et al., 2002; McKinnon & Moscovitch, 2007; Pardini & Nichelli, 2009; Sullivan & Ruffman, 2004). Subsequent studies have failed to replicate Happé and colleagues' (1998) findings using the Strange Stories task, many of whom report group differences in ToM performance in favour of younger adults (e.g., Bull, Phillips, & Conway, 2008; Maylor et al., 2002; Sullivan & Ruffman, 2004). For example, Maylor and colleagues (2002) found age-related reductions in performance on stories requiring mental state inferences (but not for non-mental state content) than their younger peers under task conditions comparable to Happé et al (1998). These age differences remained even after accounting for group differences in vocabulary, processing speed and executive function (Maylor et al., 2002). The authors postulated that older adults may have drawn correct inferences regarding mental states, but simply failed to refer to them in their answer, resulting in an incomplete response. Sullivan and Ruffman (2004) addressed this possibility in a replication study, by incorporating an extra condition to the Strange Stories task that required participants to recall facts about the stories to determine whether performance reductions were due to difficulty recalling the text, or a real impairment in mental state reasoning. Participants had no difficulty recalling key facts, and the authors agreed with Maylor et al.'s (2002) explanation that discrepancies in results from Happé and

colleagues (1998) were best explained by differences in the sample composition (Sullivan & Ruffman, 2004).

Although story paradigms are commonly used in ToM investigations, tasks used to assess mental state reasoning may vary considerably. In keeping with these findings, other recent studies have shown age-related declines in mental state reasoning using alternate tasks designed to measure ToM (Bailey & Henry, 2008; Charlton et al., 2009; McKinnon & Moscovitch, 2007; Pardini & Nichelli, 2009; Phillips, MacLean, & Allen, 2002; Saltzman, Strauss, Hunter & Archibald, 2000). These may include: verbal measures assessing the appreciation of mistaken beliefs (*Faux pas task*: MacPherson et al., 2002; Stone, Baron-Cohen, & Knight, 1998), visual tasks assessing recognition of mental states through pictures of faces (*Reading the Mind in the Eyes task*: Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997, Bull et al., 2008; Pardini & Nichelli, 2009) and interactive tasks assessing the recognition of false beliefs (*Sandbox task*: Bernstein et al., in press).

Most neuropsychological research supports the reliance of older adults' ToM upon contributions from traditional cognitive resources such as executive function, speed, and language (Bull et al., 2008; Charlton et al., 2009; German & Hehman, 2006; McKinnon & Moscovitch, 2007). Support for ToM's nonmodularity is garnered through studies that have examined older adults' performance on measures of ToM while varying the neurocognitive load (high versus low) on these tasks (Bull et al., 2008; McKinnon & Moscovitch, 2007; Newton & de Villiers, 2007). McKinnon & Moscovitch (2007) observed that

reduced efficiency in executive function adversely affected ToM performance in both younger and older adults, reinforcing the notion that ToM draws heavily from executive resources. In another study, German & Hehman (2006) used a task of belief-desire reasoning to examine the links between ToM, neuropsychological abilities and age. They found that systematically manipulating executive function demands within tasks of ToM caused the greatest performance decreases across age groups. Moreover, processing speed, inhibition and working memory accounted for the greatest variance in ToM performance in older adults. Other investigations support the role of executive abilities and speed in aging populations (Bailey & Henry, 2008; Bull et al., 2008; Maylor et al., 2002). One recent study examined the influence of language on mental state reasoning in adults using a dual-task paradigm (Newton & de Villiers, 2007). In this study, Newton & de Villiers (2007) showed that the concurrent performance of measures of language and ToM significantly disrupted participants' ability to reason about mental states, even when non-verbal tasks of ToM were used. Their results are consistent with Maylor et al. (2002), who found that vocabulary was significantly associated with reductions in mental state reasoning on the Strange Stories task among older individuals.

More recently, Charlton and colleagues (2009) examined the relation between ToM, neuropsychological and intellectual abilities, and neuroanatomical markers in older adults using the Strange Stories task (Happé, 1994). The authors reported that executive function, processing speed, and two facets of intellectual ability (WAIS-III verbal [VIQ] and performance [PIQ] indexes)

mediated age-related declines in ToM. Reductions in mental state reasoning were also associated with decreased white matter integrity, indicating the potential for ToM abilities to be (a) sensitive to widespread neuropsychological change, (b) susceptible to structural brain changes and (c) sensitive to vascular integrity (Charlton et al., 2009).

An impressive body of literature on brain activity in ToM supports this neuropsychological evidence, however the precise nature of brain networks in ToM is not well understood (see Carrington & Bailey, 2009; Gallagher & Frith, 2003 for a review). Evidence from brain-injured populations indicates that ToM and executive abilities may rely upon a common neuroanatomical system (see Bull et al., 2008 for an overview). Several anatomical regions have been implicated in ToM, most prominently the medial pre-frontal cortex, extending from the posterior end of the superior temporal sulcus and encompassing the tempoparietal junction, temporal pole, and paracingulate cortex (Frith & Frith, 2006; Saxe, Moran, Scholz, & Gabrieli, 2006; Young et al., 2010). Data suggest that these areas most likely overlap with and recruit from areas linked to other traditional cognitive resources, thus providing biological evidence for the role of supporting cognitive abilities in mental state reasoning (Gallagher & Frith, 2003; Saxe et al., 2006).

It is clear that neuropsychological factors make an important contribution to variability in older adults' mental state reasoning. What remains to be seen, however, is the extent to which age differences in ToM may persist after controlling for neurocognitive ability, and what other factors, if any, may further

explain age-related changes. Several recent studies, including one from our lab, have found age differences in ToM to remain irrespective of performance on traditional neuropsychological measures (Bernstein et al., in press; Keightley, Winocur, Burianova, Hongwanishkul, & Grady, 2006). For example, Bernstein et al. (in press) assessed adults' ToM using a first-order false belief framework that required participants to watch a short scenario, after which they would answer a critical question about the actions of a character in the story. ToM questions required participants to infer that the character held a false belief, whereas control guestions did not. Their task measured false-belief performance along a continuum, indexing not only whether individuals are capable of disregarding their own beliefs to reason from a different perspective, but to what extent this bias exists. Results demonstrated that middle-aged and older adults displayed worse performance than younger adults on questions involving mental state content. Further, these differences remained after accounting for language, executive function, speed, and memory (Bernstein et al., in press). Bernstein et al. and others' findings highlight the existence of unanswered questions in the current literature on aging and ToM. Everyday social behaviour demonstrates that individual variations in ToM exist—specifically, some people may show insight into mental states, whereas others may be less aware. Through our review of literature in this area, we have shown that variation in mental state reasoning can be partially attributed to individual differences in neuropsychological ability. What about other factors known to impact cognitive performance? Conclusions from the ToM and aging literature underscore that

neuropsychological factors may be necessary, but not sufficient, to explain age changes in mental state reasoning.

In sum, neuropsychological studies provide evidence for involvement of executive function, speed, and vocabulary in older adults' mental state reasoning (e.g., Charlton et al., 2009; German & Hehman, 2006; McKinnon & Moscovitch, 2007; Newton & de Villiers, 2007). In the current study, we included measures of inhibition, working memory, mental set-shifting, processing speed, and vocabulary as part of a comprehensive neuropsychological battery designed to assess traditional neurocognitive involvement in mental state reasoning. We also included a task of verbal memory, as memory demands are intrinsic to our dependent measure of ToM (Strange Stories task; Happé, 1994). Our primary aim was to explore potential non-cognitive modifiers of ToM; therefore, we did not focus our objectives on capturing associations between ToM and individual neurocognitive measures. Rather, we sought to examine the potential modifying influence of blood pressure on general associations between ToM and neurocognition, using composite neuropsychological indicators representing performance on domains closely associated with mental state reasoning.

### Potential Modifiers of Theory of Mind in Aging: Blood Pressure

Recent research has investigated the utility of blood pressure as a predictor of age-related changes in traditional neuropsychological domains. In general, two main indicators of blood pressure are used in neuropsychological studies: diagnosed hypertension (i.e., hypertensive versus non-hypertensive) and continuous measurements (typically taken at the time of assessment). The

prevalence of hypertension increases dramatically in older age, with recent estimates as high as 50 - 70% for North American individuals over the age of 65 (Chobanian et al., 2003; McDonald, Hertz, Unger, & Lustik, 2009). Clinical criteria used in the diagnosis of hypertension include having systolic (SBP) and diastolic blood pressure (DBP) levels of  $\geq$  140 mmHg and  $\geq$  90 mmHg, respectively (as defined by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [JNC7]; Chobian et al., 2003).

Findings regarding the impact of blood pressure on cognition generally suggest an inverse relationship (i.e., high blood pressure is associated with reduced neuropsychological performance); however the specific domains affected are not unequivocally defined (see Qiu, Winblad, & Fratiglioni, 2005 for a review). In general, chronic elevations in systolic blood pressure have been associated with reductions in attention, executive function, verbal learning and memory, and less consistently, slowed speed of processing (Dahle, Jacobs, & Raz, 2009; Elias, D'Agostino, Elias, & Wolf, 1995; Saxby et al., 2003; Raz, Rodrigue, & Acker, 2003; Waldstein et al., 2005). For example, in a crosssectional comparison, Saxby and colleagues (2003) found that older adults with diagnosed hypertension exhibited lowered performance in executive function, speed, episodic memory and working memory. A more recent study examining multiple vascular risk factors found that SBP independently accounted for 11% of global cognitive variance in adults aged 61 – 65 years, although explained variance differed by age (Knecht, Wersching, Lohmann, Berger, & Ringelstein, 2009). Additionally, longitudinal research suggests that individuals who maintain

chronically elevated SBP throughout adulthood are at increased risk of cognitive decrements in areas of memory, verbal learning, and speed in older age (Swan, Carmelli, & Larue, 1998). In general, extant research supports an inverse relationship between blood pressure and cognition; but associations are complex and follow a non-linear pattern across the lifespan (Qiu et al., 2005). Findings suggest that mid-life hypertension is associated with an increased risk of later dementia; however, this association may be weaker in old age (Kennelly, Lawlor, & Kenny, 2009). Several cross-sectional studies have also reported adverse effects of low blood pressure on tasks of global cognitive performance (see Qiu et al., 2005; Qiu, Winblad, & Fratiglioni, 2009).

The degree to which blood pressure affects neuropsychological functioning is evidenced by its role in the pathogenesis of dementing illness. For instance, elevated SBP and low DBP are both recognized as independent risk factors for Alzheimer's disease (Qiu, Winblad, Fastbom, & Fratiglioni, 2003). Possible mechanisms for deleterious blood pressure effects include: (a) atherosclerotic processes resulting in an accumulation of white matter lesions, and (b) hemodynamic processes (e.g., decreased cerebral perfusion), which may lead to an acceleration of existent neurodegenerative processes (Kennelly et al., 2009; Qiu et al., 2005). A full discussion of these areas is beyond the scope of this manuscript; however, interested readers are referred to Skoog (1997) and Qiu et al. (2005) for a more thorough review.

Much of the knowledge on cognitive effects of blood pressure has come from studies focussing on diagnosed hypertension as their main measure of

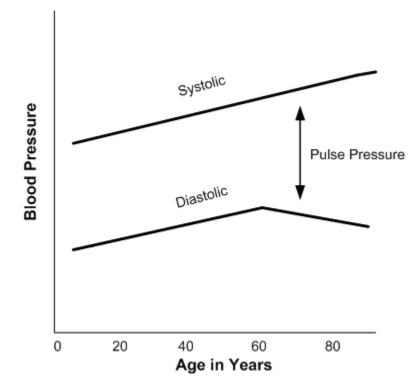
blood pressure (e.g., Brady, Spiro, & Gaziano, 2005; Saxby et al., 2003). Despite the validity of illness diagnoses as a marker, the study of individual differences in blood pressure may be improved by analyzing readings taken at the time of assessment. A strict examination of dichotomized hypertensive status may be limited in detecting potentially important differences in individuals with very low blood pressure, or those with a pre-hypertensive status (Chobanian et al., 2003). With regard to using self-reported diagnoses in studies of one recent study found that 32% of individuals aged 60 to 75 were unaware that their blood pressure levels met criteria for hypertension (Lee, 2005). These findings underscore the importance of incorporating continuous blood pressure measurements in studies of cognitive aging, in addition to examining hypertensive status (Waldstein et al., 2005). We examined both blood pressure levels measured at the time of assessment and diagnosed hypertension as potential modifiers of links between ToM and neuropsychological ability.

Using continuous blood pressure measurements (i.e., SBP and DBP readings), different predictors may display unique associations with cognition (Waldstein et al., 2008). This is particularly relevant to adults over the age of 60, where SBP and DBP may follow divergent trajectories. Specifically, elevations in SBP in late life are accompanied by falling or stabilized DBP levels driven by age-related stiffening of large central arteries (Franklin et al., 1997). Most literature examining late life relationships with cognition has demonstrated adverse effects of elevated SBP upon multiple areas of cognition (e.g., Obisesan et al., 2008). In individuals over the age of 80, other studies have observed that

low DBP is associated with an increased risk of dementia (Qiu et al., 2009). In light of the extant literature suggesting differential trajectories and cognitive effects displayed by SBP and DBP in individuals aged 60 and over (see Qiu et al., 2005 for a review), we examined SBP and DBP in separate models as predictors of ToM in the current study.

A third indicator that captures the late-life influence of blood pressure is pulse pressure (PP). Defined as the difference between SBP and DBP (i.e., SBP-DBP), PP is considered a surrogate marker of arterial stiffness (de Simone et al., 2005). More specifically, a widened PP in older age may indicate a loss of elasticity in large vessels that is needed to accommodate and compensate for ejected blood (de Simone et al., 2005). To illustrate the important relationships between SBP, DBP, and PP, a graphical depiction of the expected trajectories of these markers with increasing age is presented in Figure 1. Note that with age, PP follows linearly with SBP, thus creating a widened range between SBP and DBP levels (i.e., increased PP).

Figure 1. Hypothetical Effects of Aging on Systolic Blood Pressure, Diastolic Blood Pressure, and Pulse Pressure



*Note*. Adapted from Malhorta, A., & Townsend, R. R. (2000, October). Clinical significance of systolic and pulse pressure. *Emergency Medicine*, 1–7. Lines depicted do not represent actual data from any source.

Previous epidemiological studies indicate that the prognostic significance of blood pressure predictors is age-dependent; specifically, among older individuals, PP (followed by SBP) best predicts cardiovascular risk (Khattar, Swales, Dore, Senior, & Lahiri, 2004). Neuropsychological studies also suggest that PP represents a unique contribution to blood pressure-cognition relations beyond that accounted for by systolic and diastolic readings (Qui et al., 2003). Recent studies demonstrate that increasing levels of PP, alongside high SBP and diagnosed hypertension were associated with declines in global cognitive status (Obisesan et al., 2008). Other authors have found that widened PP is associated with prospective declines in verbal learning, nonverbal memory, and working memory (Waldstein et al., 2008). Although cut-points for what is considered a clinically relevant PP are not well-defined in the context of cognition, epidemiological studies generally suggest that a PP of  $\geq$  60 mmHg should be considered a cardiovascular risk (Safar, Lajemi, Rudnichi, Asmar, & Benetos, 2004).

In light of the expanding literature demonstrating important links between blood pressure and late life cognitive change, we examined SBP, DBP and PP taken at the time of assessment as potential modifiers of ToM relationships. We also assessed the predictive utility of diagnosed hypertension, which is an important indicator of vascular risk alongside continuous blood pressure measurements (Waldstein et al., 2005). We chose to examine blood pressure in the context of ToM for several reasons. Extant research demonstrates strong associations between elevated blood pressure and declines in cognitive areas hypothesized to support ToM (e.g., executive function, speed; Dahle et al., 2009; Saxby et al., 2003; Raz et al., 2003; Waldstein et al., 2005). High blood pressure is linked to structural damage in frontal brain regions (Raz, Rodrigue, Acker, & Kennedy, 2007); presumably, these areas may have an important role in mental state reasoning. We were interested in whether blood pressure may be associated with reductions in mental state reasoning, either as an independent predictor, or through interactive effects with neuropsychological ability. Health outcomes such as blood pressure may predict cognitive change through several pathways: (a) independent risk factors, (b) moderators, and (c) mediators (Baron

& Kenny, 1986; Kraemer, Stice, Kazdin, Offord, & Kupfer, 2001; see also McFall, Geall, Fischer, Dolcos, & Dixon et al., 2010; Thornton, Deria, Gelb, Shapiro, & Hill, 2007; Wahlin, et al., 2006). The current study makes a novel contribution to the ToM literature in our consideration of the role of blood pressure as a potential moderator and/or mediator of associations between ToM and neuropsychological performance in older adults.

### **Blood Pressure as a Moderator and/or Mediator**

Regression-based mediator and moderator analyses (Baron & Kenny, 1986) have made a significant contribution to the field of cognitive aging, and have put forward valuable evidence regarding the nature of relationships among older age, cognition and health status (e.g., McFall et al., 2010; Thornton et al., 2007; Wahlin et al., 2006). Moderator variables (e.g., blood pressure) serve to specify the conditions under which an outcome is produced by affecting the direction and/or strength of a relationship (e.g., ToM and traditional neuropsychological function). In contrast, mediator variables (e.g., blood pressure) provide a direct mechanism through which an independent variable (e.g., neuropsychological function) influences the outcome (e.g., ToM) (Baron & Kenny, 1986). Recent studies from our lab have used these analyses to explore mediating and moderating relationships between age, everyday problem solving, neuropsychological ability and health status (Thornton et al., 2007). In these investigations, neuropsychological variables (memory/executive function) mediated the links between chronic illness (diagnosed chronic kidney disease) and everyday problem solving, and between age and everyday problem solving.

In other words, health differences in everyday problem solving were directly accounted for by neuropsychological performance, and age differences in problem solving were partially accounted for by neuropsychological performance. Other published research indicates that vascular modifiers, including illness diagnoses (e.g., hypertension) and blood pressure, play both moderating and mediating roles in understanding late-life cognitive performance and should be explored (McFall et al., 2010; Raz et al., 2007; Wahlin et al., 2006). Importantly, recent work has established that a continuous independent variable can exert *both* moderating and mediating effects (cf. Wahlin et al., 2006).

Toward this end, we explored whether blood pressure indicators common to the cognitive aging literature may modify observed associations between ToM and neuropsychological performance. Specifically, we examined whether blood pressure (a) accounted for unique variance in ToM performance, and (b) moderated or mediated previously established links between ToM and neurocognitive performance in older adults.

### **OBJECTIVES AND HYPOTHESES**

Given strong theoretical support for associations between ToM and traditional neuropsychological abilities, our main objective was to examine whether these associations were modified by blood pressure in a sample of community-dwelling older adults (65+). After establishing which blood pressure indicators served as independent predictors of older adults' ToM, we conducted regression-based mediator and moderator analyses to determine whether potential blood pressure modifiers influenced the direction and/or strength of established relationships between ToM and neuropsychological ability (Baron & Kenny, 1986).

### **Research Questions and Hypotheses**

Our first research questions addressed the utility of blood pressure as an independent predictor of older adults' mental state reasoning: (1) Do hypertensive status and blood pressure at the time of assessment account for a significant proportion of variance in ToM beyond age and neuropsychological performance? Our second and third research questions pertained to potential moderating and mediating influences of blood pressure on established relationships between ToM and neurocognitive ability: (2) Do interactions between blood pressure and neuropsychological performance account for unique variance in ToM performance beyond the effects of age, neuropsychological

ability, and blood pressure alone (i.e., is there a moderating relationship)? (3) Does blood pressure mediate associations between traditional neuropsychological performance and ToM? In other words, does blood pressure fully or partially account for relationships between ToM and neuropsychological performance? Hypotheses corresponding to each research question are discussed in turn:

- Regarding the role of blood pressure as an independent predictor of ToM, we expected that diagnosed hypertension, and elevated SBP, DBP, and PP would uniquely predict reductions in mental state reasoning in older adults, beyond age and neuropsychological performance.
- 2. Concerning blood pressure as a moderator of ToM, we hypothesized that interactions between neuropsychological performance and (a) diagnosed hypertension, and (b) elevated blood pressure may account for a significant proportion of variance in ToM beyond the effects of age, neuropsychological ability, or blood pressure alone. Specifically, we expected that those individuals with elevated blood pressure would show a stronger relationship between neuropsychological ability and ToM.
- 3. We considered whether blood pressure would mediate the relationship between traditional neuropsychological performance and ToM. We expected that increased SBP, DBP, and PP and a diagnosis of hypertension would partially account for this relationship.

### METHOD

### **Participants**

A total of N = 66 cognitively intact, community-dwelling older adults aged 65 and over (*range* = 65 – 92 years) participated in this study. Participants were recruited through advertisements in community newspapers and fliers placed at local community centres and parks throughout the greater Vancouver area, and through seminars on aging and cognition hosted by Dr. Wendy Thornton. All participants were tested individually at the Cognitive Aging Laboratory at Simon Fraser University Burnaby campus between June 2010 and September 2010.

Participants were considered eligible for this study if they met the following inclusion criteria: (a) English fluency (as determined by an acculturation measure developed within our lab, see Appendix A; Thornton et al., 2007) and (b) completion of a minimum grade six education to ensure a reading level adequate for task completion. Participants were ineligible if they had a history of dementia, major psychiatric illness (e.g., schizophrenia, bipolar disorder), comorbid major illness (e.g., metastatic cancer), neurological condition (e.g., Parkinson's disease, Huntington's disease, multiple sclerosis, epilepsy), major organ failure, or self-reported colour-blindness. Further, we excluded all individuals reporting a significant past head injury (i.e., loss of consciousness > 15 minutes). Based on the visual nature of several of our tasks, we screened participants' visual acuity using a Snellen vision chart, with a set lower limit of 20/50 (corrected or

uncorrected). Unless otherwise indicated, screening of inclusion and exclusion criteria was based upon participants' self-report. No participant received a score of less than 24 on the Mini Mental Status Examination (MMSE), which is a cut-off recommended by current assessment standards to control for cognitive impairment in the absence of dementia (Folstein, Folstein, & McHugh, 1975; Lezak, 2004).

#### **Measures and Procedure**

Participants completed a 2.5-hour battery that included blood pressure measurements, health/demographic questionnaires and measures assessing ToM, neuropsychological performance and other reasoning abilities. Testing was conducted individually as part of a larger battery examining social reasoning. In general, the screening of inclusion and exclusion criteria was conducted through brief phone interviews prior to testing. Informed consent and health/demographic questionnaires were mailed out to participants to be signed and completed prior to their assessment date. Where possible, participants were asked to bring a list of current medications (or the actual bottles) to their appointment; this information was used to confirm self-reported illness diagnoses and to screen for any medication indicating a major illness not reported on our questionnaires. According to standardized protocol, all measures were administered by graduate students and trained research assistants. All participants were compensated \$20 for time and travel expenses. The study protocol was approved by the Simon Fraser University Research Ethics Board prior to data collection.

**Demographics and health.** Demographic information collected included age, gender, ethnicity, education, employment status and alcohol and/or tobacco use. Participants completed a self-report *Health Questionnaire* assessing general medical history and health concerns. This measure has been developed and used previously in our lab (e.g., Thornton et al., 2007), and was used in the current study to screen exclusionary criteria and identify diagnoses of hypertension. To confirm diagnoses, participants' objective medications were checked for the presence of drugs relevant to hypertension (if applicable; some individuals were not taking any medication or whose treatment included only lifestyle modification). This two-step diagnostic procedure has been used previously in our lab and meets current accepted standards for research diagnostic criteria (Campbell, Joffres, & McKay, 2005; Thornton et al., 2007).

**Blood pressure.** Four separate blood pressure readings were taken at the beginning of the assessment session for each participant. Measurements were taken using a standard upper arm monitor, on the right arm unless medically contraindicated (Model A&D UA-774; medium and large cuffs). After an initial reading to ensure comfort with protocol, participants sat quietly with the cuff in place and rested for five minutes. Following this, we took three individual readings, separated by one-minute rest intervals. To minimize the effect of observation, examiners were instructed to face away from participants during readings. Outcome blood pressure measurements included the average of each of the last three systolic (SBP; mmHg) and the last three diastolic readings (DBP; mmHg), and average pulse pressure (PP [SBP-DBP]; mmHg).

**Verbal memory.** The *California Verbal Learning Test-II* (CVLT-II; Delis, Kramer, Kaplan, & Ober, 2000) was used to index participant's verbal memory. This task required that a word list (16 nouns; List A) be read to participants, followed by a period of free recall, for each of five trials (A1-A5). After a 20minute delay period, participants were asked to remember these words again using free recall. Raw scores from the 20-minute Long Delay Free Recall trial were used to index verbal memory performance. The CVLT-II demonstrates high reliability within older adult age groups, based on split-half reliability estimates (ages 60-89; r = .91-.92; Delis et al., 2000; see also Woods, Delis, Scott, Kramer, & Holdnack, 2006).

**Executive function.** First, the *Color-Word Interference* subtest from the Delis-Kaplan Executive Function System was used to index inhibition (D-KEFS; Delis, Kaplan, & Kramer, 2001). Participants viewed a page of colour words printed in discordant-coloured ink, wherein they were required to inhibit their dominant response (reading the word) in order to perform a less-dominant task (naming the ink colour). Participants' latency to complete the task (seconds) indexed inhibitory control. The Color-Word test has demonstrated adequate reliability in older adults aged 60-89 (test-retest, r = .75; Delis et al., 2001). Second, we used the number-letter sequencing condition of the D-KEFS *Trail-Making* test to measure set-shifting and mental flexibility. In this task, participants were presented with a page containing scattered numbers and letters, and were instructed to draw a line alternating consecutively between numbers and letters (i.e., 1-A-2-B-3-C). Raw latencies (seconds) to complete this task represented

set shifting. Construct validity for the Trail-Making test has been established in community-dwelling older adult populations (Sanchez-Cubillo et al., 2009).

**Working Memory.** The Wechsler Adult Intelligence Scale-III (WAIS-III; Wechsler, 1997) *Letter-number Sequencing* (LNS) subtest measured working memory. In this task, an examiner read aloud sequences containing both numbers and letters and participants were asked to recall first the numbers in ascending order, followed by the letters in alphabetical order. The total number of sequences correctly recalled served as our measure of working memory. The LNS subtest as been normed on Canadian populations, and demonstrates high split-half reliability in adults aged 65-84 (test-retest;  $r_{xx}$  = .83; Wechsler, 1997).

**Processing speed.** The WAIS-III *Digit Symbol Coding* subtest (Coding; Wechsler, 1997) was used to index speed of processing. Participants were provided with a coding key of nine numbers, each matched to a specific symbol. Within a 120-second period, participants used this key to fill in rows of empty boxes with the symbol that correctly corresponded to the number indicated above each box. The total number of symbols correctly transcribed within the time limit indexed processing speed. The Coding subtest has been widely used in older adults and demonstrates high reliability (test-retest; r = .84; Wechsler, 1997).

**Receptive vocabulary.** The *Peabody Picture Vocabulary Test-III* (PPVT-III; Dunn & Dunn, 1997) measured general language ability. Participants viewed a stimulus book with pages containing four pictures. An examiner orally produced a stimulus word and participants were asked to indicate (verbally or by pointing) the picture which best represented the meaning of the target word. This task is

untimed and was administered in two separate blocks. Raw scores for the number of correctly identified stimulus words indexed receptive vocabulary. The PPVT-III has demonstrated high reliability in older adults aged 61-90 years (splithalf; r = .96; Dunn & Dunn, 1997).

Theory of mind. The Strange Stories task (Happé, 1994: hereafter referred to as the 'Stories task') is a measure of ToM that specifically assesses the construct of mental state reasoning. Participants were presented with eight short stories (vignettes), containing two types of content: mental state and non-mental state (control). The four mental state vignettes assessed both first- and second-order ToM inferences, requiring participants to infer a character's intentions or feelings. In contrast, the four control vignettes did not involve mental states, but required participants to make some sort of global inference beyond what was explicitly stated in the vignette. Each vignette was paired with one critical question, which usually took the form, "Why did X say/do that?" The subset of vignettes (Happé, 1994) used in the current study were selected based on both their relevance to older adults, and the presence of only one unambiguous correct response for each vignette. Vignettes used in this study can be found in Appendix B.

Vignettes were presented in two blocks on white 8 ½ X 11 inch sheets, organized by story type. Both mental state and control vignettes appeared alongside a small black and white drawing depicting significant characters from the corresponding story. The order of presentation (mental state versus control) was counterbalanced across participants.

Before beginning experimental protocol, a practice story (mental state content) was given to participants to ensure adequate understanding of task instructions. Participants' answers to this practice story were corrected and explained if less than a complete response was given. Vignettes were presented face up on the table in front of participants. They were instructed to carefully read each story to themselves, after which they would be asked to answer a question about the story that required them to make some sort of inference. Further, participants were told to make sure they understood each story before indicating that they were finished reading, and were encouraged to take as much time as necessary to do so. Upon finishing reading each story, participants flipped the page containing the vignette. At this time, an examiner asked the critical question aloud (i.e., Why did X say/do that?). Each critical question was also presented to participants in text format on the page immediately following each story. As per Happé (1994), if a participant's response to any critical question was vague or unclear, examiners provided one standardized query to probe whether participants could further explain their answer. Query statements included "Explain what you mean" and "Tell me more about that." The examiner recorded all participants' responses verbatim. For each story, participants' latency to read the item was recorded.

Responses to each question were rated according to Happé et al.'s (1998) 3-point criteria by graduate students and trained research assistants familiar with test protocol (i.e., 2 = complete, accurate answer, 1 = partial or implied answer, 0 = incorrect or irrelevant answer). For example, in the story

where Mrs. Smith tries to convince Jill to buy a male kitten by saying she will drown them all (see Appendix B for actual vignette), an accurate, complete answer (2-point) would require some variant of explanation that made reference to coercion or stated that Mrs. Smith is playing on Jill's sympathy for the cats. In contrast, an incomplete answer (0-point) would comprise irrelevant statements (e.g., "there were no male kittens") or a lack of realization that the Mrs. Smith did not actually intend to drown the kittens (e.g., "that is horrible that she would drown all those kittens"). One-point answers reflected a partial or implied understanding of the required inference, such as "so Jill would buy the kitten," with no further elaboration.

Where both a correct and incorrect answer were given, participants were given full credit for the better answer provided. Similarly, if a participant's answer contained both mental state and physical state inferences, they were scored for the mental state. Physical state inferences referred to physical outcomes, whereas mental state inferences included all those that referred to thoughts, feelings, desires, intentions, and goals.

Despite the existence of one clear, unambiguous response for each question, judgments of accuracy and completeness of responses are prone to some degree of subjectivity. Our scoring protocol required that each vignette was examined twice. A first rater judged responses and assigned a score for each vignette (0, 1, 2) as described above. A second rater checked these scores for accuracy in rating and consistency with scoring protocol. We conducted reliability estimates for three independent raters (A. Fischer, A. Coolin & J. Vishloff).

Excellent agreement in item scores was found between raters for a subset of 25 task protocol (intraclass correlation coefficient, ICC (3,3) = .938, 95% confidence limits from .921 to .951; McGraw & Wong, 1996; Shrout & Fleiss, 1979).

After all scoring and checking was complete, participants' scores across the four mental state vignettes were summed to create our dependent measure representing mental state reasoning ability. This allowed for a range of possible scores from zero to eight. A reduced ability to provide accurate responses with reference to mental state content were reflective of poor mental state reasoning, which we are conceptualizing as a reduction in ToM capacity.

## STATISTICAL ANALYSIS

#### **Statistical Power**

In order to ensure adequate statistical power to test the hypotheses of interest and control for type I and II error, all analyses were conducted at alpha level of p < .05. Based on a sample size of N = 66, our preliminary multiple linear regression analyses with one predictor variable on Step 1 (age), two predictors on Step 2 (neuropsychological composites), and one predictor variable on Step 3 (depending on the analysis: hypertensive status, SBP, DBP, or PP), were able to detect a large effect size ( $f^2 = 0.35$ ) in  $R^2$ . Similarly, our final regression model for the moderation analysis also lacked sufficient power to detect a medium effect size ( $f^2 = 0.15$ ), but was sufficient to determine a large effect size ( $f^2 = 0.15$ ) 0.35). Table 1 depicts the power analyses conducted for our final multiple linear regression models, and contrasts achieved power by medium and large effect size parameters (see Cohen, 1992 for details). All power analyses were conducted using G\*Power version 3.1.2 (Faul, Erdfelder, Buchner, & Lang, 2009; Faul, Erdfelder, Lang, & Buchner, 2007). Overall, limited power might have increased our chances of obtaining type II errors, thereby reducing our ability to detect significant effects. Power issues affecting interpretability are further discussed in a later section of this manuscript.

Mode	els Testing Ind	lependent Predic	ctors		
$R^2$	f²	α	n	# of predictors	Power $(1 - \beta \text{ err prob})$
-	.15	.05	66	4	.672
	.35				.973
Final	Model Testing	g Interaction Effe	ects		
$R^2$	<b>f</b> <sup>2</sup>	α	n	# of predictors	Power $(1 - \beta \text{ err prob})$
-	.15	.05	66	3	.727
	.35				.984

 Table 1. Contrasted Power for Final Multiple Linear Regression Models

#### **Data Preparation and Assumption Checking**

First, descriptive statistics were examined for each independent variable to determine the central tendency of the data (e.g., mean, median), variability (range, standard deviation) and shape of the distribution (skew, kurtosis). All cells identified as extreme outliers (i.e., more than three standard deviations from the remaining values) were re-coded to reflect a less-extreme value by adding one unit to the next-highest, non-outlying score (see Tabachnick & Fidell, 2007). Thus, outliers were adjusted, rather than removed, to make them more contiguous with the data while maintaining their distal-most ranking. Across all relevant demographic, neuropsychological and health variables, six data points (out of a possible 1122, or 0.5% of the data) were adjusted according to the above protocol. To account for missing data while retaining power, we used pairwise deletion to exclude cases that were missing data only for that specific analysis.

Next, preliminary analyses were conducted to ensure our models contained no violation of the assumptions of parametric analyses (see Tabachnick & Fidell, 2007). No individuals emerged as multivariate outliers, as determined by extreme values of Mahalanobis distance (using a conservative alpha set at p < .001). Further, no influential points were identified (i.e., Cook's distance < 1.00 for all cases). Normality and linearity between independent variables were assessed using (a) Q-Q scatterplots and histograms for each distribution, and (b) graphs of residuals plotting standardized residual values against predicted residual values. Models were examined for homoscedasticity

using  $F_{max}$  estimates (i.e., ratio of the largest cell variance compared to the smallest cell variance). Low Condition Indices (i.e., < 30) for all models indicated that our regression analyses were not adversely affected by multicollinearity between predictor variables. In sum, all parametric assumptions of multiple linear regression were met for all models.

#### Intercorrelations Among ToM, Neurocognitive Ability and Blood Pressure

A paired-samples t-test was conducted to determine whether older adults displayed the expected pattern of ToM performance. We expected to see a greater proportion of low scores (indicating fewer accurate responses with regard to mental state content) on ToM trials of the Stories task, compared to higher scores on control trials (indicating better accuracy of responses with regard to non-mental state story content).

For the correlational analyses, continuous variables examined included age, neuropsychological measures, and blood pressure (SBP, DBP, PP). Categorical variables examined included gender and hypertensive status (scored yes/no). Continuous variables were assessed using Pearson product moment correlations. For cases where correlations between one continuous variable and one dichotomous variable, point biserial coefficients were examined. First, zeroorder correlations were examined to determine which neuropsychological measures in our sample were significantly correlated with ToM. At this time, those measures that displayed significant correlations with ToM and possessed strong theoretical rationale supporting these associations were selected for

determination of composite measures of neuropsychological ability using Principle Components Analysis. The smallest number of components from the rotated matrix that best fit the data were used in subsequent analyses. We selected this method to reduce our neurocognitive data in a meaningful way, in accordance with other studies of aging and cognition (Bernstein et al., in press; Wahlin et al., 2006). Correlations between ToM and each blood pressure variable (hypertensive status, SBP, DBP, and PP) were also assessed.

Next, correlations were examined between all independent variables, demographic variables, hypertensive status and blood pressure. Correlations for demographic variables demonstrating established relationships with cognition were inspected prior to the main regression analyses (i.e., age, gender, education; Heaton, Ryan, & Grant, 2009; Lichtenberg, Ross, Millis, & Manning, 1995; Wahlin et al., 2006). Only those health and demographic variables displaying significant correlations with ToM (set at  $R \ge .3$ ) were included as predictors in the main analyses. To address our primary research questions, three sets of analyses were conducted: (1) preliminary regression analyses, (2) moderation analyses, and (3) mediation analyses. Each is outlined below.

#### **Preliminary Regression Analyses**

A series of hierarchical multiple linear regressions were conducted to determine whether the individual blood pressure predictors accounted for unique variance in ToM beyond the effects of age, demographics and neuropsychological performance (research question one). To determine the proportion of variance accounted for by demographic influences, age and other

demographic predictors were entered onto Step 1. Next, the orthogonally-derived components from our Principle Components Analysis representing neuropsychological performance were entered onto Step 2 to determine the amount of variance associated with each predictor while controlling for one another. The candidate blood pressure modifiers [SBP, DBP, PP] and hypertensive status were entered individually onto Step 3. To control for potential multicollinearity and method bias between predictors, separate models were assessed to determine whether each health modifier independently predicted ToM. For all regression analyses, F-tests and their corresponding  $\Delta R^2$  values were used to determine whether each step added predictive utility to the model beyond earlier steps. Standardized regression coefficients were examined to determine the strength and direction of any significant predictors of ToM. All continuous predictors were centred to further control for multicollinearity between the sets of independent variables (Cohen, Cohen, West, & Aiken, 2003).

#### Moderation Analyses

To address our second research question, moderation analyses were conducted to determine whether health modifiers displayed a significant interaction with neuropsychological performance on ToM (Baron & Kenny, 1986). For each candidate blood pressure moderator, separate models were constructed using each neuropsychological composite (Step 1: neuropsychological composite, blood pressure [SBP, DBP, PP, hypertensive status]; Step 2: product term [neuropsychological composite\*blood pressure]). To the extent that each interaction term accounted for significant variance beyond

neuropsychological performance and blood pressure, it was retained for inclusion into an overall model examining moderation effects. A predictor was considered to display a significant interaction effect if the  $\Delta R^2$  between Steps 3 and 4 was significant.

#### **Mediation Analyses**

For any significant independent predictors of ToM, we considered their further inclusion into analyses to investigate whether health modifiers acted as mediators between ToM and neuropsychological performance (Baron & Kenny, 1986). As is standard, models were first examined to determine whether the first two conditions of meditation were met (Baron & Kenny, 1986). The first step examined whether the changes in the independent variable (i.e., neuropsychological performance) significantly accounted for changes in the proposed mediator (i.e., blood pressure; Path A). The second step was to establish whether changes in the proposed mediator variable (i.e., blood pressure) accounted for significant changes in levels of the outcome variable (i.e., ToM; Path B). If the first two criteria were met, we examined the third condition, in that when Paths A and B are controlled, a previously significant relationship between the independent variable (i.e., neuropsychological performance) and the dependent variable (i.e., ToM) is significantly reduced in strength (Path C). Sobel's (1982) test was used to determine whether the indirect effect of neuropsychological performance on ToM via the mediator was significantly different from zero, and to quantify the strength of relationship associated with the mediator. All data entry, coding and analysis was conducted

at the SFU Cognitive Aging Laboratory using the Statistical Package for the Social Sciences version 16.0/17.0 software (SPSS, Inc., Chicago, Illinois, USA).

# RESULTS

#### **Demographic and Health Characteristics**

Participant characteristics, including demographics, health, and selfreported depressive symptoms are presented in Table 2. Overall level of education (M = 14.45, SD = 2.81) and global cognitive status (MMSE; M = 28.80, SD = 1.10) indicate that our sample was well-educated and demonstrated intact global cognitive performance. As can be seen in Table 2, 43.9% of our sample reported a physician's diagnosis of hypertension. Means and standard deviations for the demographic variables age, gender, ethnicity, depressive symptoms, and global cognitive status (MMSE), and the blood pressure variables are presented in Table 2.

Participant Characteristics	<i>n</i> = 66
Age	73.49 ± 5.78
Range	65.08 – 92.26
Female (n; %)	39; 59.1
Education	14.45 ± 2.81
Ethnicity (n; %)	
Caucasian	57; 86.4
Asian	3; 4.5
East Indian	5; 7.6
Aboriginal	1; 1.5
MMSE	28.80 ± 1.10
Hypertension (n; %)	29; 43.9
SBP (mmHg)	126.59 ± 18.35
Range	95 – 179
DBP (mmHg)	72.38 ± 8.94
Range	52 – 91
PP (mmHg)	54.20 ± 14.78
Range	31 – 96

Table 2. Demographic and Health Characteristics

*Note.* Unless otherwise indicated, means and standard deviations are presented as  $M \pm SD$ . Age and education are presented in years. MMSE = Mini Mental Status Examination; SBP = systolic blood pressure; DBP = diastolic blood pressure; PP = pulse pressure. Hypertension diagnosis includes all individuals who self-reported a physician's diagnosis of hypertension and were taking relevant antihypertensive medication.

#### **Theory of Mind Performance**

Paired-sample t-tests determined whether performance differed between ToM and control scores on the Stories task. A significant difference between ToM and control scores was observed, t (65) = -2.79, p < .01, such that participants produced more accurate and complete responses in response to non-mental state content (control: M = 6.27, SD = 1.46; *range* = 0-8) than mental state story content (ToM; M = 5.64, SD = 1.66).

#### Intercorrelations Among ToM, Neurocognitive Ability and Blood Pressure

Table 3 illustrates correlations between ToM and our neurocognitive variables of interest. As can be seen in Table 3, ToM was significantly associated with neuropsychological performance on five of our main measures. Specifically, less accurate inferences about mental state content were associated with lower memory (CVLT-II Delayed Recall; r = .35, p < .01). Further, lower vocabulary was also associated with worse less accurate mental state reasoning (PPVT; r = .25, p < .05). Slower speed of processing (WAIS-II Coding; r = .31, p < .05), lower mental flexibility (D-KEFS Trail-Making; r = -.38, p < .01) and poor inhibition (Color-Word Interference; r = .25, p < .05), were all associated with less accurate inferences about mental state content. See Table 3 for intercorrelations among the neurocognitive variables.

Principle components analysis with varimax rotation was conducted using six neuropsychological measures: CVLT-II Long Delay Free Recall, Digit Symbol Coding, Color-word Interference Inhibition subtests, Trail-Making Number-Letter Sequencing subtest, WAIS-III Letter-Number Sequencing, and PPVT-III raw score. The rotated matrix revealed the presence of two orthogonal components with eigenvalues exceeding 1.0, explaining 43% and 25% of the variance, respectively. The first component, which we labelled "Neuropsychological Ability (NPA)," included measures of processing speed, cognitive inhibition, mental set-shifting and verbal memory. We labelled the second component "Semantic Knowledge/Working Memory (SK/WM)," which included measures of receptive vocabulary and working memory.

Associations between ToM and our PCA-derived neuropsychological composites (i.e., NPA, SK/WM) were examined. As can be seen in Table 3, ToM displayed correlations with each composite such that lower NPA and SK/WM were both associated with less accurate inferences about mental state content (NPA, r = .37, p < .01; SK/WM, r = .27, p < .05). These scores were retained for use in subsequent analyses.

Variable	AGE	ТоМ	NPA	SK/WM	DR	CD	CW	TS	LN	RV
AGE										
ТоМ	27*									
NPA	48+	.37 <sup>∆</sup>								
SK/WM	.06	.37*	00							
DR	35 <sup>▲</sup>	.35 <sup>∆</sup>	.79+	17						
CD	31 <sup>∆</sup>	.31*	.82+	.10	.55 <sup>+</sup>					
CW	.42+	25*	76+	23#	38 <sup>∆</sup>	57+				
TS	.35 <sup>∆</sup>	38 <sup>∆</sup>	79+	34 <sup>Δ</sup>	48 <sup>+</sup>	57+	.61+			
LN	21 <sup>#</sup>	.32 <sup>∆</sup>	.29*	.78+	.16	.20#	38 <sup><b>Δ</b></sup>	50+		
RV	.20	.25*	05	.85+	07	.16	07	16	.38 <sup>Δ</sup>	

Table 3. Zero-order Correlations Among Theory of Mind and Neurocognitive Variables of Interest

*Note.* N = 66; \* p < .05,  $^{\Delta}p < .01$ , \* p < .001, # p < .10. ToM = Stories – Theory of Mind; NPA = Neuropsychological Ability composite; SK/WM = Semantic Knowledge/Working Memory; DR = delayed recall (CVLT-II long delay); CD = WAIS-III digit symbol coding; CW = D-KEFS Color-word Condition 3; TS = D-KEFS Trail Making test – sequencing; LN = WAIS-III Letter-Number Sequencing; RV = receptive vocabulary (PPVT raw score).

Table 4 presents correlations between ToM, demographic and health variables of interest. Increasing age was correlated with worse performance on the ToM task (r = -.27, p < .05), and on all individual and composite neuropsychological indicators (see Tables 3 & 4). Female gender displayed a trend in its association with better mental state reasoning, and was entered into our preliminary regression models because of its potential influence on cognitive performance (Table 4; Heaton et al., 2009). Higher education was also correlated with better mental state reasoning (r = .26, p < .05) and better mental flexibility, but did not display significant associations with any other neurocognitive variables of interest. Traditionally, education accounts for a large proportion of variance in neuropsychological function compared to other demographic variables (Heaton et al., 2009), and is significantly related to general intellectual functioning in fluid and perhaps especially crystallized domains (Kaufman, Kaufman, Liu, & Johnson, 2009). This is of particular relevance in a highly educated sample such as ours, where controlling for education before accounting for the influence of neuropsychological performance may prohibit detection of hypothesized effects of neurocognitive ability. Importantly, our neuropsychological composites contain measures that may capture elements of crystallized intelligence (e.g., PPVT). Toward this end, we opted a priori to exclude education as a predictor in our main regression models.

As can be seen in Table 4, the presence of hypertension was associated with lower accuracy in mental state reasoning, this correlation did not reach statistical significance (r = -.19, p = .119). With regard to blood pressure, higher

SBP (r = -.23, p = .063) and higher PP (r = -.23, p = .061) were negatively associated with accurate reasoning about mental states, but these correlations did not reach statistical significance. DBP was not significantly associated with ToM.

Variable	AGE	ED	GE	NPA	SK/WM	ТоМ	HTN	SBP	DBP	PP
AGE										
ED	04									
GE	22#	.10								
NPA	48+	.16	.48+							
SK/WM	.06	.17	13	00						
ТоМ	27*	.26*	.21#	.37^	.27*					
HTN	12	21 <sup>#</sup>	01	09	17	19				
SBP	03	16	07	.05	08	23 <sup>#</sup>	.22#			
DBP	18	06	06	.24 <sup>#</sup>	.10	09	.02	.60+		
PP	.07	17	05	09	16	23 <sup>#</sup>	.26*	.88+	.14	

Table 4. Zero-order Correlations Among Theory of Mind, Demographic, and Health Variables of Interest

*Note.* N = 66; \* p < .05,  $^{\Delta}p < .01$ , \* p < .001, # p < .10. ED = education; GE = gender; NPA = Neuropsychological Ability Composite;

SK/WM = Semantic Knowledge/Working Memory Composite; ToM = Stories – Theory of Mind; HTN = hypertension (i.e., current or history of hypertension vs. no hypertension); SBP = systolic blood pressure; DBP = diastolic blood pressure; PP = pulse pressure.

#### Research Question 1: Blood Pressure as an Independent Predictor

As expected, increasing age was associated with worse ToM performance  $(\beta = .078)$  and was retained in all regression models. Female gender did not predict ToM performance and was dropped from subsequent analyses. Higher NPA ( $\beta = .300$ ) and higher SK/WM ( $\beta = .276$ ) were associated with worse ToM ( $\Delta R^2 = .151, f^2 = .18$ ; 95% confidence limits from .00 to .29; Steiger & Fouladi, 1992). Thus, our models consisted of age in Step 1, NPA and SK/WM in Step 2, and the blood pressure predictor (SBP, DBP, PP or hypertensive status; tested in separate models) in Step 3. Results pertaining to independent predictors of ToM will be presented here, and are summarized in Table 5.

As can be seen in Table 5, SBP accounted for unique variance in ToM  $(\Delta R^2 = .052, f^2 = .05; 95\%$  confidence limits from .00 to .14) beyond age and neurocognitive performance. Specifically, a 10mmHg increase in SBP was associated with a .21-point decrease in ToM score (ToM: M = 5.64, SD = 1.66; range = 1.0 to 7.0). Altogether, 27.7% of variance in ToM was accounted for by the full model ( $R^2 = 0.277$ , F(4, 64) = 5.748, p < .001,  $f^2 = .38$ ).

DBP was assessed separately as a predictor of ToM, as its cognitive effects may be distinct from SBP, and these predictors have been suggested to contribute independent information (e.g., Glynn, L'Italien, Sesso, Jackson, & Buring, 2002; Qiu, et al., 2005). A 10mmHg increase in DBP was associated with a .43-point decrease in ToM ( $\Delta R^2 = .050$ ,  $f^2 = .05$ ; 95% confidence limits from

.00 to .14). The model accounted for 27.6% of the variance in ToM ( $R^2$  =0.276, F (4, 64) = 5.704, p < .001,  $f^2$  =.38). Refer to Table 5 for details.

Contrary to our predictions, the presence of hypertension did not account for significant variance in ToM (see Table 5)

Theory of Mind										
Variable	(s) Entered	В	S.E.	β	p	$\Delta R^2$	$\Delta F$	Model R <sup>2</sup>	f <sup>2</sup>	
Step 1	Age	078	.035	273	.028	.075	5.084*			
	NPA Composite	.501	.214	.300	.022					
Step 2	SK/WM Composite	.455	.186	.276	.017	.151	5.925**	.225+	.18	
Step 3										
Model 1	: Systolic Blood Pres									
	SBP	021	.010	229	.042	.052	4.302*	.277*	.38	
Model 2	: Diastolic Blood Pre	ssure								
	DBP	043	.021	223	.046	.050	4.167*	.276 <sup>+</sup>	.38	
Model 3	: Pulse Pressure									
	PP	018	.013	156	.175	.024	1.886	.249 <sup>▲</sup>	.33	
Model 4	Diagnosis of Hyper	tension								
	HTN	488	.385	147	.210	.020	1.603	.245 ^	.32	

# Table 5. Hierarchical Multiple Regressions Examining Main Effects of Age, NeuropsychologicalPerformance, and Blood Pressure on ToM

*Note.* n = 66; \* p < .05,  $^{\Delta}p < .01$ , \* p < .001, #p < .10.

#### **Research Question 2: Blood Pressure as a Moderator**

Because both SBP and DBP were significant independent predictors of ToM, we examined these variables as potential moderators of the association between ToM and neuropsychological ability. Further, given strong correlations between PP and SBP (see Table 4) and their close biological association (Schiffrin, 2004; Waldstein et al., 2008), we also considered PP in our moderator analyses.

We used procedures described previously to ensure our product terms were orthogonal with respect to the lower-order terms, thereby eliminating the potential for confounds introduced by multicollinearity of predictors (Burrill, 2006; Draper & Smith, 1981). In this case, each variable displays zero correlation with lower-order variables and represents a "pure" effect at its hierarchical level, thereby eliminating the need to fit multiple models. We followed a simple procedure to create our orthogonalized product terms (Burrill, 2006; Draper & Smith, 1981). For example, consider the 2-way interaction between SBP and NPA. A simple product term was formed using the original predictor variables (i.e., SBP by NPA). This product term was then regressed on the two original predictors according to Equation 1. The unstandardized residual for Equation 1 was saved and used in our moderation analyses to represent the orthogonal interaction between systolic blood pressure and Neuropsychological Ability (i.e., SBP\*NPA). This procedure was repeated for all 2-way interactions between SBP/DBP, NPA, and age, and between SBP/DBP, SK/WM, and age.

We then considered the possibility of 3-way interactions among age, neuropsychological performance and blood pressure. Orthogonal product terms for the 3-way interactions were constructed by regressing the simple product of the three original independent variables on the three 2-way interactions and the three original variables (see Equation 2). For instance, the simple product of age, SBP and NPA, was regressed on the three 2-way interactions (i.e. age\*SBP, age\*NPA, NPA\*SBP) and the three original independent variables (age, SBP, NPA) as described in Equation 2.

Age\*NPA\*SBP = 
$$a + b1$$
 age +  $b2$  NPA +  $b3$  SBP +  $b4$  age\*NPA +  $b5$   
age\*SBP +  $b6$  NPA\*SBP + residual (2)

For each candidate blood pressure moderator (SBP, DBP), two preliminary, separate models were constructed to test interactions with each neurocognitive composite (Step 1: age, neuropsychological composite [NPA or SK/WM], blood pressure predictor [SBP, DBP, PP]; Step 2: the three 2-way product terms; Step 3: one 3-way interaction). Using this approach, we started by examining all available candidate predictors of ToM (i.e., all original independent variables and all possible interactions between), then simplified by discarding predictors that did not contribute to variability in ToM. To the extent that each interaction term accounted for significant variance beyond neuropsychological

performance and blood pressure, it was included into a final model testing moderation effects.

Across all preliminary models, three of the interaction terms were significant: SBP\*SK/WM (p = .034), DBP\* SK/WM (p = .040), and PP\*NPA (p = .006), and were entered into a final, simplified model. Table 6 provides details regarding the three preliminary models containing significant interaction effects.

			Theo	ory of Mind				
Variable(s)	) Entered	В	S.E.	β	Р	$\Delta R^2$	$\Delta F$	Model R <sup>2</sup>
Preliminar	y Model 1: Systolic Bloo	od Pressur	е					
Step 1	Age	085	.033	297	.012			
	SBP	020	.010	218	.062			
	SK/WM	.443	.189	.269	.023	.203	$5.17^{\Delta}$	
Step 2	Age*SK/WM	.031	.047	.074	ns			
	Age*SBP	.001	.002	.040	ns			
	SBP*SK/WM	.027	.012	.247	.034	.070	1.85	
Step 3	Age*SK/WM*SBP	.004	.003	.138	ns	.019	.1.53	<b>291</b> <sup>∆</sup>
Preliminar	y Model 2: Diastolic Blo	od Pressu	re					
Step 1	Age	093	.034	325	.008			
	DBP	033	.022	179	.ns			
	SK/WM	.504	.192	.306	.011	.186	$4.65^{\Delta}$	
Step 2	Age*SK/WM	.037	.048	.090	ns			
	Age*DBP	.001	.004	.019	ns			
	DBP*SK/WM	.041	.020	.240	.040	.063	1.61	
Step 3	Age*SK/WM*DBP	005	.006	092	ns	.008	.648	.259*

# Table 6. Preliminary Models for Interaction Effects Among Age, Blood Pressure, and NeurocognitivePerformance

Variable(s) Entered		В	S.E.	β	Р	$\Delta R^2$	$\Delta F$	Model R <sup>2</sup>
Prelimin	nary Model 3: Pulse Pro	essure						
Step 1	Age	034	.038	118	Ns			
	PP	022	.013	197	ns			
	NPA	.496	.220	.297	.027	.188	<b>4</b> .70 <sup>∆</sup>	
Step 2	Age*NPA	.017	.020	.094	ns			
	Age*PP	.005	.003	.214	ns			
	PP*NPA	.046	.016	.358	.006	.108	2.96*	
Step 3	Age*NPA*PP	.005	.004	.136	ns	.018	1.53	.314 <sup>∆</sup>

*Note.* N = 66; \* p < .05,  $^{\Delta}p < .01$ ,  $^{+}p < .001$ ,  $^{\#}p < .10$ . All significant interaction terms from the preliminary models presented above were entered into a final reduced model.

To build our final model examining moderation effects, we ran the three significant, orthogonalized interaction terms in one model with age, to determine whether each interaction retained its significance while controlling for one another. We entered age as an independent predictor on Step 1, and SBP\*SK/WM, DBP\* SK/WM, and PP\*NPA entered simultaneously on Step 2. The backward elimination approach required two steps to arrive at the final model, which is the three variable model presented in Table 7. Variables were retained in the model at a significance level of *p* < .05. The final model revealed that age ( $\beta$  = -.356, *p* <.01), SBP\*SK/WM ( $\beta$  = .281, *p* <.05), and PP\*NPA ( $\beta$  = .259, *p* <.05) each uniquely accounted for variance in older adults' mental state reasoning. Together, these variables accounted for 21.5% of variance in ToM (*F* (3, 64) = 5.566, *p* < .01, *f*<sup>2</sup> =.27).

Theory of Mind											
Variable (s) Entered	В	S.E.	β	р	F	Model R <sup>2</sup>	f²				
Age	102	.033	356	.003							
SBP*SK/WM	.028	.012	.259	.027							
PP*NPA	.036	.015	.281	.018	5.57 <sup><b>^</b></sup>	.215	.27				

 Table 7. Final Model Assessing Moderating Effects of Blood Pressure

*Note.* N = 66; \* p < .05, <sup> $\Delta$ </sup> p < .01, <sup>+</sup> p < .001, <sup>#</sup> p < .10.

#### **Research Question 3: Blood Pressure as a Mediator**

After establishing the presence of moderating effects, we addressed whether blood pressure mediated the association between ToM and neuropsychological performance. Since SBP and DBP were significant independent predictors of ToM (Table 5), we examined these variables as mediators in separate analyses. We also examined PP as a mediator given its strong association with SBP. The first step was to conduct a regression with the independent variables (i.e., NPA, SK/WM) predicting the proposed mediator. N neither NPA nor SK/WM was associated with SBP, DBP, or PP. Thus, for all three variables, the first condition of mediation was not met, precluding further investigation of blood pressure as a mediator in our sample.

### DISCUSSION

Current findings from the cognitive aging literature provide evidence that successful performance on tasks that require mental state reasoning, or ToM, draws heavily from traditional neurocognitive resources as well (e.g., Charlton et al., 2009; German & Hehman, 2006; McKinnon & Moscovitch, 2007). Within this framework, we considered the utility of blood pressure taken at the time of assessment and diagnosed hypertension as modifiers of this relationship in a sample of cognitively intact, community dwelling older adults. To our knowledge, this is the first study to assess the utility of individual differences in blood pressure as independent predictors of older adults' mental state reasoning. Further, it is the first to examine whether blood pressure may exert moderating or mediating effects on established associations between ToM and supporting neuropsychological resources.

Our first research questions addressed whether blood pressure accounted for unique variance in older adults' mental state reasoning. We predicted that elevated blood pressure and hypertensive status would be associated with reductions in older adults' mental state reasoning. Increased systolic (SBP) and diastolic blood pressure (DBP) emerged as significant independent predictors of ToM beyond the effects of age and neuropsychological performance. Counter to these predictions, self-reported hypertensive status did not contribute to

variability in older adults' mental state reasoning, and was not further examined as a mediator or moderator of ToM relationships.

Our second research question concerned potential moderating influences of blood pressure on associations between ToM and neurocognitive abilities. We anticipated that an interaction between neuropsychological performance and blood pressure would account for significant variance in older adults' ToM. Our predictions were supported in that two important interactions (i.e., Pulse pressure by the Neuropsychological Ability composite [PP\*NPA] and systolic blood pressure by the Semantic Knowledge/Working Memory composite [SBP\*SK/WM]) were observed. The interaction between PP and NPA revealed that older adults with low NPA scores showed less accurate mental state reasoning than older adults with high NPA scores. Importantly, this effect was more pronounced at greater PP levels.<sup>3</sup> An interaction between SBP and SK/WM revealed that individuals with low SK/WM scores also showed less accurate mental state reasoning than individuals with high SK/WM scores. The link between SK/WM and ToM was stronger in older adults with moderate to high levels of SBP.

Our third research question explored whether blood pressure acted as a mediator of links between ToM and neuropsychological performance. We hypothesized that hypertensive status and blood pressure would partially account for the relationship between ToM and neuropsychological performance. Counter

<sup>&</sup>lt;sup>3</sup> Although PP was not identified as a significant independent predictor of ToM in the first research question, we considered it as a potential moderator and mediator given strong theoretical rationale supporting its close biological relationship with SBP and documented effects on domain-specific cognitive function (Bucur & Madden, 2010; Waldstein et al., 2008).

to our predictions, none of our candidate mediators (i.e., SBP, DBP, PP) satisfied the conditions necessary to test for mediation (cf. Baron & Kenny, 1986), thus, hypotheses concerning blood pressure as a mediator could not be confirmed or disconfirmed with this approach. Blood pressure may act as a mediator in more diverse samples that include individuals with severe illnesses, and where greater variance in levels of education, neuropsychological ability, and blood pressure control exist.

Our results highlight important associations between blood pressure and cognition, in that certain groups of older adults may be at greater risk for reductions in ToM. We demonstrated the critical influence of blood pressure taken at the time of assessment, such that for older adults with elevated SBP and/or greater PP, neurocognitive performance was an important predictor of reduced mental state reasoning. However, this relationship was less salient in older adults with low blood pressure. Further, our findings regarding SBP and DBP as important independent predictors of reduced mental state reasoning are in accord with previous literature documenting inverse relationships between blood pressure and traditional cognitive abilities (e.g., learning and memory, executive function, speed; Bucur & Madden, 2010; Saxby et al., 2003; Waldstein et al., 2008). These variables explained variance in ToM beyond the effects of supporting neuropsychological resources.

According to the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, cardiovascular risk doubles with each 20/10 mmHg rise in blood pressure, starting at 115/75 mmHg

(Chobanian et al., 2003). Recent attention has been paid to individuals whose SBP levels fall between 120-139 mmHg (and DBP levels 80-89 mmHg), as these "pre-hypertensive" individuals are considered to be at increased risk for progression to hypertension and other cardiovascular illness (Chobanian et al., 2003). A large proportion of the current sample (i.e., n = 26, 39.3%) had an average SBP that fell within the 120-139 mmHg range, suggesting that older adults with SBP levels in this "pre-hypertensive" range may be at risk for reductions in mental state reasoning and in addition to other cognitive abilities.<sup>4</sup> Along these lines, our range of PP (i.e., 31-96 mmHg) was restricted in comparison to other studies describing its negative association with cognition (e.g., range = 22-161 mmHq, Robbins, Elias, Elias, & Budge, 2005; range = 18-136 mmHg, Waldstein et al., 2008). Even so, the important interactions we observed between PP and neurocognitive ability emphasize that negative effects on mental state reasoning may be present even at mildly elevated blood pressure levels.

The similarity in outcomes for SBP and PP is apparent and may reflect their close biological association and tendency to follow a similar trajectory in late life (Schiffrin, 2004; Swan et al., 1998). Although these indicators displayed a similar direction of effect on ToM relationships, their interactions with cognitive ability were different. Specifically, increased arterial stiffness (i.e., PP) was associated with NPA, but not SK/WM. The opposite was true for elevated SBP—

<sup>&</sup>lt;sup>4</sup> It is of note that although "low" scores on ToM and neurocognitive tasks generally fell within the normal range and are <u>not</u> clinically *impaired* (as per dementia, for example), these lower scores are clinically *meaningful* in that they reveal important information about the critical influence of elevated blood pressure.

it displayed important associations with the SK/WM composite, but not NPA. The interaction between PP & the NPA composite is expected, given contemporary literature documenting the influence of high PP on neurocognitive domains such as verbal and nonverbal memory, attention, and executive function (Elias, Elias, Robbins, & Budge, 2004; Hajjar et al., 2009; Pase et al., 2010; Waldstein et al., 2008). Other research has supported a strong association between widened PP and poor language ability (Nation et al., 2010); however, our results did not support such an interaction (i.e., absence of an interaction between PP and the SK/WM composite).

It is less clear why older adults with high SBP displayed a stronger association between ToM and the SK/WM composite, but not between ToM and the NPA composite. Given similar associations among SBP, PP and neurocognitive performance, we would expect an interaction between SBP and NPA (e.g., Bucur & Madden, 2010; Knecht et al., 2009; Waldstein et al., 2005; Qiu et al., 2005). It is possible that the SBP\*SK/WM interaction may be driven by associations with our measure of working memory that was represented in the SK/WM composite (i.e., WAIS-III Letter-Number Sequencing). Declines in working memory have been associated with the presence of vascular-related neuropathology (e.g., white matter lesions), which may arise from chronically elevated blood pressure (Raz et al., 2007; van Dijk, et al., 2004). Less research has demonstrated links between high blood pressure and crystallized abilities (e.g., Robbins et al., 2004), such as receptive vocabulary, which is the other

measure represented in our SK/WM composite.<sup>5</sup>

The absence of an association between hypertensive status and our cognitive variables of interest is in apparent contrast with studies demonstrating that hypertensive status accounts for significant variance in executive function, speed and memory (Brady et al., 2005; Bucur & Madden, 2010; Knopman, Mosley, Catellier, & Coker, 2009; Saxby et al., 2003). Other literature has shown the influence of health status differences in neuropsychological abilities in illness populations closely related to hypertension (e.g., type 2 diabetes: Fischer, de Frias, Yeung, & Dixon; Yeung, Fischer, & Dixon, 2009; chronic kidney disease: Thornton et al., 2007). One explanation for discrepant findings may pertain to the overall health and small size of our sample. Indeed, our N = 66 participants represent high-functioning older adults who are free of major co-morbid illness, live independently, and most likely engage in a number of lifestyle activities. Further, our diagnostic criteria for hypertension included the presence of objective medication for blood pressure control (see methods), which may be a factor benefiting cognitive performance (Birns, Morris, Donaldson, & Kalra, 2006). We also did not account for severity of hypertension, unlike previous

<sup>&</sup>lt;sup>5</sup> Consistent with procedures seen in previous studies examining ToM and aging (e.g., Bernstein et al., in press) and blood pressure and cognition (Elias, Robbins, Schultz, & Pierce, 1990; Saxby et al., 2003), we used Principle Components Analysis to characterize neuropsychological performance in our sample and to reduce the number of independent variables in a meaningful way. It is interesting to note that working memory (as measured by WAIS-III Letter-Number Sequencing; Wechsler, 1997) preferentially loaded on the factor containing semantic knowledge, rather than the NPA factor, which contained our measures of inhibitory control, mental set-shifting, processing speed and memory. This may reflect the semantic demands inherent to our task of working memory (i.e., alphabetically sequencing target letters). The high loading of LNS with our measure of language may represent shared variance in task demands, which both require the manipulation of verbal material (Acheson & MacDonald, 2009).

investigations that may have included a greater proportion of individuals with severe illness (e.g., Saxby et al., 2003 criteria for hypertension: blood pressure ≥ 160/90 mmHg). Overall, our findings suggest that the analysis of the three continuous blood pressure predictors (i.e., SBP, DBP, PP) may more accurately reflect the vascular health of our sample than a dichotomous analysis of hypertensive status. However, this should not preclude further investigation of hypertensive status in the context of older adults' mental state reasoning.

It is important to discuss potential mechanisms that may explain the independent and interactive effects of blood pressure and traditional neuropsychological abilities on older adults' mental state reasoning. Recent imaging studies note the greatest brain activation in frontal, temporal and medial prefrontal cortex in response to mental state stimuli (Saxe, 2006; Stuss, Gallop, & Alexander, 2001). Elevations in vascular risk (e.g., chronic hypertension) are associated with both the volume and progression of white matter lesions in these regions (esp. frontal; Raz et al., 2007; Strassburger et al., 1997). Cognitive processes that rely on the structural and functional integrity of these regions may be particularly vulnerable to these effects (Brady et al., 2005; Raz et al., 2007). Conceivably, vascular pathology may affect regions directly implicated in the generation of mental state inferences, or rather; it may operate indirectly, through deleterious effects on regions involved in executive (or other) abilities (cf. Brady et al., 2005; Charlton et al., 2009).

Blood pressure associations with cognition may also be influenced by environmental and genetic factors. Sex, education and ethnicity have each been

demonstrated to modify blood pressure effects on cognitive performance (Waldstein, 2003 for a review). We considered the role of gender in our approach; however, it was not significantly associated with variable mental state reasoning in our sample. Other factors may confound the measurement of blood pressure taken at the time of assessment and may include the history and chronicity of uncontrolled blood pressure (Elias et al., 1995; Swan et al., 1998). This is a particularly important point as an earlier onset of hypertensive illness may confer an increased risk for reductions in neuropsychological abilities in later life (Launer, Masaki, Petrovitch, Foley, & Havlik, 1995; Waldstein, 1995). However, even in the context of diagnosed hypertension, it is difficult to ascertain the duration of elevated blood pressure, as a large proportion of older individuals are unaware of their blood pressure levels (Lee, 2007). Elevated blood pressure may also interact with medical comorbidities and other cardiovascular risk factors to influence cognitive change (Waldstein, 2003). Factors such as impaired glucose tolerance and changes to serum lipid levels are known to be independently associated with cognitive decline (e.g., Fillit, Nash, Rundek, & Zuckerman, 2008; Fischer et al., 2009; Yeung et al., 2009), and may exacerbate adverse cognitive effects when present comorbid with hypertension (e.g., Hassing et al., 2004). Considering the role of other health influences in reductions in ToM in older age will be an important area for future investigation.

The study of ToM may raise questions as to why mental state reasoning is such a relevant construct to consider in aging populations. As such, we provide a brief example to illustrate how mental state reasoning permeates everyday social

interactions (adapted from Frith, Happé, & Siddons [1994]). Imagine you are watching a colleague shuffling through papers in a filing cabinet. In most cases, you are likely to assume your colleague *wants* a document that he or she *believes* is in the cabinet. Most individuals will understand the purpose of the colleague's activity, even if they know the document is not actually in the cabinet—this implies an understanding that the colleague's activity is driven by his or her beliefs about the world (cf. Frith et al., 1994). Although this small illustration provides only a glimpse into the functional utility of ToM, it serves to underscore the importance of mental state reasoning as an important social tool. This is reflected in its necessity of use in daily interactions including the understanding of humour and lies, deception, and irony (Happé, 1994; Hughes & Leekam, 2004). Conceivably, reductions in mental state reasoning could have important implications for older adults in a variety of areas, which may include health management, decision-making, or vulnerability to fraud.

At the confluence of health psychology and cognitive aging, a growing body of evidence suggests that blood pressure may play an important role in clarifying the nature of late-life cognitive changes. We provide a novel perspective to this literature in our examination of the role of blood pressure in age-related reductions in mental state reasoning. Blood pressure may interact with neuropsychological performance to exacerbate reductions in mental state reasoning, and for certain groups of older adults, this relationship is particularly important. We underscore the utility of analyzing blood pressure in future studies of ToM and aging, such that assessing the contributions of neuropsychological

resources alone may be insufficient to capture the full picture behind age changes in mental state reasoning. Key questions remain as to whether the cognitive correlates (i.e., ToM and other supporting cognitive abilities) of elevated blood pressure may impact the daily function or quality of life of older individuals.

#### Limitations and future directions

The current findings should be considered within the context of certain limitations. Inherent to the nature of our hypotheses of interest, a limitation with our statistical approach is the number of independent variables and interactions examined in our analyses. For instance, while age was a significant independent predictor of mental state reasoning in all our models, we did not find any significant 2-way or 3-way interactions between our blood pressure predictors, age, and neuropsychological performance. Specifically, in our sample, relationships among ToM, blood pressure and neurocognitive ability were not stronger in certain age groups (e.g., young-old versus old-old). We acknowledge that small cell sizes and the use of multiple comparisons limited our power to draw conclusions from these data (refer to Table 1 for a power comparison between medium and large effect size parameters). A standard way of maintaining the familywise error rate is to use the Bonferroni correction to examine each comparison at a significance level of  $\alpha/n$  (i.e., p-value divided by the number of hypotheses been tested; Mundform, Perrett, Schaffer, Piccone, & Roozebaum, 2006). We acknowledge that use of the Bonferroni correction reduces the probability of capitalizing on chance associations (i.e., thereby reducing the type I error rate). A type I error may occur when significance test

results in the incorrect rejection of a true null hypothesis. We weighed this against the presence of type II error due to the small sample size used in the current study (i.e., type II error = failing to reject a false null hypothesis). Given the preliminary nature of our examination of associations among ToM, blood pressure and neuropsychological ability, we elected to forgo the application of Bonferroni correction to these data. Our small sample size significantly reduced our power, thus increasing our chances of making a type II error, in that we did not have sufficient power to provide strong evidence against a full null hypothesis. Considering the emerging nature of this field, our overarching aim was to identify potential significant blood pressure predictors that will be important to pursue in future investigations of ToM, and we consider the current results carefully in light of our small sample size and low power..

The cross-sectional nature of our study design limits our ability to draw causal inferences and establish long-term temporal relationships between ToM, neuropsychological ability, and blood pressure. The question remains whether individuals with chronically elevated blood pressure may experience accelerated decline in ToM abilities over time. To date, we are not aware of any studies that have examined longitudinal patterns of ToM in an aging population.

Our sample comprised healthy, cognitively intact community-dwelling individuals; this means that results may not be representative of the population of Canadian adults aged 65 and over as a whole. As shown in Table 2, older adult volunteers were primarily Caucasian (86%), well educated, and free of any major functional or cognitive limitations. Further, our exclusion criteria were stringent,

and applied to many members of the older adult community. This restricted our sample to those without severe medical illness, which likely obscured our ability to detect even stronger effects regarding hypertensive status. Additionally, we cannot be certain that our use of self-reported diagnoses to determine hypertensive status accurately captured all individuals with objective illness. This issue is compounded by the increased prevalence of vascular conditions in later life. As we did not have access to participants' medical records to confirm diagnoses, we followed a two-step diagnostic procedure based upon both a self-reported physician's diagnosis *and* objective confirmation of relevant medication (Campbell et al., 2005). However, previous studies provide support for the accuracy of self-reported diagnoses (Kriegsman, Penninx, van Eijk, Boeke, & Deeg, 1996; Midthjell, Holmen, Bjørndal, & Lund-Larsen, 1992).

The use of blood pressure may be limited by our single-occasion method of assessment. "Gold-standard" measures such as ambulatory blood pressure monitoring are expensive and time-consuming but may yield greater reliability. In the current study, multiple measurements were taken at the beginning of the assessment session for each participant, in accordance with procedures commonly observed within the aging literature (e.g., Knecht et al., 2008; Qiu et al., 2003; Yeung et al., 2009). Specific precautions were also taken to reduce the potential for "white coat" hypertension, as participants were given time to rest before and between readings, and examiners were trained to face away from participants during measurement. Within aging populations, it is particularly important to incorporate continuous measurements in addition to self-reported

diagnoses, as a high proportion of individuals have been found to be unaware of their hypertensive status (Lee, 2007). Future studies may want to target individuals with without diagnoses of hypertension (e.g., prehypertensive, normotensive) to further elucidate associations between ToM and blood pressure. As blood pressure is a modifiable risk factor, implications exist for the importance of early detection and control of changes in blood pressure levels. Theoretically, interventions aimed at improving blood pressure control, such as use of antihypertensive agents and/or lifestyle modification may yield a positive effect on both older adults' mental state reasoning and traditional neuropsychological abilities (Birns et al., 2006). Research in these areas may assist health care professionals in their recommendation of treatment options, as well as in the identification of cognitive difficulties that may be partially attributable to vascular risk.

Finally, our use of a common measure of ToM (i.e., *Strange Stories* task: Happé, 1994) allows our results to be contrasted more meaningfully against the extant literature on ToM and aging. Although this task is common in the literature and may be construed as "standard," the Stories task arguably requires greater manipulation of verbal material than other ToM tasks. Varying methods of assessing ToM may place vastly different demands on the involvement of neuropsychological resources, underscoring the importance of careful task selection (Bull et al., 2008; Lough et al., 2006; Saltzman et al., 2000). Discrepant patterns of correlations with neurocognitive performance, as well as modest correlations between ToM tasks themselves reinforce the notion that ToM is

likely a multi-faceted, non-unitary construct, perhaps representing a varied compilation of cognitive and social abilities (see Bernstein et al., in press; Lough et al., 2006 for similar arguments). Further explorations of similar research questions would benefit from inclusion of multiple measures of ToM within a larger sample size, which are key considerations necessary to demonstrate convergent validity of these results.

To our knowledge, this is the first study to test the hypothesis that blood pressure is an important modifier of ToM relationships in older age. We emphasize findings suggesting the critical influence of blood pressure in determining the strength of associations between ToM and supporting neuropsychological resources. In neuropsychological research and practice there is a need for a better understanding of what factors may influence cognition in later life. Expanding upon traditional neuropsychological literature, we emphasize that even among healthy older adults, normal but elevated levels of blood pressure may negatively influence age-sensitive tasks of mental state reasoning. Neuropsychological predictors of ToM are necessary, but in isolation may not be sufficient to understanding the nature of age changes in ToM. Future research may examine these areas with other health modifiers common to the aging literature (e.g., self-rated health, other indicators of vascular risk). Results may inform research and clinical practice regarding potentially important healthcognition relationships to be targeted in designing future interventions extending beyond cognition to more global improvements older adults' quality of life.

# APPENDICES

## Appendix A

### Acculturation Questionnaire

<u>Please fill out the following information:</u> Note that the information you provide will be kept confidential.

1. Age:
2. Gender:
3. Race/Ethnicity:
4. Handedness (Right/Left):
5. Do you have any visual problems? (Y/N)
If YES, please explain:
6. Do you have any hearing problems? (Y/N)
If YES, please explain:
7. As a child, did you have any developmental difficulties (e.g. learning disabilities, giftedness, delayed development) or disorders (e.g. autism, attention deficit hyperactive disorder – ADHD)? (Y/N)
If YES, please elaborate:

# 8. Have you ever been diagnosed with or received treatment for any serious medical conditions? (Y/N)

If YES, please explain:\_\_\_\_\_

# 9. Have you ever been diagnosed with or received treatment for any psychological disorders? (Y/N)

If YES, please explain:\_\_\_\_\_

10. Were you born in Canada? (Y/N)\_\_\_\_\_

11. If you were <u>not</u> born in Canada, please answer the following questions, otherwise please skip to question 12:

a) Where were you born? (City/Country):

b) At what age did you arrive in Canada?

c) How many years have you lived in Canada?

d) Have you had schooling in a country other than Canada? If so, where? And for how many years?

e) Have you had schooling in Canada? If so, for how many years?

12. What is your first language?\_\_\_\_\_

13. What is your preferred language?\_\_\_\_\_

14. Do you speak any other language(s), if so which ones (s)?

15. If you speak a language other than English, please answer the following questions, otherwise please skip to question 16:

b)	What language do you prefer to use when speaking?
c) \	What language do you prefer to use when thinking?
d) '	What language do you prefer to use when reading?
e) \	What language do you prefer to use when writing?

17. Are you currently working? (Y/N): \_\_\_\_\_

Occupation:

**18. Estimated Income:** please check the category that you believe best describes your situation:

- □ Below \$20,000
- □ \$20,000 **-** \$40,000
- □ \$40,000-\$60,000
- □ \$60,000 \$80,000
- □ Above 80,000

### Appendix B

Theory of Mind and Control Vignettes Used in the Current Study (adapted

from Happé's [1994] Strange Stories)

### THEORY OF MIND VIGNETTES

1. SIMON IS A BIG LIAR. SIMON'S BROTHER JIM KNOWS THIS, HE KNOWS THAT SIMON NEVER TELLS THE TRUTH! NOW YESTERDAY SIMON STOLE JIM'S PING-PONG PADDLE, AND JIM KNOWS SIMON HAS HIDDEN IT SOMEWHERE, THOUGH HE CAN'T FIND IT. HE'S VERY CROSS. SO HE FINDS SIMON AND HE SAYS, "WHERE IS MY PING-PONG PADDLE? YOU MUST HAVE HIDDEN IT EITHER IN THE CUPBOARD OR UNDER YOUR BED, BECAUSE I'VE LOOKED EVERYWHERE ELSE. WHERE IS IT, IN THE CUPBOARD OR UNDER YOUR BED?" SIMON TELLS HIM THE PADDLE IS UNDER HIS BED.

Q: WHY WILL JIM LOOK IN THE CUPBOARD FOR THE PADDLE?

2. JILL WANTED TO BUY A KITTEN, SO SHE WENT TO SEE MRS. SMITH, WHO HAD LOTS OF KITTENS SHE DIDN'T WANT. NOW MRS. SMITH LOVED THE KITTENS, AND SHE WOULDN'T DO ANYTHING TO HARM THEM, THOUGH SHE COULDN'T KEEP THEM ALL HERSELF. WHEN JILL VISITED SHE WASN'T SURE SHE WANTED ONE OF MRS. SMITH'S KITTENS, SINCE THEY WERE ALL MALES AND SHE HAD WANTED A FEMALE. BUT MRS. SMITH SAID, "IF NO ONE BUYS THE KITTENS I'LL JUST HAVE TO DROWN THEM!"

Q: WHY DID MRS. SMITH SAY THAT?

3. DURING THE WAR, THE RED ARMY CAPTURES A MEMBER OF THE BLUE ARMY. THEY WANT HIM TO TELL THEM WHERE HIS ARMY'S TANKS ARE; THEY KNOW THEY ARE EITHER BY THE SEA OR IN THE MOUNTAINS. THEY KNOW THAT THE PRISONER WILL NOT WANT TO TELL THEM, HE WILL WANT TO SAVE HIS ARMY, AND SO HE WILL CERTAINLY LIE TO THEM. THE PRISONER IS VERY BRAVE AND VERY CLEVER, HE WILL NOT LET THEM FIND HIS TANKS. THE TANKS ARE REALLY IN THE MOUNTAINS. NOW WHEN THE OTHER SIDE ASK HIM WHERE HIS TANKS ARE, HE SAYS, "THEY ARE IN THE MOUNTAINS".

Q: WHY DID THE PRISONER SAY THAT?

- 4. BRIAN IS ALWAYS HUNGRY. TODAY AT SCHOOL IT IS HIS FAVORITE MEAL - SAUSAGES AND BEANS. HE IS A VERY GREEDY BOY, AND HE WOULD LIKE TO HAVE MORE SAUSAGES THAN ANYBODY ELSE, EVEN THOUGH HIS MOTHER WILL HAVE MADE HIM A LOVELY MEAL WHEN HE GETS HOME! BUT EVERYONE IS ALLOWED TWO SAUSAGES AND NO MORE. WHEN IT IS BRIAN'S TURN TO BE SERVED, HE SAYS, "OH, PLEASE CAN I HAVE FOUR SAUSAGES, BECAUSE I WON'T BE HAVING ANY DINNER WHEN I GET HOME!"
- Q: WHY DOES BRIAN SAY THIS?

#### CONTROL VIGNETTES

 JOHN IS GOING SHOPPING. HE BUYS A NICE NEW DESK LAMP, FOR HIS STUDY. HE NEEDS A LIGHT BULB FOR HIS NEW LAMP. HE GOES FROM THE FURNITURE SHOP TO THE ELECTRICAL SHOP. IN THE ELECTRICAL SHOP HE FINDS THAT THERE ARE TWO BRANDS OF LIGHT BULB OF THE RIGHT KIND. EVER-BRIGHT LIGHT BULBS COST LESS IN SINGLE PACKS THAN LIGHT-RIGHT BULBS. HOWEVER, ONLY LIGHT-RIGHT BULBS COME IN MULTI-PACKS OF SIX. JOHN BUYS THE MULTI-PACK, EVEN THOUGH HE ONLY NEEDS ONE BULB.

Q: WHY DOES JOHN BUY THE LIGHT-RIGHT BULBS?

2. MRS SIMPSON WORKS IN A MUSEUM. ONE DAY SHE RECEIVES A VERY SPECIAL OLD COAT AND HAS TO DECIDE WHERE TO PUT IT IN THE MUSEUM. THE MUSEUM IS VERY BIG, AND HAS MANY DIFFERENT SECTIONS. THE COAT USED TO BELONG TO A MEMBER OF THE FRENCH ROYAL FAMILY AND IS COVERED IN VERY DELICATE LACE. HOWEVER, MRS SIMPSON DOES NOT PUT IT IN THE FRENCH ROYALTY SECTION. SHE DOES NOT PUT IT IN THE CLOTHING SECTION EITHER. INSTEAD, SHE CAREFULLY TAKES IT INTO A SEPARATE ROOM. IN THIS ROOM ALL THE CLOTHES ARE KEPT IN SPECIAL CASES, AND THE TEMPERATURE IS KEPT CONSTANT.

Q: WHY DID SHE DO THIS?

3. TWO ENEMY POWERS HAVE BEEN AT WAR FOR A VERY LONG TIME. EACH ARMY HAS WON SEVERAL BATTLES, BUT NOW EITHER SIDE COULD WIN. THE TWO SIDES ARE EQUALLY STRONG. HOWEVER, THE BLUE ARMY IS STRONGER THAN THE YELLOW ARMY IN FOOT SOLDIERS AND TANKS. BUT THE YELLOW ARMY IS STRONGER THAN THE BLUE ARMY IN AEROPLANES. ON THE DAY OF THE FINAL BATTLE, WHICH WILL DECIDE THE OUTCOME OF THE WAR, THERE IS HEAVY FOG OVER THE MOUNTAINS WHERE THE FIGHTING IS ABOUT TO OCCUR. LOW CLOUDS HANG ABOVE THE SOLDIERS. BY THE END OF THE DAY THE BLUE ARMY HAS WON.

Q: WHY DID THE BLUE ARMY WIN?

4. MRS BROWN HAS VERY POOR EYESIGHT. SHE HAS ONLY ONE PAIR OF GLASSES, WHICH SHE KEEPS LOSING. TODAY SHE HAS LOST HER GLASSES AGAIN AND SHE NEEDS TO FIND THEM. SHE HAD THEM YESTERDAY EVENING WHEN SHE LOOKED UP THE TELEVISION PROGRAMMES. SHE MUST HAVE LEFT THEM SOMEWHERE THAT SHE HAS BEEN TODAY. SHE ASKS TED TO FIND HER GLASSES. SHE TELLS HIM THAT TODAY SHE WENT TO HER REGULAR EARLY MORNING SWIMMING CLASS, THEN TO THE POST OFFICE, AND LAST TO THE FLOWER SHOP. TED GOES STRAIGHT TO THE POST OFFICE.

Q: WHY IS THE POST OFFICE THE MOST LIKELY PLACE TO LOOK?

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