Individual Differences in Cognitive Plasticity and Variability as Predictors of Cognitive Function in Older Adults

by

Jacob Harold Gross Grand

B.Sc., Queen's University, 2002
B.A., University of British Columbia, 2008

A Thesis Submitted in Partial Fulfillment
of the Requirements for the Degree of

MASTER OF SCIENCE

in the Department of Psychology

Supervisory Committee

Individual Differences in Cognitive Plasticity and Variability as Predictors of Cognitive Function in Older Adults

by

Jacob Harold Gross Grand

B.Sc., Queen's University, 2002
B.A., University of British Columbia, 2008

Supervisory Committee

Dr. Stuart W. S. MacDonald, (Department of Psychology)
Supervisor

Dr. Holly A. Tuokko, (Department of Psychology)
Departmental Member

Dr. David F. Hultsch (Department of Psychology)
Departmental Member

Abstract

Supervisory Committee

Dr. Stuart W. S. MacDonald (Department of Psychology)
Supervisor

Dr. Holly A. Tuokko (Department of Psychology)
Departmental Member

Dr. David F. Hultsch (Department of Psychology)
Departmental Member

Background: With the growth in elderly populations worldwide, there is a pressing need to characterize the changes in cognition and brain function across the adult lifespan. The evolution of cognitive abilities is no longer considered to reflect a universal, cumulative process of decline. Rather, significant inter- and intra-individual differences exist in cognitive trajectories, with the maintenance of functions ultimately determined by multi-dimensional biological and psychological processes. The current study examined the relationship between intra-individual variability, cognitive plasticity, and long-term cognitive function in older adults. ***Methods***: Data were analyzed from *Project Mental Inconsistency in Normals & Dementia (MIND)*, a 6-year longitudinal burst design study, integrating micro-weekly assessments (reaction time (RT) tasks), with macro-annual evaluations (cognitive outcome measures). Participants included 304 community-dwelling adults, ranging in age from 64 to 92 years (M = 74.02, SD = 5.95). Hierarchical multiple regression models were developed to examine long-term cognitive function, along with multilevel modeling (HLM) techniques for the analysis of specific predictors of longitudinal rates of cognitive change. ***Results***: Baseline intraindividual variability (ISD) emerged as a robust and highly sensitive predictor, with increased variability associated with decreased long-term cognitive performance. Complex baseline cognitive plasticity (1-Back 4-Choice RT Task) uniquely predicted subsequent cognitive function for measures of processing speed, fluid reasoning, episodic memory, and crystallized verbal ability. Multilevel models revealed chronological age to be a significant predictor across cognitive domains, while intraindividual variability selectively predicted rates of change for performance on measures of episodic memory and crystallized verbal ability. ***Conclusion***: These findings underscore the potential utility of intraindividual variability and cognitive plasticity as dynamic predictors of longitudinal change in older adults.

Table of Contents

List of Tables

List of Figures

Acknowledgments

First and foremost I would like thank my research supervisor, Dr. Stuart MacDonald for his unwavering support and advice. His inspirational mentorship has guided me throughout this process, and motivated me to continue developing a comprehensive program of research. Thank you to my clinical supervisor, Dr. Holly Tuokko and my committee member, Dr. David Hultsch for their expert feedback and insightful commentary on the development of this project. I would like to recognize the many individuals involved in Project MIND, including participants, research assistants, and the significant contributions of Dr. Esther Strauss, without whom this research would not be possible. I would also like to acknowledge Dr. Howard Feldman and my colleagues at the University of British Columbia for fostering my interest in Clinical Neuropsychology and aging research, and for their collaborations early in my career. Additional thanks to the Canadian Institutes for Health Research (CIHR) and the University of Victoria for generous graduate fellowships in support of this research.

On a more personal note, thank you to the constellation of unique individuals – both friends and family - who are closest to me. To my family reaching across the country, thank you for your support, encouragement, and caring words. To my siblings, for the special bond that ties us together and our many shared experiences. To my wonderful parents for their trust, support, and understanding over the many years. Finally, to my incredible wife, Danyael, for her extraordinary patience, compassion, and enduring love. I dedicate this body of work to our shared life and the exciting promise of our future together. Thank you for everything you do, every single day.

Introduction

Given the increase in aging populations worldwide, there is a growing need to characterize changes in cognition and brain function across the adult lifespan and to identify early indicators of impairment. Traditionally, the evolution of cognitive abilities in older adults was considered to reflect a universal, cumulative process of decline. However, dissatisfaction with this limited point of view has given rise to an increased research emphasis on multi-dimensional and multi-directional aging processes (Baltes & Singer, 2001; Christensen, Mackinnon, Jorm, Henderson, & Scott, 1994; Hultsch, MacDonald, & Dixon, 2002; MacDonald, Hultsch, & Dixon, 2003; Schaie & Willis, 1986). Considerable inter- and intra-individual heterogeneity exists in trajectories of change among older adults, with differences in rates of cognitive decline, as well as fluctuations in cognitive function with advancing age (see Figure 1; Baltes, Staudinger, & Lindenberger, 1999; Dixon, Garrett, Lentz, MacDonald, Strauss, Hultsch, 2007; Hultsch, Hertzog, Small, & Dixon, 1999; Hultsch et al., 2002; MacDonald, Hultsch, & Dixon, 2008; Williams, Hultsch, Strauss, Hunter, & Tannock, 2005; Wilson et al., 2002).

Research on human development and psychological functioning has typically assumed that outcome measures represent enduring, stable characteristics of an individual (e.g., intellectual abilities, personality traits). Consequently, mean level of performance or single sample measurements have traditionally been used as primary outcomes of interest (Williams et al., 2005). This general stability perspective assumes within-person variation in level of performance to represent intrinsic testing error, and should be interpreted as experimental 'noise'. However, Nesselroade (1991) proposed a model of development that is characterized by two types of change: *Intraindividual change*, which occurs slowly

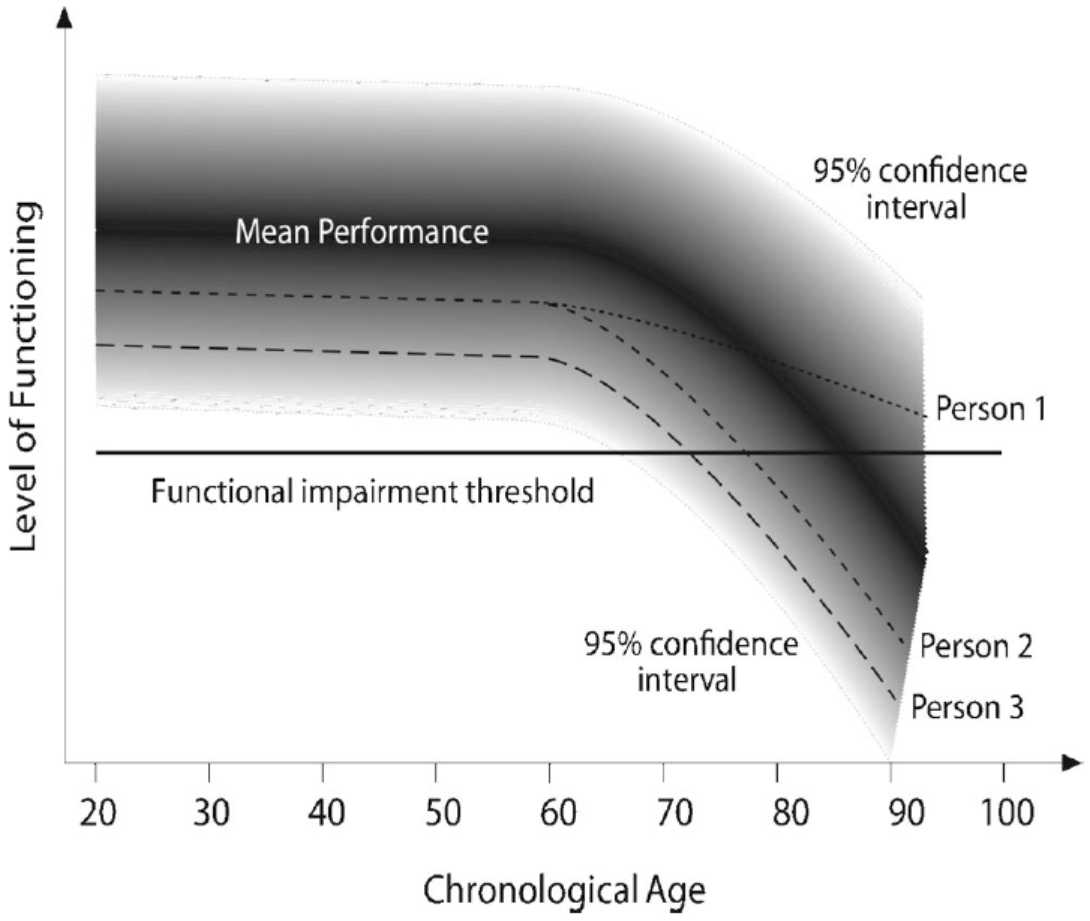

Figure 1) Individual differences in trajectories of cognitive change across the lifespan.

Schematic univariate description of the hallmarks of adult development of fluid intelligence. Performance at a particular point in time displays normal distribution with substantial interindividual differences. Until the seventh decade of life, individuals travel in parallel to a high degree. As indicated by comparison of the trajectories of Person 1 and Person 2, interindividual differences in change are apparent in old age. The age at which functional impairment thresholds (e.g., dementia) are reached is codetermined by level of performance (compare the trajectories of Persons 2 and 3) and change in performance in old age (compare trajectories of Persons 1 and 2) (Lövdén, Bäckman, Lindenberger, Schaefer, & Schmiedek, 2010).

over relatively long periods of time (e.g., year-to-year), and *intraindividual variability*, which occurs quickly over relatively short time periods (e.g., moment-to-moment). Intraindividual change tends to result in enduring changes in an individual (e.g., learning of new abilities), whereas intraindividual variability (or *inconsistency*) is a more labile short-term process (e.g., rapid fluctuations in cognitive performance). Performance variability is typically indexed by computing across-trial intraindividual standard deviations (ISD) about each individual's mean performance on a specific outcome measure (e.g., response time, accuracy; Hultsch, Strauss, Hunter, & MacDonald, 2008). Potential confounding influences can then be partialed out using multilevel statistical techniques. By using the resulting residuals, it ensures that any systematic within-person (i.e., trial) and between-person (i.e., age group) sources of variance have been removed, and each individual's unsystematic portion of variance can be evaluated. An interactive, dynamic relationship between intraindividual change and variability likely exists, whereby short-term fluctuations help to facilitate long-term developmental changes (Nesselroade, 1991). Recent research has demonstrated that intraindividual variability in cognitive performance is significant in magnitude (relative to interindividual differences), is a relatively stable trait-like characteristic, and may function as a predictor of longitudinal rates of change (Hultsch et al. 2000, 2008; Nesselroade & Salthouse, 2004; Rabbitt, Osman, Moore, & Stollery, 2001).

Epidemiological and population-based studies of adult cognitive aging have demonstrated individual differences in levels of performance in abilities such as working memory, reasoning, episodic memory, and spatial orientation (Rönnlund & Nilsson, 2006; Rönnlund, Nyberg, Bäckman, & Nilsson, 2005), as well as variability in rates of

cognitive change over time (DeFrias, Lövdén, Lindenberger, & Nilsson, 2007; Lindenberger & Ghisletta, 2009). According to the *cognitive-enrichment hypothesis* (Hertzog, Kramer, Wilson, & Lindenberger, 2009), a lifestyle rich in mental stimulation, physical activity, and social engagement exerts beneficial influences on levels of cognitive functioning across the adult lifespan (Bäckman, Small, Wahlin, & Larsson, 2000; Hertzog, Kramer, Wilson, & Lindenberger, 2009; Hultsch, Hertzog, Small, & Dixon, 1999; Kramer, Behere, Colcombe, Dong, & Greenough, 2004). However, the underlying mechanisms through which these factors influence cognitive aging remain to be fully characterized. Specifically, it is not known if the beneficial impact of an enriched lifestyle reflects direct effects of cognitive stimulation on performance, or if underlying mechanisms act indirectly to reduce negative effects on cognition (e.g., vascular health, depression, stress; Lövdén, Bäckman, Lindenberger, Schafer, & Schmiedek, 2010). To address these questions, current research must investigate how processes involved in plasticity shape adult cognitive development at behavioural and neural levels of functioning (Baltes & Singer, 2001; Li, 2003; Lustig, Shah, Seidler, & Reuter-Lorenz, 2009; MacDonald, Nyberg, & Bäckman, 2006).

The term cognitive plasticity has been widely used in the behavioural and brain sciences, and its meaning has undergone considerable evolution and proliferation. In general, cognitive plasticity refers to a fundamental distinction between present levels of functioning and potential changes in performance (i.e., an individual's latent capacity to learn by taking advantage of experience). Baltes & Willis (1982) operationally defined cognitive plasticity as "the extent to which a given individual can alter their performance on a given task following training or exposure to performance-optimizing conditions".

Current theoretical frameworks for our understanding of cognitive plasticity revolve around the capacity for reactive change within an individual's range of functioning. In this view, cognitive plasticity reflects a secondary change in response to a primary change in the system (Lövdén et al., 2010). For example, when experience (e.g., prior exposure to cognitive tasks) is thought to result in plastic alterations of brain and behaviour, it is the secondary responses (e.g., performance gains, structural and functional brain changes) that are considered to be manifestations of plasticity.

The current study focuses on three primary research questions examining data derived from *Project Mental Inconsistency in Normals & Dementia (Project MIND)*: **1)** Does baseline intraindividual variability predict long term (5 year) cognitive function; **2)** Does baseline cognitive plasticity predict long term (5 year) cognitive function; and **3)** Do specific factors (age, education, intraindividual variability, cognitive plasticity) predict long term rates of cognitive change, and do the observed patterns vary as a function of domain.

Theoretical Models of Cognitive Plasticity

Historically, the term plasticity has permeated the fields of psychology and neuroscience. However, plasticity remains a conceptually ambiguous construct with varied understandings of its neural correlates and functional presentation. Given the different meanings of plasticity in contemporary science, it is necessary to operationally define the term and to sharpen its conceptual distinctiveness in relation to the more encompassing notion of change.

Selection, Optimization, and Compensation (SOC) Model: Initial studies by Baltes and colleagues provided support for a general framework of plasticity by conceptualizing maximization of gains and minimization of losses in cognitive performance across the adult lifespan (Baltes, 1987; Baltes, Ditman-Kohli, & Dixon, 1984; Baltes, Kuhl, & Sowarka, 1992; Baltes & Willis, 1982). These seminal studies lead to the development of the *Selection, Optimization, and Compensation* (SOC) model, which is based on the assumption that individuals continually seek to successfully balance the processes of developmental regulation. *Selection* involves focusing an individual's resources on a subset of potentially available options, thereby giving development its direction. A central function of selection is to efficiently utilize limited cognitive resources available in old age. *Optimization* involves the acquisition, refinement, and coordination of resources directed at achieving outcomes and attaining higher levels of functioning. Optimization requires an individual to monitor and evaluate the discrepancy between actual and desired states of functioning. A key element of optimization is practice. Repeated practice develops the refinement of skill components, which leads to the integration and automatization of acquired abilities. Consequently, the newly acquired skill becomes less resource-demanding, freeing additional cognitive resources that can be devoted to other goal-directed processes. *Compensation* addresses the regulation of loss in development. It involves the application of cognitive processes that have been maintained and enhanced throughout the adult lifespan. These well-developed skills function to offset impaired processes that have become less efficient. Whereas selection refers to restructuring one's goals, compensation implies the maintenance of goals by using alternative means (Freund & Baltes, 2000).

Scaffolding Theory of Aging and Cognition (STAC): The Scaffolding Theory of Aging and Cognition (STAC) is an integrative, adaptive model of plasticity that suggests the brain responds to age-associated neural insults by engaging in continuous functional reorganization, resulting in self-generated support of cognitive functions (Park & Reuter-Lorenz, 2009). According to the STAC model, behavioural performance in older adults can be understood in terms of a homeostatic interaction of neurocognitive declines and compensatory 'scaffolding' processes (see Figure 2). Scaffolding is considered a normal process present across the entire lifespan and involves the use and development of complementary, alternative neural circuits to achieve a particular behavioural output or cognitive goal. Scaffolding involves the recruitment of additional neural circuitry as a compensatory mechanism that offsets declining structures whose functioning has become noisy, inefficient, or both. The STAC model is based primarily on research evidence from the functional brain-imaging literature of greater bilateral and over-activation of frontal brain regions in older adults, particularly the inferior, lateral, and rostral regions of the prefrontal cortex (Cabeza, 2002). STAC also provides for mechanisms that can bolster compensatory scaffolding, including novel learning, cognitive training, physical exercise, and social engagement. STAC therefore places neurocognitive aging within the context of both plasticity and challenge, and provides a broad integrative framework for understanding the relationship between structural and functional changes in the brain in combination with life experiences in order to understand cognitive functioning in older adulthood (Park & Reuter-Lorenz, 2009).

Mismatch Model of Cognitive Plasticity: Lövdén and colleagues (2010) recently proposed a theoretical framework whereby adult cognitive plasticity is driven by a

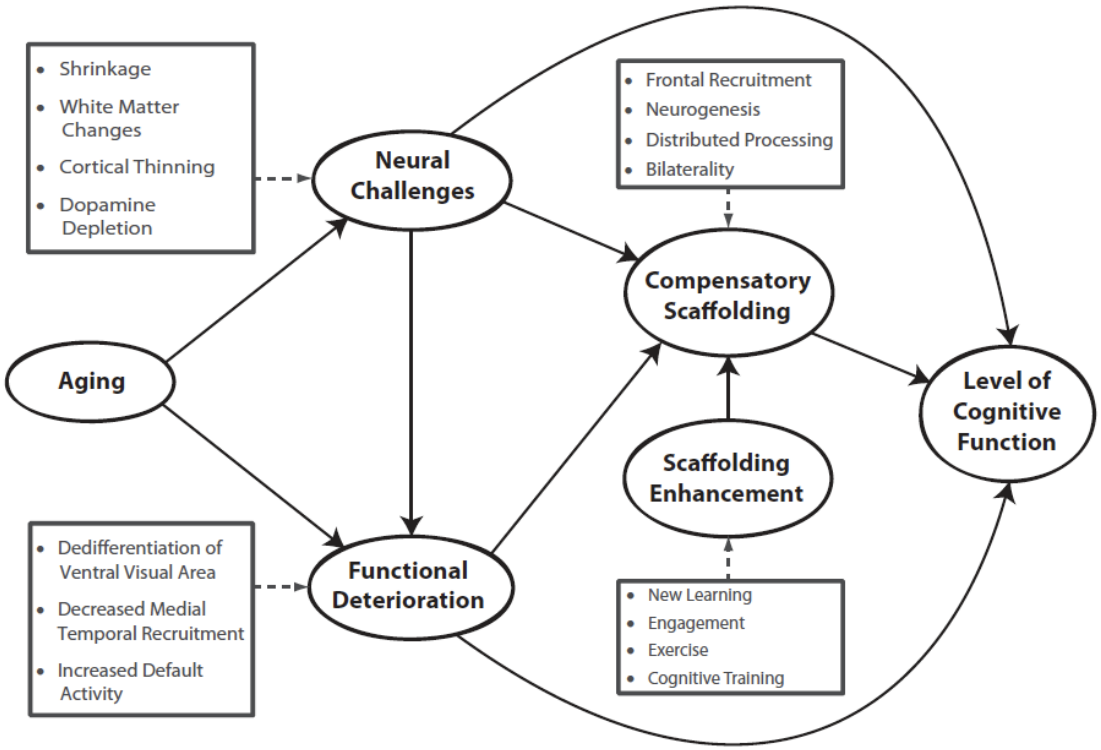

Figure 2) The Scaffolding Theory of Aging and Cognition (STAC).

STAC posits that behavior is maintained at a relatively high level with age, despite neural challenges and functional deterioration, due to the continuous engagement of compensatory scaffolding—the recruitment of additional circuitry that shores up declining structures whose functioning has become noisy, inefficient, or both. The pervasive evidence in the functional brain-imaging literature of greater bilateral activation and over activation of frontal areas in older adults reflects the engagement of "compensatory scaffolding"— the patterns of brain activation that include both declining networks and the associated compensatory circuitry recruited to meet the task demands. STAC also provides for mechanisms that can bolster compensatory scaffolding (Park & Reuter-Lorenz, 2009).

prolonged mismatch between an individual's functional supply and environmental demands (see Figure 3). In this model, plasticity is conceptualized as the capacity for reactive change within a range of functioning (i.e., flexibility). Similar to the concept of baseline reserve capacity (Baltes, 1987; Stern, 2002), flexibility denotes the capacity to optimize the brain's performance within the limits of the current state of functional supply. From an interindividual differences perspective, both a less and a more flexible individual may perform accurately when faced with low demands on a cognitive task, whereas only the more flexible individual may perform accurately when challenged with high environmental demands. The mismatch model also fits the typical learning curve of initially rapid, but then diminishing increases in performance approaching an asymptotic level. As such, the mismatch model holds that functional supply initially responds to increased environmental demands, but later, when supply meets the demands, further impetus for plastic change is lost. From this perspective, stable levels of cognitive performance over defined periods of time can be interpreted as dynamic equilibrium states of reactive change within an individual's system. A key proposition within the framework is that some unknown duration of the supply-demand mismatch must be reached in order to drive the system away from its current dynamic equilibrium state (Bäckman & Dixon, 1992). Always responding to supply-demand mismatches with plastic changes would be functionally and economically maladaptive. However, the degree of responses to a mismatch may differ among various manifestations of plasticity, perhaps a function of the metabolic costs associated with their implementation. For example, structural processes involved in gliogenesis may take months to develop, whereas synaptogenesis and alterations involved in long-term potentiation (LTP) may

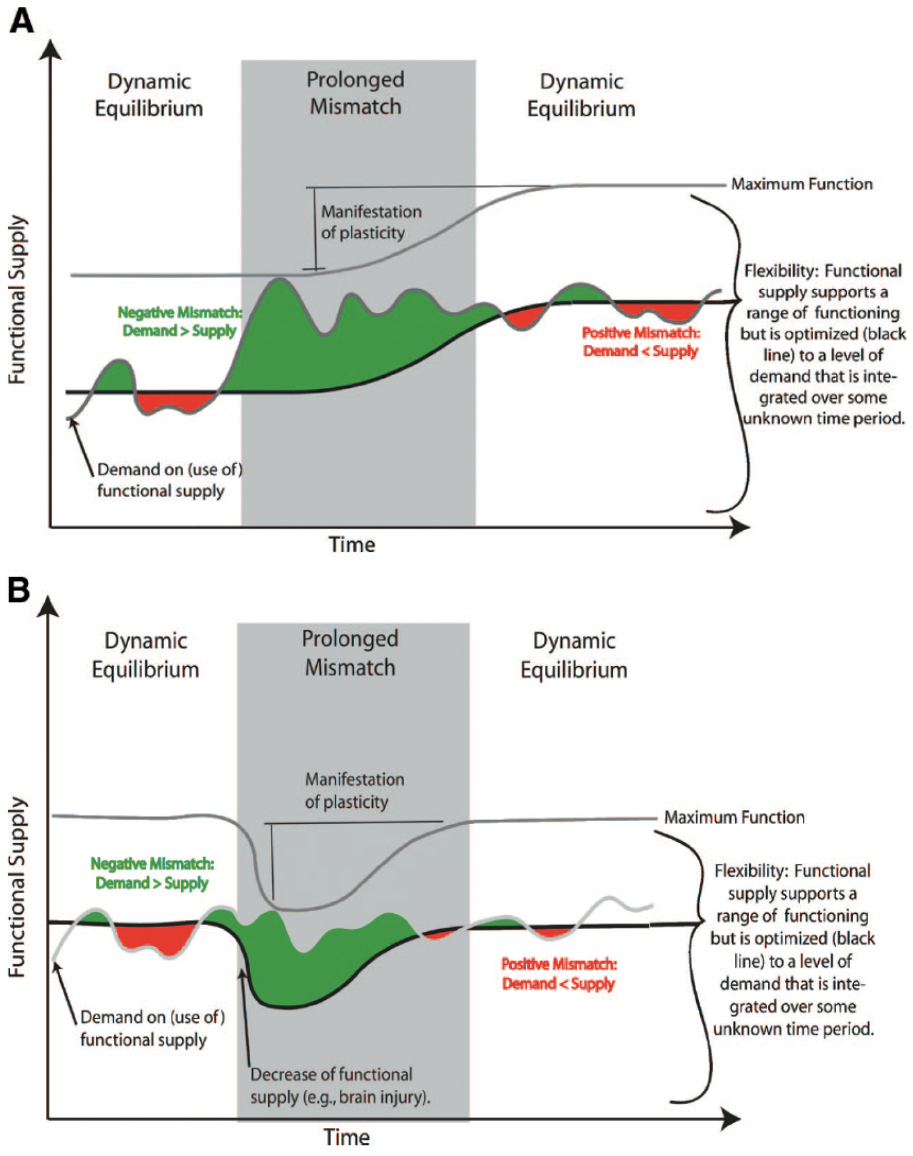

Figure 3) The Mismatch Model of adult cognitive plasticity.

Schematic model of a mismatch between functional supply and experienced environmental demands caused by primary changes in demand (Figure 3A) and primary changes in functional supply (Figure 3B). Functional supply (i.e., the structural constraints imposed by the brain on function and performance) allows for range of performance and functioning. Flexibility denotes the capacity to optimize the brain's performance within the limits of the current state of functional supply. Due to the sluggishness of plasticity, structural supply optimizes its support for function to a level of demand (i.e., use of functional supply) that is averaged over some unknown time period, and mismatches need to be prolonged to overcome the inertia and sluggishness of plasticity and to push the system away from its dynamic equilibrium. Deviations in demand that are within the current range of functional supply constitute the mismatch that constitutes the impetus for change. Alternatively, decreases in functional supply combined with unaltered demand (Figure 3B), decreases in demands (not shown), or increases in supply may constitute impetus for change through the same principle of a mismatch between demand and supply (Lövdén, Bäckman, Lindenberger, Schaefer, & Schmiedek, 2010).

develop over hours, minutes or seconds. These diverse neural alterations do not allow for an absolute time metric of plasticity to be defined, however the mismatch model stipulates that the phase of development of a plastic response must be longer than the time it takes to induce the initial and primary plasticity-inducing change in demand or supply. The mismatch model also recognizes that functional outcomes of supply-demand alterations may result in cognitive performance improvements because an individual has acquired knowledge relevant to the particular task, has improved in task-relevant processing efficiency, or through a combination of both processes. For example, improvements in performance attributed to knowledge acquisition include declarative memory (e.g., mathematical problems of a particular nature can be solved by applying a specific algorithm or equation), learned stimulus-response mappings (e.g., yes response = left button), and functional strategies (e.g., test-taking strategies, vigilance). Improvements in processing efficiency are due to one or more cognitive processes (e.g., working memory, perceptual speed, inhibitory control, associative binding) that generalize to task-specific content and result in increased performance gains (Lövdén et al., 2010). The mismatch model is an empirically-based theoretical framework that provides a useful operational definition of plasticity, and allows for the meaningful investigation of cognitive plasticity across the adult lifespan.

Plasticity as a Predictor of Cognitive Impairment

Characterizing the performance of older adults at risk for cognitive impairment (e.g., Mild Cognitive Impairment (MCI)/Cognitive Impairment No Dementia (CIND)) has become a major focus of aging research in recent years. To date, most studies investigating the predictive utility of cognitive plasticity have used the Testing-the-Limits

(TtL) experimental design. The TtL approach is composed of three phases: First, the subject performs a series of cognitive tasks (e.g., word list memorization) and baseline performance is assessed. Second, the subject is exposed to performance-enhancing conditions. The range of training conditions can vary from simple retest exposure, to targeted cognitive strategies (e.g., method of loci). Finally, the subject is retested under standard conditions. Baseline and retest measurements are calculated, and the difference represents a measure of cognitive plasticity (Baltes, Kuhl, & Sowarka, 1992).

Using a TtL design, Schreiber and Schneider (2007) evaluated the discriminative ability of the *Adaptive Figure Series Learning Test* (ADAFI) to identify individuals diagnosed with MCI versus healthy matched controls (n = 42; age range = 55-80 years). The ADAFI is a computer based learning test designed to assess fluid intelligence. A series of 12 coloured figures, with one figure missing, is presented to the subject. The task is to search and identify the correct missing figure from a pool of alternatives. Very easy items are initially presented and task items increase in difficulty after each correct solution. Following an error, subjects receive specific feedback aids as a form of cognitive training. Cognitive plasticity is measured by an algorithm that combines the number of tasks and number of aids provided to the subject (Schreiber, Schneider, Schweizer, Beckmann, & Baltissen, 2000). Results of the training intervention indicate significant improvements in post-test performance for both groups, however the MCI subjects profited less (i.e., displayed reduced levels of cognitive plasticity) from the intervention compared to healthy controls (Schreiber & Schneider, 2007).

In a series of similarly designed studies, Calero and Navarro (2004; 2007) evaluated the *Auditory Verbal Learning Test of Learning Potential* (AVLT-LP) and the

Position Learning Potential Test (PLPt) as measures of cognitive plasticity in a sample of individuals diagnosed with MCI (n = 203; age range = 60-93 years), who were followed longitudinally with assessments at 9-months, 12-months, and 24-months. The AVLT-LP is a test of verbal recall, and is an adaptation of the original Rey Verbal Learning Test (Rey, 1964). In the learning potential version, word list presentations three and four constitute a training phase and include reinforcement, feedback on performance, and repetition of forgotten words. Following the sixth and final word list presentation, a gain score of more than 2.5 words (Presentation 1 vs. Presentation 6 pre-post difference) is considered evidence of cognitive plasticity (Calero & Navarro, 2004). The PLPt is an adaptation of the original Fixing Positions test (Rey, 1964), designed to evaluate memory, spatial learning, and orientation. Subjects are presented with a series of charts and instructed to learn and memorize specific locations within a grid. In the learning potential version, performance feedback and assistance are provided to subjects with each successive failed attempt. In accordance with the TtL experimental approach, pre-post total gain scores are calculated and considered to represent a measure of cognitive plasticity. Results of the Calero & Navarro longitudinal studies revealed significant levels of cognitive plasticity in both MCI and control groups, measured on the AVLT-LP and the PLPt. Of particular interest is the finding that subjects with high baseline levels of cognitive plasticity maintained stable levels of cognitive functioning at 12- and 24-month follow-up (Calero & Navarro, 2004; 2007).

Fernandez-Ballesteros and colleagues (2003) provided additional support for measures of cognitive plasticity as potential diagnostic tools for the assessment of cognitive impairment. The *Battery of Learning Potential Assessment for Dementia*

(BEPAD) was evaluated for its discriminative power in identifying healthy adults from those with MCI and Alzheimer's Disease (AD; n = 200; M age = 74 years). The BEPAD measures four cognitive domains including verbal recall (AVLT-LP), verbal fluency (Verbal Fluency Test (VFt)), visuospatial processing (PLPt), and executive control (Hanoi Tower Learning Potential Test (HTLPt). A series of standardized training intervention procedures have been developed for each of the tests and include feedback, reinforcement, practice, and cognitive representation. Results of the BEPAD study revealed comparable baseline cognitive performance across all measures for the MCI and AD groups. However, post-test training gains on measures of verbal recall, visuospatial processing, and executive control were greater for the MCI versus AD group, suggesting more efficient learning and increased cognitive plasticity (Fernandez-Ballesteros, Zamarron, Tarraga, Moya, & Iniguez, 2003).

Two main findings have been drawn from research studies of cognitive plasticity as a predictor of cognitive impairment: 1) older adults at risk for dementia profit less (i.e., show reduced levels of cognitive plasticity) from cognitive training interventions compared to healthy matched controls; and 2) cognitive plasticity scores magnify inter-individual differences to a greater degree than traditional baseline status-oriented tests (Raykov et al, 2002; Schreiber & Schneider, 2007). Despite these promising findings, there are a number of important limitations associated with the TtL experimental design. Typically, repeated measures (i.e., Between x Within) analysis of variance (ANOVA) is used to evaluate group differences across multiple trials. Additionally, most studies use several measures to assess cognitive plasticity. Scores from these tests are then rescaled into a common mean and variance, and compared against each other as factors in the

ANOVA (McArdle & Pringle, 2008). When comparing mean-level, pretest-posttest changes between treatment and control groups, many assumptions are made about the causal factors driving changes in cognitive performance. By focusing exclusively on mean-level changes, important pieces of information about the dynamics of plasticity-related alterations are missing and individual differences are largely ignored. For example, what magnitude of training effects is transferred from a learned skill to additional unlearned skills? Does the training intervention apply to all populations, or are individualized strategies required to unlock cognitive reserve capacity and active compensatory mechanisms? To what degree do uncontrolled covariates influence the effects of training interventions? It will be important for future studies of cognitive plasticity in aging to recognize these assumptions and develop appropriate a priori methodological approaches.

Variability as a Predictor of Cognitive Function

Three dimensions of variability should be considered when examining normative and maladaptive aging processes. First, interindividual (between-person) differences can be evaluated on a single task, at a single point in time. Second, intraindividual (within-person) variability can be measured for a single individual on multiple tasks on a single occasion. The third type of variability is also evaluated within one individual (intra-individual) on a single task, but measured over multiple occasions (Hultsch et al., 2000). In general, studies of intraindividual variability have demonstrated that: a) individuals tend to perform in fluctuating patterns over time; b) these fluctuations are not necessarily attributable to the unreliability of measures; and c) the magnitude of variability is

negatively correlated to levels of performance (Dixon et al., 2007; Nesselroade & Salthouse, 2004; Rabbitt et al., 2001; Ram, Rabbitt, Stollery, & Nesselroade, 2005).

In terms of normative aging processes, intraindividual variability can be represented by a U-shaped curve across the lifespan, with greater variability in childhood and older adulthood (Li et al., 2004; Williams, Strauss, Hultsch, & Hunter, 2007; Williams et al., 2005). Importantly, adult age-related increases in variability have been observed both cross-sectionally (Li, Huxhold, & Schmiedek, 2004; Li et al., 2004; Shammi et al., 1998) and longitudinally, with increased acceleration of variability in old-old adulthood (Deary & Der, 2005; Der & Deary, 2006; MacDonald et al., 2003). Additionally, intraindividual variability has been shown to be an enduring trait-like characteristic, highly correlated across time points and cognitive domains (Fuentes, Hunter, Strauss, & Hultsch, 2001; Hultsch et al., 2002; Hultsch et al., 2000; Rabbitt et al., 2001), is associated with risk of attrition (MacDonald, et al., 2003), and predicts impending death (MacDonald et al., 2008).

With regard to pathological aging processes, increased intraindividual variability is associated with a range of maladaptive behaviours including poorer cognitive ability (Hultsch et al., 2002), decreased physical performance (Li, Aggen, Nesselroade, & Baltes, 2001), and reduced lifestyle engagement (Bielak, Hughes, Small, & Dixon, 2007). Intraindividual variability is also associated with a variety of neurological conditions, including traumatic brain injury (TBI; Stuss, Murphy, Binns, & Alexander, 2003), Mild Cognitive Impairment (MCI; Christensen et al., 2005), and neurodegenerative diseases (dementia, Hultsch et al., 2000; Parkinson's disease, Burton, Strauss, Hultsch, Moll, & Hunter, 2006). Evidence from the cognitive neuroscience literature has demonstrated

associations between increased intraindividual variability in performance and various brain markers (MacDonald et al., 2006) including structural brain characteristics (Anstey et al., 2007; Bunce et al., 2007), functional activation (Bellgrove, Hester, & Garavan, 2004; MacDonald, Nyberg, Sandblom, Fischer, & Bäckman, 2008), and modulatory neurotransmitters (MacDonald, Cervenka, Farde, Nyberg, & Bäckman, 2009).

Education as a Moderator of Cognitive Function

It is well established that the impact of aging on cognitive function is a complex process, influenced by interactive environmental and biological variables. Experimental studies suggest that changes facilitated by enriched environments and formal training in behavioural tasks result in a range of positive outcomes including increased neurogenesis and synaptogenesis, increased supportive glial cells, increased neural capillary networks, and a cascade of neurochemical processes (Black, Isaacs, Anderson, Alcantrara, & Greenough 1990; Kempermann, Kuhn, & Gage, 1997; Rosenzweig & Bennett, 1996). Human studies have investigated the influence of environmental richness by evaluating the impact of the number of years of formal education on cognitive abilities. Although education is not a pure measure of environmental richness or cognitive stimulation, it is assumed that formal educational training is a critical experience that evolves over many years, and its impact is likely to modulate cognitive functioning in older adulthood (Kramer, Bherer, Colcombe, Dong, & Greenough, 2004).

A number of longitudinal studies have examined the effects of education and other environmental factors on cognitive abilities across the adult lifespan (Schaie & Hofer, 2001). Many such studies found that the correlation between cognitive functioning and years of education in older adults to be highly dependent on the type of cognitive

outcome measured used (Anstey & Christensen, 2000). For example, studies using measures of general mental status (e.g., Mini-Mental Status Examination (MMSE)), which are known to have poor diagnostic sensitivity among highly functioning individuals, generally showed a protective effect of formal education (Lyketsos, Chen, & Anthony, 1999). Similarly, studies reporting changes in memory performance and crystallized intelligence also reveal a protective effect for number of years of education. The MacArthur Studies of Successful Aging, a large-scale longitudinal study, identified lower education as the strongest predictor of cognitive decline on measures of verbal and non-verbal memory, conceptualization, and non-verbal abilities, when examining cognitive changes in older adults (age range = 70-79 years) over 2.5 years (Albert, Jones, Savage, et al. 1995). In contrast, education appears to be a less powerful predictor of change in fluid abilities and processing speed. Christensen and colleagues (1997) studied a comparable sample of individuals (age range = 70-79 years) over 3.6 years and found that education predicted performance on measures of general mental status and verbal abilities (e.g., verbal fluency, similarities), but not on measures of processing speed. Despite such findings of positive effects of education on cognitive functioning, some longitudinal studies of aging have not observed comparable protective effects. For example, the PAQUID study (n = 547; age range = 65-94 years) found that education is associated with better baseline MMSE scores, but does not predict cognitive decline over a 10-year period (Winnock et al., 2002). The varied results of such studies suggest that education may serve as a moderator of cognitive decline in older adults. However, the specificity of this relationship and its interaction with other related factors (e.g., expertise, lifestyle engagement, socioeconomic status) remains to be clearly established.

Objectives & Hypotheses

A considerable body of recent research has demonstrated meaningful heterogeneity in trajectories of cognitive change among older adults. However, few studies have systematically evaluated plasticity and variability as predictors of longitudinal change – and to my knowledge, none have done so in the same study. The current research study investigates the relationship between cognitive plasticity, intraindividual variability, and long term cognitive function in older adults.

Specific Research Questions:

1. Does baseline intraindividual variability predict subsequent cognitive function?

This research question looks to verify the longitudinal relationship between intraindividual variability in baseline performance (indexed as individual standard deviations (ISD) on Reaction Time (RT) tasks) and long-term (5 year) cognitive function (Bielak, Hultsch, Strauss, MacDonald, & Hunter, 2010a, 2010b; Hultsch, et al., 2002; MacDonald et al., 2003, 2008).

2. Does baseline cognitive plasticity predict subsequent cognitive function?

Individual differences in cognitive plasticity (indexed as RT performance gains across weekly reassessments at the baseline measurement wave) will be investigated as a significant predictor of long-term (5 year) cognitive function. Our conceptualization of cognitive plasticity is based on the mismatch model (Lövdén et al., 2010), which suggests that adult cognitive plasticity is driven by reactive changes in response to a prolonged mismatch between an individual's functional supply and environmental demands.

3. Do specific factors (age, education, intraindividual variability, cognitive plasticity) predict long-term rates of cognitive change, and do the observed patterns vary as a function of cognitive domain?

This research question aims to determine whether individual differences in intraindividual variability and cognitive plasticity predict longitudinal rates of cognitive change, and whether these associations vary as a function of cognitive domain. In terms of intraindividual variability, we expect the RT task with a greater cognitive load (i.e., 1-Back 4-Choice RT (BRT)) to share a stronger association with cognitive decline for more fluid (Digit Symbol, Letter series) versus crystallized (Word Recall, Verbal Fluency, Vocabulary) cognitive measures. With regards to cognitive plasticity, we expect to find increased positive slope estimates in rates of plasticity (i.e., performance gains across Year 1 weekly burst assessments), to share a stronger association with cognitive change for more fluid versus crystallized tasks. Overall, we predict that individuals who display lower levels of baseline variability and higher levels of cognitive plasticity will maintain greater cognitive stability (or reduced cognitive decline) across time, relative to individuals who exhibit greater variability and lesser cognitive plasticity at baseline. Chronological age (years) and total years of formal education are included in all analysis, in order to investigate the possible moderating effects of these demographic variables on the relationship between intraindividual variability, cognitive plasticity, and longitudinal cognitive function.

Methods

Data for the current study are derived from Project MIND, a longitudinal study conducted at the University of Victoria (Victoria, British Columbia, Canada) from 2001-2007. Project MIND was designed to investigate short-term inconsistency, reflecting moment-to-moment fluctuations in cognitive performance, as well as long-term changes in a range of cognitive, physical, and psychological measures associated with aging. As previous reports have described the Project MIND methodological design and baseline demographic characteristics in detail, only sections relevant to the current study will be summarized (Bielak et al., 2010a, 2010b; Burton, Strauss, Hultsch, & Hunter, 2009; Strauss, Bielak, Bunce, Hunter, & Hultsch, 2007).

Participants

A total of 304 community-dwelling older adults (females n = 208, males n = 96), aged 64 to 92 years (M age = 74.02, SD = 5.95), comprised the baseline sample. All participants were of Caucasian descent, resided in the greater Victoria, British Columbia, Canada metropolitan area, and were recruited through advertisements in local media (e.g., newspaper, radio) requesting healthy volunteers concerned about their mental functioning. Initial exclusionary criteria included a diagnosis of dementia by a physician, a Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) score less than 24, a history of significant head injury (defined as loss of consciousness for more than 5 minutes), other neurological or major medical illness (e.g., Parkinson's disease, heart disease, cancer), severe sensory impairment (e.g., difficulty reading newspaper-size print, hearing a normal conversation), drug or alcohol abuse, a current

psychiatric diagnosis, psychotropic drug use, and lack of fluency in English. Informed written consent was obtained from each participant, and the study was approved by the University of Victoria Human Research Ethics Board.

Participants provided demographic (e.g., age, years of education) and self-reported health information during an initial intake interview. In addition to the MMSE, several benchmark cognitive measures were administered, including the Wechsler Adult Intelligence Scale-III (WAIS-III; Wechsler, 1997) Block Design and Vocabulary subtests, and the North American Adult Reading Test (NAART; Blair & Spreen, 1989). Estimates of full scale IQ (FSIQ) were computed based on age-adjusted Block Design and Vocabulary subtests (Sattler & Ryan, 1999), while premorbid IQ was based on NAART performance (Blair & Spreen, 1989).

Procedure

An initial telephone interview was conducted to identify eligible Project MIND participants, based on inclusion and exclusion criteria. Following initial screening, participants were administered the full range of study measures, across seven sessions (1 group, 6 individual), scheduled over approximately 3 months. The complete testing battery was repeated annually, for a total of six waves of data (baseline + Year 2 testing + Year 3 testing + Year 4 testing + Year 5 Interview + Year 6 testing) (see Figure 4).

Group testing sessions were held in the Project MIND laboratories at the University of Victoria, while individual testing sessions were conducted in the participants' home. For each annual wave, the first two sessions were used to obtain demographic and health information, and to assess participants' cognitive ability. Participants then completed a '*burst'* evaluation of five individual testing sessions, each

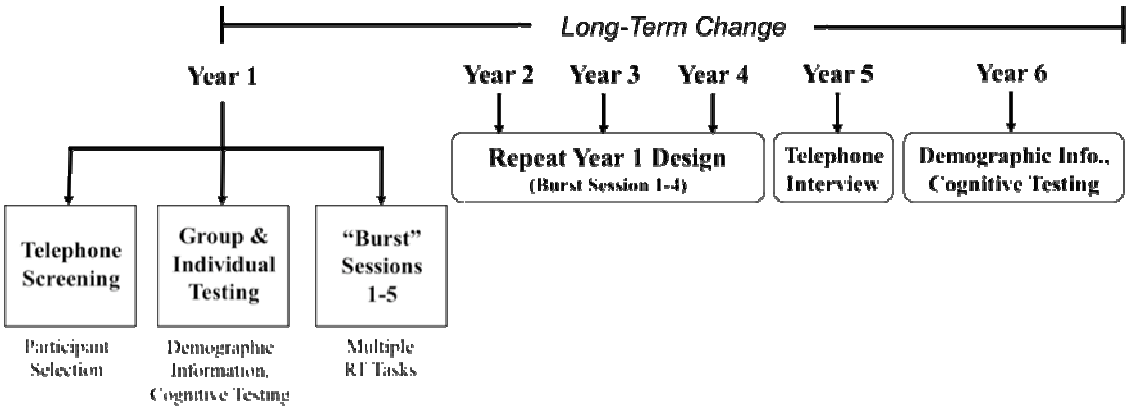

Figure 4) Project MIND Study Design.

scheduled approximately two weeks apart (for waves 2 through 4, only four individual burst testing sessions were conducted). During each of the burst sessions, participants completed a battery of reaction time (RT) tasks, designed to assess short-term fluctuations in response speed. For each annual wave, the burst RT measures were identical and the order of presentation was invariant. However, scheduling of the burst sessions was distributed across days of the week and times of the day, because a primary goal of Project MIND was to investigate individual variability in performance.

Measures

Cognitive Tasks

Cognitive ability was based on a neuropsychological test battery comprised of a series of measures assessing a range of cognitive processes and domains. The test battery was administered once per annual wave, using standardized group procedures.

Processing Speed: Perceptual processing speed was assessed with the WAIS-Revised Digit Symbol Substitution task (Wechsler, 1981). Participants were presented with a

coding key pairing nine numbers (1 through 9), with nine corresponding symbols. The task requires participants to transcribe as many symbols as possible into rows of randomly ordered numbers with empty boxes, in 90 seconds. The number of correctly completed items represented the outcome measure.

Fluid Reasoning: Participants' fluid reasoning was assessed with the Letter Series Test (Thurstone, 1962). In the Letter Series Test, participants were presented with sets of letter strings that formed a distinct pattern. The task required participants to inductively decipher the pattern and to generate the next letter in the string that was congruent with the pattern. The number of correct responses generated in 6 minutes from a total of 20 strings of letters was the outcome measure.

Episodic Memory: Episodic memory was assessed using a word recall task consisting of immediate free recall of 30 English words (Hultsch, Hertzog, & Dixon, 1990). The word list consisted of 6 words from 5 taxonomic categories (e.g., birds, flowers), presented on a single page in unblocked order. Participants were given 2 minutes to study the list and 5 minutes to write their recall of as many words as possible. The number of correctly recalled words was used as the outcome measure.

Verbal Fluency: Participants' verbal fluency was assessed using the Controlled Associations Test (Ekstrom, French, Harman, & Dermen, 1976), which required participants to generate as many synonyms as possible in response to a set of four target words. Participants were given 6 minutes to complete the test. The outcome measure was the total number of correct synonyms.

Crystallized Ability: Crystallized ability was assessed using a 36-item multiple-choice recognition vocabulary test (Ekstrom et al., 1976). Participants were instructed to select

the correct definition of a target word from five possible definitions. Participants were given 10 minutes to complete the test. The total number of correct items was the outcome measure.

Global Cognitive Functioning: The Mini-Mental State Examination (MMSE; (Folstein et al., 1975) was administered as a measure of global cognitive functioning. Participants responded to a series of basic questions related to orientation (time and place), memory, attention and concentration, language functioning, arithmetic calculations, and visuospatial processing. A total score out of 30 was the outcome measure.

Reaction Time (RT) Tasks

A series of multi-trial computer-based tasks, varying in complexity, were used to assess participants' reaction time (RT) to the nearest millisecond (ms). RT tasks were presented on a 14" colour laptop screen, with a specifically configured external keyboard attached to the computer. For all tasks, participants were instructed to emphasize speed in responding to stimuli, while minimizing errors to the best of their ability. The RT tasks were administered 5 times for the baseline burst testing wave, and 4 times for each subsequent wave of annual burst testing (Waves 2-4). At each wave, the RT testing sessions were scheduled approximately 2 weeks apart, and tasks were individually administered at the participants' home.

Four-choice RT (CRT) task: Participants were presented with a horizontal row of four plus (+) signs, with a matching arrangement of keys on a response keyboard. Following a 1000ms delay, one plus sign changed into a box, and the participant was required to press the key corresponding to its location as quickly as possible. The location of the box was

randomly equalized across trials. Practice trials (n = 10) were administered first, followed by 60 test trials. The latencies and percent correct for the test trials were recorded.

Four-choice one-back RT (BRT) task: The BRT task used the same display, response keyboard, and stimulus presentation design as the CRT task. However, participants were instructed to press the key corresponding to the location of the box on the previous trial as quickly as possible. A total of 10 practice trials and 61 test trials were administered. Because participants made no response on Trial 1, the latencies and percent correct of the remaining 60 test trials were assessed.

Statistical Analyses

Data Preparation

Age Classification: All analyses in the current study include age as a predictive factor to determine whether it can significantly account for a proportion of the between-person variance in inconsistency, cognitive plasticity, and cognitive function. To describe the Project MIND sample characteristics, all participants were classified into two groups based on age at first occasion of testing: a Young-Old group (ages 64-74 years), and an Old-Old group (ages 75-92 years). This classification represents a commonly used division between older adults (Hultsch et al., 2002; MacDonald et al., 2003; Strauss et al., 2007), with this division reflecting the approximate mean age of the overall sample (M = 74.29). For research questions 1 and 2, chronological age (in years) at baseline testing was entered as a continuous predictor in a series of hierarchical multiple regression models. For research question 3, age was centered at 75 years and added as a continuous predictor for all multilevel model analyses.

Outliers & Missing Values: The complete RT data set was examined for outliers by evaluating the distributions of raw latency scores at the level of individual trials. Extremely fast or slow responses likely represent sources of measurement error (e.g., accidental key press, distraction of participant), and prior research has suggested valid lower bounds for responses (150 ms; Hultsch et al., 2002). Upper boundaries were identified by computing the mean and standard deviation for each task and occasion of measurement and any trials that exceeded the mean by three or more standard deviations were removed. Missing value estimates were imputed using a regression substitution procedure that forms individual equations of response times across all trials, which is then used to predict the missing RT entry (Hultsch et al., 2000). By applying these data preparation procedures for eliminating outliers and imputing missing values, within-subject variation is reduced, thus representing a conservative approach to examining intraindividual variability and cognitive plasticity in response time performance.

Computation of Intraindividual Variability: A general index of each individual's performance distribution was computed as the across-trial within-person individual standard deviation (ISD) about each individual's mean RT (Hultsch et al., 2008). Potential confounding effects (e.g., age differences in mean RT) were controlled for using a split-plot regression:

$$Y = a + b(\text{Age Group}) + c(\text{Trial}) + d(\text{Age Group x Trial}) + e.$$

Using the resulting residuals from this regression ensures that any systematic within-subject (i.e., trial) and between-subject (i.e., age group) sources of variance in mean RT are removed. Therefore, each individual's level of performance variability can be effectively measured. To facilitate comparisons across tasks, the residual scores were

converted to standardized T scores (M = 50, SD = 10). ISD values were then individually averaged across the five sessions (4 sessions for Waves 2-4) for each RT task, producing one ISD score per task per wave for each individual.

Computation of Cognitive Plasticity: In the current study, cognitive plasticity refers to levels of performance attained following repeated exposure to RT tasks. This conceptualization of basic cognitive plasticity is in accordance with the mismatch model (Lövdén et al., 2010) which asserts that some unknown duration of supply-demand mismatch must occur in order to disrupt an individual's dynamic equilibrium state (between functional supply and environmental demands), and drive the system to respond with increased cognitive performance. Our operationalization of cognitive plasticity is computed as within-person RT performance gains across trials and 5 weekly burst sessions for the first year of measurement (see Figure 4). Specifically, cognitive plasticity is indexed as individual slopes of cognitive change for the CRT and BRT tasks, derived from 2-level multilevel models of cognitive change (mean response latency for weekly burst assessments nested within individuals). Response latencies (in milliseconds) were analyzed from all trials, including correct and incorrect responses.

Multilevel Models of Change

In contrast to cross-sectional studies, longitudinal research designs are based on repeated observations of the same individual over multiple time points, allowing for greater examination of the factors involved in rates of change associated with cognitive aging (Singer & Willett, 2003). Advanced statistical techniques, such as multilevel modeling (also known as hierarchical linear models (HLM), random-effects models,

mixed-effects models, random regression models, or growth curve models), are very flexible frameworks for the study of repeated measurements across time and are currently used to analyze longitudinal data sets. There are a number of advantages of multilevel modeling relative to other longitudinal statistical approaches (e.g., repeated measures ANOVA) including: 1) the examination of all available data, thus maximizing the number of participants and increasing the statistical power to detect change; 2) relaxed assumptions regarding comparable change across all participants (both mean change and variance about the mean are estimated); and 3) simultaneous assessment of individual differences at baseline and change over time (Chu et al., 2007).

Given that the focus of multilevel modeling is on change at the individual level, two separate questions can be asked. First, how does each person change over time at a micro-level (*Level 1; within-individual differences in change*). Second, which variables differentiate individual patterns of change at a macro-level (*Level 2; between-individual differences in within-individual change over time*). Multilevel modeling integrates these hierarchical levels of analysis by fitting separate Level 1 trajectories for each individual, with these subject-specific parameters serving as the outcomes to be predicted by Level 2 models. Typical Level 1 models can be described by the following equation:

$$\text{Level 1:} \quad Y_{ij} = \beta_{0i} + \beta_{1i}\,(x_{ij}) + e_{ij}$$

In this equation, a change in Y (e.g., cognitive performance on a specific measure) for a given individual (*i*) at a given measurement occasion (*j*) is a function of that individual's performance for x = 0 (the intercept: β_{0i}), plus the individual's average linear rate of change per unit change in x (the slope; β_{1i}), plus an error term (e_{ij}) reflecting within-individual residual variance remaining to be explained after controlling for x (time

metric). The selection of an appropriate Level 1 time metric (x) for the data, based on relative best fit, is a necessary condition before Level 2 moderators can be examined (Sliwinski, Hofer, Hall, Buschke, & Lipton, 2003). A typical Level 2 model can be represented by the following equations:

$$\text{Level 2:} \quad \beta_{0i} = \gamma_{00} + \gamma_{01}(\text{GROUP}_i) + u_{0i}$$
$$\beta_{1i} = \gamma_{10} + \gamma_{11}(\text{GROUP}_i) + u_{1i}$$

For the Level 2 models, each individual's intercept (β_{0i}) is estimated as a function of the population average intercept (γ_{00}) for x = 0 and GROUP = 0, plus the population average difference in intercepts (γ_{01}), plus the residual variance from between-individual differences in intercept (u_{0i}). Correspondingly, the Level 1 slopes (β_{1i}) for each individual are modeled as a function of the population average change (the slope; γ_{10}) for x = 1 and GROUP = 0, plus the population average difference in slopes (γ_{11}) for x = 1 and GROUP = 1, plus the residual variance about the true slope (u_{1i}) remaining to be explained. The Level 2 equations can be understood as explanatory models to which the effects of moderating variables (e.g., age, education) influence individual differences in starting points (intercepts) and rates of change (slope) on outcomes of interest (e.g., performance on specific cognitive tasks). An example of a multilevel model including such moderators can be represented by:

$$\text{Level 1: Cognitive Performance}_{ij} = \beta_{0i} + \beta_{1i}(\text{Time in Study}_{ij}) + e_{ij}$$

$$\text{Level 2:} \quad \beta_{0i} = \gamma_{00} + \gamma_{01}(\text{Age}) + u_{0i}$$
$$\beta_{1i} = \gamma_{10} + \gamma_{11}(\text{Age}) + u_{1i}$$

Model estimation is an additional benefit of using multilevel modeling for the analysis of longitudinal change. Maximum likelihood estimates are computed through multiple (log) iterations, to produce values of the unknown population parameters that maximize the probability of having observed the sample of data. Full information maximum likelihood (FIML) modeling maximizes estimates of both fixed and random parameters.

Results

Participant Characteristics

Baseline demographic characteristics of the Project MIND sample are summarized in Table 1 as a function of age group (Young-Old versus Old-Old). Overall, the study participants were highly educated (M = 15.16, SD = 3.14), ranging from 7 to 24 years of education, with only 10.2% (n = 31) having less than 12 years of formal education. The participants were relatively healthy, with 65.5% (n = 199) having 3 or fewer chronic health conditions. The participants' global cognitive functioning was quite high (MMSE; M = 28.74, SD = 1.23), but consistent with an independent sample (Victoria Longitudinal Study (VLS)) of older adults recruited from the same geographic population (Dixon et al., 2007). Limited sample attrition was observed across the six year study, with 84.5% (n = 257) of the original sample completing Years 2 and 3, 79.6% (n = 242) completing Years 4 and 5, and 71.4% (n = 217) completing Year 6.

To examine group differences in age, a multivariate analysis of variance (MANOVA) including all dependent variables was conducted. There were significant overall multivariate effects for age group, $F(8, 293) = 5.49$, $p < .001$, $\eta^2 = 0.13$. Specifically, there were significant age group differences for education, $F(1, 300) = 14.03$, $p < .001$, $\eta^2 = 0.05$; total chronic health conditions, $F(1, 300) = 8.89$, $p < .005$, $\eta^2 = 0.03$; MMSE, $F(1, 300) = 26.28$, $p < .001$, $\eta^2 = 0.08$; WAIS-III estimated FSIQ, $F(1, 300) = 5.58$, $p < .05$, $\eta^2 = 0.02$; and NAART estimated IQ, $F(1, 300) = 5.14$, $p < .05$, $\eta^2 = 0.02$. The young-old individuals had significantly more years of education (M = 15.70, SD = 2.95) and reported fewer chronic health conditions (M = 2.56, SD = 1.77) compared to the old-old adults (Education; M = 14.41, SD = 3.26; Chronic Health Conditions; M =

3.42, *SD* = 1.99). In addition, the young-old adults performed significantly better on the MMSE (*M* = 29.03, *SD* = 1.01), and had higher estimated WAIS-III FSIQs (*M* = 120.66, *SD* = 11.86) and NAART estimated IQs (*M* = 117.04, *SD* = 6.62) than the old-old adults (MMSE; *M* = 28.35, *SD* = 1.30; WAIS-III FSIQ; *M* = 118.22, *SD* = 13.44; NAART IQ; *M* = 115.69, *SD* = 6.87).

Table 1) Project MIND Baseline Demographic Characteristics

Variable (*M*, *SD*)	**Young-Old (64-74 years) *n* = 170**	**Old-Old (75-92 years) *n* = 134**	**MANOVA**
Gender (Female: Male)	110:60	98:36	$F(8, 293) = 2.50$ $p<.05$, $\eta^2 = 0.06$
Age (Years)	70.09 (2.91)	80.06 (4.01)	$F(8, 293) = 5.49$ $p<.001$, $\eta^2 = 0.13$
Education (Total Years)	15.70 (2.95)	14.41 (3.26)	$F(1, 300) = 14.03$ $p<.001$, $\eta^2 = 0.05$
Chronic Health Conditions (Total #)	2.56 (1.77)	3.42 (1.99)	$F(1, 300) = 8.89$ $p<.005$, $\eta^2 = 0.03$
MMSE (Total Score)	29.03 (1.01)	28.35 (1.30)	$F(1, 300) = 26.28$ $p<.001$, $\eta^2 = 0.08$
WAIS-III Estimated FSIQ	120.66 (11.86)	118.22 (13.44)	$F(1, 300) = 5.58$ $p<.05$, $\eta^2 = 0.02$
NAART Estimated IQ	117.04 (6.62)	115.69 (6.87)	$F(1, 300) = 5.14$ $p<.05$, $\eta^2 = 0.02$

M = mean; *SD* = Standard Deviation; MANOVA = Multivariate Analysis of Variance; Total Chronic Health Conditions = self-reported presence of 16 chronic health problems (e.g., diabetes, arthritis, high blood pressure); MMSE = Mini-Mental State Examination; WAIS-III = Wechsler Adult Intelligence Scale-III; NAART = North American Adult Reading Test

Variability & Plasticity as Predictors of Cognitive Function

To investigate the relationship between baseline intraindividual variability (Research Question 1) and cognitive plasticity (Research Question 2) as predictors of subsequent (Year 6) cognitive function, six unique hierarchical multiple regression models, varying in sequential blocked entry, were generated for each of the five cognitive outcome measures (Letter Series, Digit Symbol, Word Recall, Verbal Fluency, Vocabulary). The relative contributions of demographic variables (age in years, total years of education), intraindividual variability (CRT ISD, BRT ISD), and cognitive plasticity (CRT plasticity, BRT plasticity) were assessed by adding each of the variables into the models as univariate or multivariate predictors of subsequent cognitive function.

First, pearson correlation coefficients were estimated for the relationships between intraindividual variability (ISD) and cognitive plasticity on each of the RT tasks (CRT, BRT) (Table 2). Significant associations were found for each of the variables, with correlations ranging from small to large (r <. 30 small, r = .30 - .50 moderate, r > .50 large; Cohen, 1977). The highest correlations were observed for the ISD-ISD association, along with the ISD-plasticity association for BRT, but not for CRT, perhaps reflecting task differences in cognitive load.

Table 2) Intercorrelations between Intraindividual Variability (ISD) and Cognitive Plasticity on Reaction Time (RT) tasks (CRT, BRT)

Variable	1.	2.	3.	4.
1. CRT ISD	1			
2. BRT ISD	.675**	1		
3. BRT Plasticity	-.385**	-.611**	1	
4. CRT Plasticity	-.307**	-.284**	.211**	1

**p<0.01; ISD = Intraindividual Standard Deviation; CRT = 4-Choice RT; BRT = 1-Back 4-Choice RT

Univariate Hierarchical Regression Analyses

Model 1 (Univariate CRT ISD & CRT Plasticity): In Model 1, univariate intraindividual variability and cognitive plasticity on the Four-Choice RT task (CRT) were evaluated as predictors of cognitive function using blocked order of entry in hierarchical regression. In the first block, demographic variables (chronological age in years and total number of years of formal education) were added, followed by CRT ISD (Block 2) and CRT plasticity (Block 3). As shown in Table 3, age and education significantly accounted for the largest proportion of variance in each of the five cognitive outcomes measures (Digit Symbol = 24.5%, Letter Series = 26.8%, Word Recall = 13.6%, Verbal Fluency = 10.7%, Vocabulary = 6.4%). Age uniquely contributed to Digit Symbol (β = -.497, p<.001) and Word Recall (Age: β = -.343, p<.001), Education uniquely contributed to Vocabulary (β = .234, p<.01), while both Age and Education each contributed significantly to performance on Letter Series (Age: β = -.409, p<.001; Education: β = .232, p<.001), and Verbal Fluency (Age: β = -.197, p<.01; Education: β = .220, p<.01). In block 2, CRT ISD significantly accounted for additional variance, above and beyond that accounted for by demographic variables, for each of the five cognitive tasks (Digit Symbol = 7.6%, Letter Series = 5.2%, Word Recall = 6.4%, Verbal Fluency = 2.4%, Vocabulary = 5.7%). With the exception of Verbal Fluency, CRT ISD made unique contributions, relative to the total set of variables, in predicting subsequent cognitive performance (Digit Symbol: β = -.310, p<.001; Letter Series: β = -.2.57, p<.001; Word Recall: β = -.284, p<.001; Vocabulary: β = -.267, p<.001). In the third block, CRT plasticity only accounted for further unique variance on the Word Recall task (η^2 = .015), albeit uniquely significant (β = -.130, p<.05) independent of Block 1 (age, education) and Block 2 (CRT ISD) effects.

Table 3) Model 1: Hierarchical Regression Analysis for CRT ISD & CRT Plasticity as Predictors of Year-6 Cognitive Function

Digit Symbol	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.972	.121	-.497***	-.687	.129	-.351***	-.687	.129	-.351***
Education	-.035	.226	-.010	.039	.216	.011	.039	.217	.011
CRT ISD				-1.791	.369	-.310***	-1.792	.387	-.310***
CRT Plasticity							.000	.091	.000
R^2		.245			.321			.321	
$R^2\Delta$					.076			.000	
F for Δ in R^2		34.418***			23.553***			.000	
Letter Series	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.334	.049	-.409***	-.235	.054	-.287***	-.234	.054	-.287***
Education	.358	.093	.232***	.383	.090	.248***	.385	.091	.250***
CRT ISD				-.624	.155	-.257***	-.600	.163	-.247***
CRT Plasticity							.019	.038	.030
R^2		.268			.320			.321	
$R^2\Delta$					.052			.001	
F for Δ in R^2		38.993***			16.192***			.249	
Word Recall	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.300	.058	-.343***	-.183	.063	-.210**	-.183	.062	-.209**
Education	.121	.108	.074	.151	.105	.092	.142	.104	.087
CRT ISD				-.734	.179	-.284***	-.846	.186	-.327***
CRT Plasticity							-.088	.044	-.130*
R^2		.136			.200			.215	
$R^2\Delta$					.064			.015	
F for Δ in R^2		16.752***			16.781***			4.052*	

Table 3) (continued) **Model 1**: Hierarchical Regression Analysis for CRT ISD & CRT Plasticity as Predictors of Year-6 Cognitive Function

Verbal Fluency	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.196	.066	-.197**	-.117	.073	-.117	-.119	.073	-.119
Education	.412	.124	.220**	.428	.123	.228**	.416	.123	.222**
CRT ISD				-.513	.213	-.172	-.613	.222	-.206**
CRT Plasticity							-.081	.052	-.105
R^2		.107			.131			.141	
$R^2\Delta$					.024			.010	
F for Δ in R^2		12.875***			5.787*			2.405	
Vocabulary	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.039	.048	-.055	.048	.052	.068	.048	.053	.068
Education	.311	.091	.234**	.328	.088	.247***	.327	.088	.246***
CRT ISD				-.565	.153	-.267***	-.575	.160	-.272***
CRT Plasticity							-.008	.038	-.014
R^2		.064			.120			.121	
$R^2\Delta$					.057			.000	
F for Δ in R^2		7.272***			13.70***			.043	

* p<0.05; **p<0.01; ***p<0.001; CRT = 4-Choice RT; ISD = Intraindividual Standard Deviation

Model 2 (Univariate CRT Plasticity & CRT ISD): In order to more fully examine the relative contributions of CRT predictors, the hierarchical regression analysis was re-run, reversing the order of entry for CRT Plasticity and CRT ISD (relative to Model 1). Table 4 demonstrates that, as the order of model entry did not change, the proportion of variance accounted for by the Block 1 demographic variables (age, education) was identical to the Table 3 estimates for each of the five cognitive outcomes measures (Digit Symbol = 24.5%, Letter Series = 26.8%, Word Recall = 13.6%, Verbal Fluency = 10.7%, Vocabulary = 6.4%). Notably, when CRT Plasticity was entered at Block 2, it failed to account for any additional variance, above and beyond the demographic variables, for any of the cognitive measures. In contrast, when CRT ISD was entered in the final step (Block 3), it was still able to account for a significant proportion of variance in cognitive performance for each of the five tasks (Digit Symbol $\eta^2 = .069$, $\beta = -.310$, $p<.001$; Letter Series $\eta^2 = .044$, $\beta = -.247$, $p<.001$; Word Recall $\eta^2 = .077$, $\beta = -.327$, $p<.001$; Verbal Fluency $\eta^2 = .031$, $\beta = -.206$, $p<.001$; Vocabulary $\eta^2 = .054$, $\beta = -.272$, $p<.001$).

Table 4) Model 2: Hierarchical Regression Analysis for CRT Plasticity & CRT ISD as Predictors of Year-6 Cognitive Function

Digit Symbol	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.972	.121	-.497***	-.947	.122	-.485***	-.687	.129	-.351***
Education	-.035	.226	-.010	-.016	.226	-.004	.039	.217	.011
CRT Plasticity				.125	.091	.082	.000	.091	.000
CRT ISD							-1.792	.387	-.310***
R^2		.245			.252			.321	
$R^2\Delta$		.245			.007			.069	
F for Δ in R^2		34.418***			1.871			21.390***	
Letter Series	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***B***	***B***	***SE B***	***β***
Age	-.334	.049	-.409***	-.321	.050	-.393***	-.234	.054	-.287***
Education	.358	.093	.232***	.368	.093	.239***	.385	.091	.250***
CRT Plasticity				.061	.038	.096	.019	.038	.030
CRT ISD							-.600	.163	-.247***
R^2		.268			.277			.321	
$R^2\Delta$					.009			.044	
F for Δ in R^2		38.993***			2.617			13.611***	
Word Recall	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.300	.058	-.343***	-.306	.059	-.350***	-.183	.062	-.209**
Education	.121	.108	.074	.116	.109	.071	.142	.104	.087
CRT Plasticity				-.029	.044	-.043	-.088	.044	-.130*
CRT ISD							-.846	.186	-.327***
R^2		.136			.138			.215	
$R^2\Delta$					.002			.077	
F for Δ in R^2		16.752***			.446			20.588***	

Table 4) (continued) Model 2: Hierarchical Regression Analysis for CRT Plasticity & CRT ISD as Predictors of Year-6 Cognitive Function

Verbal Fluency	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.196	.066	-.197**	-.205	.067	-.205**	-.119	.073	-.119
Education	.412	.124	.220**	.404	.125	.216**	.416	.123	.222**
CRT Plasticity				-.040	.051	-.051	-.081	.052	-.105
CRT ISD							-.613	.222	-.206**
R^2		.107			.110			.141	
$R^2\Delta$					.003			.031	
F for Δ in R^2		12.875***			.603			7.608**	
Vocabulary	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.039	.048	-.055	-.032	.049	-.046	.048	.053	.068
Education	.311	.091	.234**	.316	.091	.238**	.327	.088	.246***
CRT Plasticity				.031	.037	.057	-.008	.038	-.014
CRT ISD							-.575	.160	-.272***
R^2		.064			.067			.121	
$R^2\Delta$		.064			.003			.054	
F for Δ in R^2		7.272***			.715			12.965***	

* p<0.05; **p<0.01; ***p<0.001; CRT = 4-Choice RT; ISD = Intraindividual Standard Deviation

Models 3 & 4 (Univariate BRT ISD & BRT Plasticity): Models 3 and 4 added predictor variables into the regression analysis in the same sequential blocked order as Models 1 and 2 respectively, however univariate intraindividual variability and cognitive plasticity were evaluated for the more cognitively demanding 1-Back 4-Choice RT task (BRT) (see Tables 5 & 6). For both Model 3 and Model 4, age and education were found to significantly account for the largest proportion of variance in each of the five cognitive outcomes measures when entered in the first block.

In Model 3, BRT ISD was added in Block 2, and significantly accounted for additional variance, above and beyond that accounted for by demographic variables, for each of the five cognitive tasks (Digit Symbol $\eta^2 = .102$, $\beta = -.393$, $p<.001$; Letter Series $\eta^2 = .144$, $\beta = -.470$, $p<.001$; Word Recall $\eta^2 = .075$, $\beta = -.337$, $p<.001$; Verbal Fluency $\eta^2 = .044$, $\beta = -.259$, $p<.001$; Vocabulary $\eta^2 = .060$, $\beta = -.304$, $p<.001$). In the third block, BRT plasticity only added additional variance for Letter Series ($\eta^2 = .024$), providing significant unique contributions to the total set of variables (BRT Plasticity: $\beta = -.193$, $p<.01$).

To fully examine the relative contributions of BRT plasticity as a predictor of cognitive function, the order of entry was reversed in Model 4. Age and education were added first, followed by BRT plasticity, then BRT ISD. By adding BRT plasticity into the model in the second block, considerable differences were found compared to Model 3. Specifically, BRT plasticity in Model 4 accounted for a significant amount of unique additional variance, above and beyond that accounted for by demographic variables, for four of the five cognitive tasks (Digit Symbol $\eta^2 = .027$, $\beta = .176$, $p<.01$; Letter Series $\eta^2 = .107$, $\beta = .351$, $p<.001$; Word Recall $\eta^2 = .027$, $\beta = .174$, $p<.01$; Vocabulary $\eta^2 = .016$, β

= .137, $p<.05$). In the third block, BRT ISD once again accounted for significant additional variance for each of the five cognitive tasks (Digit Symbol $\eta^2 = .075$, $\beta = -.391$, $p<.001$; Letter Series $\eta^2 = .061$, $\beta = -.356$, $p<.001$; Word Recall $\eta^2 = .049$, $\beta = -.317$, $p<.001$; Verbal Fluency $\eta^2 = .048$, $\beta = -.316$, $p<.01$; Vocabulary $\eta^2 = .044$, $\beta = -.301$, $p<.01$).

Table 5) Model 3: Hierarchical Regression Analysis for BRT ISD & BRT Plasticity as Predictors of Year-6 Cognitive Function

Digit Symbol	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.972	.121	-.497***	-.525	.137	-.269***	-.525	.137	-.269***
Education	-.035	.226	-.010	-.043	.211	-.012	-.043	.212	-.012
BRT ISD				-1.517	.264	-.393***	-1.510	.308	-.391***
BRT Plasticity							.001	.017	.003
R^2		.245			.347			.347	
$R^2\Delta$					.102			.000	
F for Δ in R^2		34.418***			32.961***			.002	
Letter Series	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.334	.049	-.409***	-.107	.054	-.131*	-.104	.053	-.128
Education	.358	.093	.232***	.357	.084	.231***	.374	.082	.242***
BRT ISD				-.760	.105	-.470***	-.575	.120	-.356***
BRT Plasticity							.020	.007	.193**
R^2		.268			.412			.436	
$R^2\Delta$					.144			.024	
F for Δ in R^2		38.993***			52.118***			8.996***	
Word Recall	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.300	.058	-.343***	-.129	.067	-.147	-.128	.067	-.146
Education	.121	.108	.074	.118	.104	.072	.121	.104	.074
BRT ISD				-.583	.130	-.337***	-.548	.151	-.317***
BRT Plasticity							.004	.009	.034
R^2		.136			.212			.212	
$R^2\Delta$					.075			.001	
F for Δ in R^2		16.752***			20.095***			.199	

Table 5) (continued) **Model 3**: Hierarchical Regression Analysis for BRT ISD & BRT Plasticity as Predictors of Year-6 Cognitive Function

Verbal Fluency	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.196	.066	-.197**	-.044	.079	-.044	-.044	.079	-.045
Education	.412	.124	.220**	.411	.122	.219**	.404	.122	.215**
BRT ISD				-.512	.155	-.259**	-.624	.179	-.316**
BRT Plasticity							-.012	.010	-.097
R^2		.107			.151			.157	
$R^2\Delta$					.044			.006	
F for Δ in R^2		12.875***			10.953***			1.528	
Vocabulary	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.039	.048	-.055	.088	.057	.124	.088	.057	.124
Education	.311	.091	.234**	.310	.088	.233**	.310	.088	.233**
BRT ISD				-.427	.112	-.304***	-.423	.130	-.301**
BRT Plasticity							.000	.007	.005
R^2		.064			.124			.124	
$R^2\Delta$					.060			.000	
F for Δ in R^2		7.272***			14.639***			.004	

* p<0.05; **p<0.01; ***p<0.001; BRT = 1-Back 4-Choice RT; ISD = Intraindividual Standard Deviation

Table 6) Model 4: Hierarchical Regression Analysis for BRT Plasticity & BRT ISD as Predictors of Year-6 Cognitive Function

Digit Symbol	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.972	.121	-.497***	-.849	.127	-.434***	-.525	.137	-.269***
Education	-.035	.226	-.010	-.002	.223	-.001	-.043	.212	-.012
BRT Plasticity				.044	.016	.176**	.001	.017	.003
BRT ISD							-1.510	.308	-.391***
R^2		.245			.272			.347	
$R^2\Delta$					.027			.075	
F for Δ in R^2		34.418***			7.901**			24.043***	
Letter Series	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.334	.049	-.409***	-.228	.049	-.280***	-.104	.053	-.128
Education	.358	.093	.232***	.388	.087	.252***	.374	.082	.242***
BRT Plasticity				.037	.006	.351***	.020	.007	.193**
BRT ISD							-.575	.120	-.356***
R^2		.268			.375			.436	
$R^2\Delta$					.107			.061	
F for Δ in R^2		38.993***			36.417***			22.901***	
Word Recall	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.300	.058	-.343***	-.246	.061	-.281***	-.128	.067	-.146
Education	.121	.108	.074	.136	.107	.083	.121	.104	.074
BRT Plasticity				.020	.008	.174**	.004	.009	.034
BRT ISD							-.548	.151	-.317***
R^2		.136			.163			.212	
$R^2\Delta$					.027			.049	
F for Δ in R^2		16.752***			6.724**			13.108***	

Table 6) (continued) **Model 4**: Hierarchical Regression Analysis for BRT Plasticity & BRT ISD as Predictors of Year-6 Cognitive Function

Verbal Fluency	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.196	.066	-.197**	-.181	.071	-.182*	-.044	.079	-.045
Education	.412	.124	.220**	.415	.125	.222**	.404	.122	.215**
BRT Plasticity				.005	.009	.042	-.012	.010	-.097
BRT ISD							-.624	.179	-.316**
R^2		.107			.109			.157	
$R^2\Delta$					.002			.048	
F for Δ in R^2		12.875***			.365			12.124***	
Vocabulary	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.039	.048	-.055	-.005	.051	-.007	.088	.057	.124
Education	.311	.091	.234**	.318	.090	.239**	.310	.088	.233**
BRT Plasticity				.013	.006	.137*	.000	.007	.005
BRT ISD							-.423	.130	-.301**
R^2		.064			.080			.124	
$R^2\Delta$					.016			.044	
F for Δ in R^2		7.272***			3.808*			10.595***	

* $p<0.05$; ** $p<0.01$; *** $p<0.001$; BRT = 1-Back 4-Choice RT; ISD = Intraindividual Standard Deviation

Multivariate Hierarchical Regression Analyses

Models 5 & 6: Multivariate ISD and Plasticity: Finally, to examine the relative contributions of intraindividual variability and cognitive plasticity as predictors irrespective of cognitive-load demands, a series of hierarchical multivariate regression analyses were conducted.

For Model 5 (see Table 7), demographic variables (age, education) were entered in the first block, with CRT and BRT ISD added in the second block, followed by CRT and BRT plasticity in the third block. For each of the five cognitive outcome measures, intraindividual variability (ISD) significantly accounted for an additional proportion of variance in the model, above that which can be explained by the effects of age and education (Digit Symbol = 12.2%, Letter Series = 14.8%, Word Recall = 9.5%, Verbal Fluency = 4.8%, Vocabulary = 8.0%). BRT ISD uniquely contributed to each of the five cognitive tasks (Digit Symbol: β = -.300, p<.001; Letter Series: β = -.434, p<.001; Word Recall: β = -.246, p<.01; Verbal Fluency: β = -.217, p<.05; Vocabulary: β = -.213, p<.05), whereas CRT ISD selectively predicted performance for Digit Symbol (β = -.181, p<.05), Word Recall (β = -.178, p<.05), and Vocabulary (β = -.177, p<.05). In the third block, BRT plasticity selectively provided additional explained variance for Letter Series (2.6%, β = .205, p<.01), whereas CRT plasticity uniquely contributed to Word Recall (2.5%, β = -.166, p<.05).

To fully investigate the relative contributions of intraindividual variability and cognitive plasticity predictors, their entry order was reversed for Model 6 (Table 8). Demographic variables were added first, followed by CRT and BRT plasticity (Block 2), and then CRT and BRT ISD (Block 3). Adding both plasticity predictors in the second

block resulted in significant additional variance explained, however only BRT plasticity provided unique contributions (Digit Symbol: 2.9%, β = .165, p<.05; Letter Series: 10.8%, β = .347, p<.001; Word Recall: 3.4%, β = .197, p<.01). In the third block, BRT ISD accounted for significant additional unique variance for all five cognitive tasks (Digit Symbol = 9.4%, β = -.294, p<.01; Letter Series = 6.6%, β = -.313, p<.001;Word Recall = 8.5%, β = -.227, p<.05; Verbal Fluency = 6.0% β = -.283, p<.01, Vocabulary = 6.4%, β = -.208, p<.05).

Table 7) Model 5: Hierarchical Multivariate Regression Analysis for ISD and Plasticity as Predictors of Cognitive Function

Digit Symbol	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.972	.121	-.497***	-.465	.137	-.238**	-.460	.138	-.235**
Education	-.035	.226	-.010	.002	.209	.000	.000	.211	.000
CRT ISD				-1.043	.405	-.181*	-1.097	.418	-.190**
BRT ISD				-1.158	.296	-.300***	-1.133	.339	-.294**
CRT Plasticity							-.048	.090	-.031
BRT Plasticity							.005	.017	.019
R^2		.245			.367			.368	
$R^2\Delta$					.122			.001	
F for Δ in R^2		34.418***			20.240***			.158	
Letter Series	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.334	.049	-.409***	-.098	.055	-.119	-.091	.054	-.111
Education	.358	.093	.232***	.364	.084	.236***	.380	.083	.247***
CRT ISD				-.173	.163	-.071	-.228	.165	-.094
BRT ISD				-.700	.119	-.434***	-.505	.134	-.313***
CRT Plasticity							-.025	.036	-.039
BRT Plasticity							.022	.007	.205**
R^2		.268			.416			.442	
$R^2\Delta$					.148			.026	
F for Δ in R^2		38.993***			26.637***			4.955**	
Word Recall	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.300	.058	-.343***	-.102	.068	-.117	-.091	.067	-.104
Education	.121	.108	.074	.138	.103	.084	.132	.102	.080
CRT ISD				-.461	.200	-.178*	-.583	.203	-.226**
BRT ISD				-.424	.146	-.246**	-.391	.165	-.227*
CRT Plasticity							-.112	.044	-.166*
BRT Plasticity							.008	.008	.074

R^2	.136			.231			.256		
$R^2\Delta$				.095			.025		
F for Δ in R^2	16.752***			12.910***			3.464*		
Verbal Fluency	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.196	.066	-.197**	-.031	.080	-.031	-.026	.080	-.027
Education	.412	.124	.220**	.419	.122	.224**	.398	.122	.213**
CRT ISD				-.239	.239	-.080	-.317	.243	-.106
BRT ISD				-.430	.175	-.217*	-.559	.198	-.283**
CRT Plasticity							-.092	.053	-.119
BRT Plasticity							-.009	.010	-.073
R^2	.107			.155			.173		
$R^2\Delta$				.048			.018		
F for Δ in R^2	12.875***			5.979**			2.260		
Vocabulary	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.039	.048	-.055	.108	.058	.152	.109	.058	.154
Education	.311	.091	.234**	.322	.087	.242***	.320	.088	.240***
CRT ISD				-.375	.171	-.177*	-.397	.175	-.187*
BRT ISD				-.298	.125	-.213*	-.291	.143	-.208*
CRT Plasticity							-.021	.038	-.038
BRT Plasticity							.002	.007	.019
R^2	.064			.143			.145		
$R^2\Delta$				.080			.001		
F for Δ in R^2	7.272***			9.865***			.164		

* p<0.05; **p<0.01; ***p<0.001; CRT = 4-Choice RT; BRT = 1-Back 4-Choice RT; ISD = Intraindividual Standard Deviation

Table 8) Model 6: Hierarchical Multivariate Regression Analysis for Plasticity and ISD as Predictors of Cognitive Function

Digit Symbol	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.972	.121	-.497***	-.843	.127	-.431***	-.460	.138	-.235**
Education	-.035	.226	-.010	.006	.224	.002	.000	.211	.000
CRT Plasticity				.067	.093	.045	-.048	.090	-.031
BRT Plasticity				.041	.016	.165*	.005	.017	.019
CRT ISD							-1.097	.418	-.190**
BRT ISD							-1.133	.339	-.294**
R^2		.245			.274			.368	
$R^2\Delta$					.029			.094	
F for Δ in R^2		34.418***			4.205*			15.452***	

Letter Series	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.334	.049	-.409***	-.227	.049	-.278***	-.091	.054	-.111
Education	.358	.093	.232***	.390	.087	.253***	.380	.083	.247***
CRT Plasticity				.010	.036	.016	-.025	.036	-.039
BRT Plasticity				.037	.006	.347***	.022	.007	.205**
CRT ISD							-.228	.165	-.094
BRT ISD							-.505	.134	-.313***
R^2		.268			.376			.442	
$R^2\Delta$					.108			.066	
F for Δ in R^2		38.993***			18.168***			12.452***	

Word Recall	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.300	.058	-.343***	-.250	.061	-.286***	-.091	.067	-.104
Education	.121	.108	.074	.128	.107	.078	.132	.102	.080
CRT Plasticity				-.060	.044	-.088	-.112	.044	-.166*
BRT Plasticity				.022	.008	.197**	.008	.008	.074
CRT ISD							-.583	.203	-.226**
BRT ISD							-.391	.165	-.227*

R^2		.136			.170			.256	
$R^2\Delta$					.034			.085	
F for Δ in R^2		16.752***			4.285*			11.946***	
Verbal Fluency	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.196	.066	-.197**	-.187	.071	-.187	-.026	.080	-.027
Education	.412	.124	.220**	.407	.125	.217**	.398	.122	.213**
CRT Plasticity				-.050	.052	-.064	-.092	.053	-.119
BRT Plasticity				.007	.009	.057	-.009	.010	-.073
CRT ISD							-.317	.243	-.106
BRT ISD							-.559	.198	-.283**
R^2		.107			.113			.173	
$R^2\Delta$					.005			.060	
F for Δ in R^2		12.875***			.629			7.642***	
Vocabulary	**Block 1**			**Block 2**			**Block 3**		
Variable	***B***	***SE B***	***β***	***B***	***SE B***	***β***	***B***	***SE B***	***β***
Age	-.039	.048	-.055	-.003	.051	-.005	.109	.058	.154
Education	.311	.091	.234**	.320	.090	.241***	.320	.088	.240***
CRT Plasticity				.015	.038	.028	-.021	.038	-.038
BRT Plasticity				.012	.007	.130	.002	.007	.019
CRT ISD							-.397	.175	-.187*
BRT ISD							-.291	.143	-.208*
R^2		.064			.081			.145	
$R^2\Delta$					.017			.064	
F for Δ in R^2		7.272***			1.977			7.846***	

* p<0.05; **p<0.01; ***p<0.001; CRT = 4-Choice RT; BRT = 1-Back 4-Choice RT; ISD = Intraindividual Standard Deviation

Summary of Hierarchical Regression Analyses (Models 1-6): A summary of the overall *F*-test results (for change in R^2) for each of the six hierarchical regression models is presented in Table 9.

Overall, intraindividual variability (ISD) emerged as a consistent predictor of subsequent cognitive function for each of the five cognitive outcome measures. This trend was generally observed for both CRT and BRT indices of intraindividual variability (i.e. regardless of cognitive load), and ISD significantly accounted for additional variance despite order of entry into the hierarchical models.

Cognitive plasticity also emerged as a unique predictor of long-term cognitive function, although its effects were more limited and selective. With the exception of Word Recall, CRT plasticity did not significantly account for unique variance in the models, regardless of order of entry. In contrast, BRT plasticity (i.e., increased cognitive load) accounted for a significant proportion of additional explained variance for four of the five cognitive measures (Letter Series, Digit Symbol, Word Recall, Vocabulary). However, the unique predictivity of BRT plasticity was primarily observed when entered into the models prior to the ISD predictors.

Table 9) Summary of Hierarchical Regression Analyses

		Digit Symbol	Letter Series	Word Recall	Verbal Fluency	Vocabulary
Model 1: ***CRT ISD & CRT Plasticity***	**Block 1:** Age, Education	***	***	***	***	***
	Block 2: CRT ISD	***	***	***	*	***
	Block 3: CRT Plasticity	ns	ns	*	ns	ns
Model 2: ***CRT Plasticity & CRT ISD***	**Block 1:** Age, Education	***	***	***	***	***
	Block 2: CRT Plasticity	ns	ns	ns	ns	ns
	Block 3: CRT ISD	***	***	***	**	***
Model 3: ***BRT ISD & BRT Plasticity***	**Block 1:** Age, Education	***	***	***	***	***
	Block 2: BRT ISD	***	***	***	***	***
	Block 3: BRT Plasticity	ns	***	ns	ns	ns
Model 4: ***BRT Plasticity & BRT ISD***	**Block 1:** Age, Education	***	***	***	***	***
	Block 2: BRT Plasticity	**	***	**	ns	*
	Block 3: BRT ISD	***	***	***	***	***
Model 5: ***Multivariate ISD & Plasticity***	**Block 1:** Age, Education	***	***	***	***	***
	Block 2: CRT ISD, BRT ISD	***	***	***	**	***
	Block 3: CRT Plasticity, BRT Plasticity	ns	**	*	ns	ns
Model 6: ***Multivariate Plasticity & ISD***	**Block 1:** Age, Education	***	***	***	***	***
	Block 2: CRT Plasticity, BRT Plasticity	*	***	*	ns	ns
	Block 3: CRT ISD, BRT ISD	***	***	***	***	***

* $p<0.05$; ** $p<0.01$; *** $p<0.001$; CRT = 4-Choice RT; BRT = 1-Back 4-Choice RT; ISD = Intraindividual Standard Deviation

Variability & Plasticity as Predictors of Cognitive Change

Research question 3 aims to determine whether individual differences in specific predictors (age, education, intraindividual variability, cognitive plasticity) selectively moderate longitudinal rates of cognitive change (Baseline through Year 6), and whether these associations vary as a function of cognitive domain. Two-level multilevel models were used to examine mean intraindividual change, as well as interindividual (between-person) differences in intraindividual (within-person) change on the five cognitive outcome measures (Digit Symbol, Letter Series, Word Recall, Similarities, Vocabulary). For all HLM analyses (Models 1-5), chronological age was entered as a continuous predictor centered at 75 years, reflecting the approximate mean age of the overall Project MIND sample (M = 74.29). For the education predictor, total years of formal education was coded as a categorical variable, grouped as ≤ 12 years of education (i.e., secondary education or 'low' education) and > 12 years of education (i.e., post-secondary education or 'high' education). All multilevel analyses were performed with HLM Version 6.08, using Full Information Maximum Likelihood (FIML) for estimates of both fixed and random parameters. Level-1 models were analyzed separately for all five cognitive measures based on the following equation:

Level-1 (within-person model)

$$\text{Cognitive performance}_{it} = \beta_{0i} + \beta_{1i}\,(\text{Time in Study}_{it}) + e_{it} \qquad \textbf{(1)}$$

In equation **(1)**, cognitive performance for a given individual (i) at a given time (t) is modeled as a function of that person's performance at the first wave of testing (β_{0i}; intercept), plus the individual's average linear rate of change (β_{1i}; slope) in cognitive

performance across time in study, plus a random within-individual error term reflecting residual variance remaining to be explained after controlling for time in study (e_{it}; deviation from the individual regression line). Random coefficients are estimated for each cognitive task in the model to determine whether there are within-person fluctuations in change over time (slope), as well as interindividual differences in performance for baseline and slope.

At Level-1, each person's rate of change is represented by a unique individual trajectory (β_{0i}; intercept, β_{1i}; slope) **(1)**. For Level-2, these parameters become the outcomes that depend on stable between-person sources of variation. As such, these variables now represent an intercept (β_{0i}) and slope (β_{1i}) as outcomes model. Separate two-stage models were analyzed for each cognitive task. A sample description using age (centered at 75 years) and education (categorized as ≤ or > 12 years of education) as Level-2 predictors follows:

Level-2 (between-person model)

$$\beta_{0i} = \gamma_{00} + \gamma_{01}\,(\text{Age}) + \gamma_{02}\,(\text{Education}) + u_{0i} \quad \textbf{(2)}$$

$$\beta_{1i} = \gamma_{10} + \gamma_{11}\,(\text{Age}) + \gamma_{12}\,(\text{Education}) + u_{1i} \quad \textbf{(3)}$$

In equation **(2)**, each individual's intercept (β_{0i}; Initial Status) is modeled as a function of the starting point for the average 75 year-old with ≤ 12 years of education (γ_{00}), plus the average difference for a 1-unit increase in age (in years) (γ_{01}), plus the average difference in a 1-unit increase in education (i.e., average difference between ≤ 12 and > 12 years of education) (γ_{02}), plus a random effect (error) reflecting between-individual differences in intercept (u_{0i}).

In equation **(3)**, each individual's linear average rate of change in cognitive performance (β_{1i}; slope) is modeled as a function of the average change for a 1-unit increase in time in study for a prototypical 75 year-old with ≤ 12 years of education (γ_{10}), plus the average difference in slope associated with a 1-unit increase in time in study with a corresponding 1-unit increase in age above 75 years (γ_{11}), plus a 1-unit increase in time in study with a corresponding 1-unit increase in education (> 12 years of education) (γ_{12}), plus a random effect (u_{1i}) that reflects between-person differences in rates of change.

Multilevel Models of Cognitive Change

Multilevel Model 1: Age & Education: An initial multilevel analysis (Model 1) was conducted to determine if significant differences exist between demographic variables (age in years and total years of formal education) as predictors of cognitive change across 5 years. A summary of the Model 1 change findings is presented in Table 10. An examination of fixed effects (initial status) coefficients (β_{0i}) revealed significant baseline intercepts (γ_{00}) for each of the five cognitive outcome measures (i.e., the average performance for a prototypical 75 year old with ≤ 12 years of education; Digit Symbol γ_{00} = 37.28, p_{diff} <.001; Letter Series γ_{00} = 6.93, p_{diff} <.001; Word Recall γ_{00} = 14.69, p_{diff} <.001; Verbal Fluency γ_{00} = 10.60, p_{diff} <.001; Vocabulary γ_{00} = 27.92, p_{diff} <.001). Significant age differences (γ_{01}), in cognitive performance at baseline were found on all tasks, except Vocabulary, with poorer cognitive performance observed per additional year of age older than 75 years (Digit Symbol γ_{01} = -0.85, p_{diff} <.001; Letter Series γ_{01} = -0.35, p_{diff} <.001; Word Recall γ_{01} = -0.18, p_{diff} <.001; Verbal Fluency γ_{01} = -0.11, p_{diff} <.05; Vocabulary γ_{01} = -0.04, p_{diff} >.05). For example, a typical 85 year-old recalled 1.8

less words on the Word Recall task at baseline compared to the average 75 year-old. Significant education differences (γ_{02}), independent of age as a predictor, were found in baseline cognitive performance, with high education (i.e., > 12 years) conferring significant improvements in each of the five cognitive tasks. (Digit Symbol $\gamma_{02} = 5.57$, $p_{diff} < .001$; Letter Series $\gamma_{02} = 2.54$, $p_{diff} < .001$; Word Recall $\gamma_{02} = -2.53$, $p_{diff} < .001$; Verbal Fluency $\gamma_{02} = 3.68$, $p_{diff} < .001$; Vocabulary $\gamma_{02} = 2.74$, $p_{diff} < .001$). For example, an average 75 year-old with high education (i.e., > 12 years) transcribed 5.57 more symbols on the Digit Symbol Substitution task compared to the average 75 year-old with low education (≤ 12 years).

In terms of rates of change (β_{1i} ;Slope), there were small, non-significant, positive slopes (γ_{10}) over 5 years for Digit Symbol, Letter Series, and Word Recall, while Similarities and Vocabulary displayed minimal, non-significant, negative slopes over time (see Table 10 for γ_{10} and *p*-values). However, age as a predictor of rate of change (γ_{11}) significantly moderated performance on all five cognitive tasks (Digit Symbol $\gamma_{11} = -0.04$, $p_{diff} < .05$; Letter Series $\gamma_{11} = -0.01$, $p_{diff} < .05$; Word Recall $\gamma_{11} = -0.04$, $p_{diff} < .001$; Verbal Fluency $\gamma_{11} = -0.02$, $p_{diff} < .05$; Vocabulary $\gamma_{11} = -0.01$, $p_{diff} < .05$). For example, with each additional year in study and each additional year older beyond 75 years, the average participant's rate of change decreased by .04 units ($p_{diff} < .05$) on the Digit Symbol task. There were no significant effects of education (γ_{12}) as a moderator of rates of change on any of the cognitive tasks.

Examination of the random effects variance revealed significant individual differences in starting points for cognitive performance at baseline (u_{0i}; Intercept) for each

of the cognitive outcome measures (Digit Symbol u_{0i} = 53.46, *df* = 269, *p*<.001; Letter Series u_{0i} = 13.49, *df* = 269, *p*<.001; Word Recall u_{0i} = 10.56, *df* = 269, *p*<.001; Verbal Fluency u_{0i} = 17.50, *df* = 269, *p*<.001; Vocabulary u_{0i} = 15.07, *df* = 269, *p*<.001). Similarly, there were significant between-person differences in rates of intraindividual change (u_{1i}; Slope) for all cognitive tasks, except Letter Series (Digit Symbol u_{1i} = 0.64, *df* = 269, *p*<.001; Letter Series u_{1i} = 0.00, *df* = 269, *p*>.05; Word Recall u_{1i} = 0.20, *df* = 269, *p*<.001; Verbal Fluency u_{1i} = 0.17, *df* = 269, *p*<.05; Vocabulary u_{1i} = 0.02, *df* = 269, *p*<.01). A substantial amount of variance in changes within each individual (e_{it}; fluctuations from their own regression line) was also found across cognitive measures. Overall, the random effects components suggest there is significant variance in Model 1, both within and between individuals, remaining to be explained by other factors (e.g., intraindividual variability, cognitive plasticity).

Table 10) Model 1: Multilevel Model of Cognitive Change as a Function of Time in Study, Age, & Education

		Digit Symbol	Letter Series	Word Recall	Verbal Fluency	Vocabulary
Fixed Effects: Coefficient (SE)						
Initial Status **(β_{0i})**						
	Intercept (γ_{00})	37.28 (099)***	6.93 (0.47)***	14.69 (0.44)***	10.60 (0.58)***	27.92 (0.49)***
	Age (γ_{01})	-0.85 (0.08)***	-0.35 (0.04)***	-0.18 (0.04)***	-0.11 (0.05)*	-0.04 (0.04)
	Education (γ_{02})	5.57 (1.15)***	2.54 (0.55)***	2.53 (0.51)***	3.68 (0.67)***	2.74 (0.56)***
Rate of Change **(β_{1i})**						
	Intercept (γ_{10})	0.37 (0.22)	0.01 (0.07)	0.09 (0.10)	-0.01 (0.13)	-0.01 (0.06)
	Age (γ_{11})	-0.04 (0.02)*	-0.01 (0.01)*	-0.04 (0.01)***	-0.02 (0.01)*	-0.01 (0.00)*
	Education (γ_{12})	-0.35 (0.25)	-0.07 (0.08)	-0.15 (0.12)	-0.01 (0.15)	0.01 (0.07)
Random Effects: Variance Component (SD)						
	Initial Status (u_{0i})	53.46 (7.31)***	13.49 (3.67)***	10.56 (3.25)***	17.50 (4.19)***	15.07 (3.88)***
	Rate of Change (u_{1i})	0.64 (0.80)***	0.00 (0.07)	0.20 (0.44)***	0.17 (0.41)*	0.02 (0.13)**
	Level 1 Residual (e_{it})	24.29 (4.93)	3.50 (1.87)	4.88 (2.21)	9.27 (3.04)	2.41 (1.55)

NOTE: For all multilevel analyses, Age was centered at 75 years and Education was categorized as > or ≤ 12 years of formal education
* p<0.05; **p<0.01; ***p<0.001; SE = Standard Error; SD = Standard Deviation

Multilevel Models 2 & 3: Age, Education, & ISD: Multilevel models were developed to examine intraindividual variability (ISD) as a predictor of longitudinal rates of cognitive change over 5 years. The same equations from Model 1 (Age & Education) were used, with each of the RT ISD factors (CRT, BRT) added as additional Level-2 predictors, for Models 2 and 3 respectively. A sample equation for Model 2 (CRT ISD) follows:

Model 2 (CRT ISD) Level-1

$$\text{Cognitive performance}_{it} = \beta_{0i} + \beta_{1i}\,(\text{Time in Study}_{it}) + e_{it} \quad \textbf{(1)}$$

Model 2 (CRT ISD) Level-2

$$\beta_{0i} = \gamma_{00} + \gamma_{01}\,(\text{Age}) + \gamma_{02}\,(\text{Education}) + \gamma_{03}\,(\text{CRT ISD}) + u_{0i} \quad \textbf{(2)}$$

$$\beta_{1i} = \gamma_{10} + \gamma_{11}\,(\text{Age}) + \gamma_{12}\,(\text{Education}) + \gamma_{13}\,(\text{CRT ISD}) + u_{1i} \quad \textbf{(3)}$$

Results of the Model 2 (CRT ISD) and Model 3 (BRT ISD) HLM analyses are presented in an aggregate format in Table 11. Significant differences in baseline intercepts (γ_{00}) were once again observed for each of the five cognitive tasks for both Models 2 and 3 (see Table 11 for γ_{00} and *p*-values). For both models, age (γ_{01}) exhibited select effects on cognitive performance at baseline, independent of all other predictors in the model. For Model 2 (CRT ISD), age differences were significant for Digit Symbol (γ_{01} = -0.50, p_{diff} <.001) and Letter Series (γ_{01} = -0.20, p_{diff} <.001), whereas in Model 3 (BRT ISD), age differences were significant for Digit Symbol (γ_{01} = -0.34, p_{diff} <.001), Verbal Fluency (γ_{01} = 0.11, p_{diff} <.05), and Vocabulary (γ_{01} = 0.12, p_{diff} <.05). Significant education differences (γ_{02}) were found in baseline cognitive performance, with high education (i.e., > 12 years) conferring improvements in each of the five cognitive tasks for both CRT ISD and BRT ISD models (see Table 11 for γ_{02} and *p*-values). Significant

differences were found for both intraindividual variability predictors (Model 2: CRT ISD, Model 3: BRT ISD) in relation to baseline performance on each of the five cognitive measures (see Table 11 for γ_{03} and *p*-values). In both models, increased intraindividual variability (ISD) was associated with decreased cognitive performance at baseline. For example, with each 1-unit increase in CRT ISD, the average 75 year-old transcribed 1.60 less symbols on the Digit Symbol Substitution task at baseline (γ_{03}). Similarly, with each 1-unit increase in BRT ISD, the average 75 year-old recalled 0.44 less words on the Word Recall task at baseline (γ_{03}).

For both Models 2 and 3, no significant rates of change were observed across time for a prototypical individual aged 75 years, in the low education group, at the sample average for intraindividual variability however, there were select significant effects for age and ISD predictors (see Table 11). In Model 2 (CRT ISD Model), each additional year in study and each additional year older beyond 75 years (γ_{11}) significantly moderated rates of change, in a negative direction, on Letter Series (γ_{11} = -0.02, p_{diff} <.05), Word Recall (γ_{11} = -0.03, p_{diff} <.01), and Verbal Fluency (γ_{11} = -0.03, p_{diff} <.05). For Model 3 (BRT ISD Model), a similar pattern was observed with age as a predictor significantly moderating rates of cognitive change on Letter Series (γ_{11} = -0.02, p_{diff} <.05) and Word Recall (γ_{11} = -0.02, p_{diff} <.05). There were no significant effects of education (γ_{12}) as a moderator of rates of change for either Model 2 or 3 on any of the cognitive tasks. For Model 2, CRT ISD selectively moderated individual rates of cognitive change for Word Recall (γ_{13} = -0.03, p_{diff}<.01) and Vocabulary (γ_{13} = -0.03, p_{diff}<.05). For example, with each additional year in study and a corresponding 1-unit increase in CRT variability, the average 75 year old's slope decreased by 0.03 units (p_{diff} <.01) on Word Recall. For

Model 3, BRT ISD only moderated rates of change for Word Recall (γ_{13} = -0.05, p_{diff} <.05). Overall, the random effects for Models 2 and 3 reflecting between-individual differences in intercept (u_{0i}) and slope (u_{1i}) were significant for all cognitive measures, except Letter Series (see Table 11), suggesting there is significant variance remaining to be explained by other Level-1 and Level-2 predictors (e.g., cognitive plasticity).

Table 11) Models 2 & 3: Multilevel Models of Cognitive Change as a Function of Time in Study, Age, Education, & Intraindividual Variability

		Digit Symbol	Letter Series	Word Recall	Verbal Fluency	Vocabulary
Fixed Effects: Coefficient (SE)						
Initial Status **(β_{0i})**						
Model 2: CRT ISD	Intercept (γ_{00})	37.54 (0.91)***	7.04 (0.44)***	14.79 (0.42)***	10.72 (0.55)***	28.01 (0.47)***
	Age (γ_{01})	-0.50 (0.09)***	-0.20 (0.04)***	-0.06 (0.04)	0.05 (0.05)	0.07 (0.05)
	Education (γ_{02})	5.65 (1.05)***	2.58 (0.51)***	2.55 (0.48)***	3.71 (0.63)***	2.77 (0.54)***
	CRT ISD (γ_{03})	-1.60 (0.20)***	-0.68 (0.10)***	-0.56 (0.09)***	-0.71 (0.12)***	-0.47 (0.11)***
Model 3: BRT ISD	Intercept (γ_{00})	38.40 (0.88)***	7.54 (0.40)***	15.01 (0.43)***	11.09 (0.55)***	28.27 (0.47)***
	Age (γ_{01})	-0.34 (0.09)***	-0.06 (0.04)	-0.04 (0.04)	0.11 (0.06)*	0.12 (0.05)*
	Education (γ_{02})	4.73 (1.01)***	2.08 (0.45)***	2.29 (0.49)***	3.31 (0.63)***	2.49 (0.54)***
	BRT ISD (γ_{03})	-1.59 (0.17)***	-0.88 (0.07)***	-0.44 (0.08)***	-0.68 (0.10)***	-0.49 (0.09)***
Rate of Change **(β_{1i})**						
Model 2: CRT ISD	Intercept (γ_{10})	0.36 (0.22)	0.00 (0.07)	0.08 (0.10)	-0.02 (0.13)	-0.02 (0.06)
	Age (γ_{11})	-0.04 (0.02)	-0.02 (0.01)*	-0.03 (0.01)**	-0.03 (0.01)*	-0.01 (0.01)
	Education (γ_{12})	-0.35 (0.25)	0.07 (0.08)	-0.15 (0.12)	-0.01 (0.15)	0.01 (0.07)
	CRT ISD (γ_{13})	-0.02 (0.06)	0.01 (0.02)	-0.06 (0.03)*	-0.01 (0.03)	-0.04 (0.02)*
Model 3: BRT ISD	Intercept (γ_{10})	0.40 (0.22)	-0.01 (0.07)	0.11 (0.10)	-0.01 (0.13)	-0.00 (0.06)
	Age (γ_{11})	-0.03 (0.02)	-0.02 (0.01)*	-0.02 (0.01)*	-0.02 (0.01)	-0.01 (0.01)
	Education (γ_{12})	-0.36 (0.25)	-0.06 (0.08)	-0.18 (0.12)	-0.02 (0.15)	0.01 (0.07)
	BRT ISD (γ_{13})	-0.02 (0.04)	0.02 (0.01)	-0.05 (0.02)*	-0.01 (0.02)	-0.01 (0.01)
Random Effects: Variance Component (SD)						
Model 2: CRT ISD	Initial Status (u_{0i})	42.01 (6.48)***	11.42 (3.38)***	9.14 (3.02)***	15.30 (3.91)***	14.04 (3.75)***
	Rate of Change (u_{1i})	0.64 (0.80)***	0.00 (0.07)	0.19 (0.43)***	0.16 (0.40)*	0.02 (0.13)**
	Level 1 Residual (e_{it})	24.25 (4.92)	3.50 (1.87)	4.87 (2.21)	9.25 (3.04)	2.39 (1.55)
Model 3: BRT ISD	Initial Status (u_{0i})	37.71 (6.14)***	8.60 (2.93)***	9.32 (3.05)***	14.63 (3.82)***	13.52 (3.68)***
	Rate of Change (u_{1i})	0.64 (0.80)***	0.00 (0.07)	0.18 (0.43)***	0.16 (0.40)*	0.02 (0.12)**
	Level 1 Residual (e_{it})	24.24 (4.92)	3.50 (1.87)	4.87 (2.21)	9.25 (3.04)	2.40 (1.55)

NOTE: For all multilevel analyses, Age was centered at 75 years and Education was categorized as > or ≤ 12 years of formal education
CRT = 4-Choice RT; BRT = 1-Back 4-Choice RT; ISD = Intraindividual Standard Deviation; SE = Standard Error; SD = Standard Deviation; * $p<0.05$; ** $p<0.01$; *** $p<0.001$

Multilevel Models 4 & 5: Age, Education, & Cognitive Plasticity: Additional multilevel models were developed to fully explore cognitive plasticity as a predictor of long-term rates of cognitive change. The same equations from the ISD HLM analyses were used, with each of the RT plasticity factors (CRT, BRT) added as additional Level-2 predictors (along with Age and Education), for Models 4 and 5 respectively. A sample equation for Model 4 (CRT Plasticity) follows:

Model 4 (CRT Plasticity) Level-1

$$\text{Cognitive performance}_{it} = \beta_{0i} + \beta_{1i}\,(\text{Time in Study}_{it}) + e_{it} \quad \textbf{(1)}$$

Model 4 (CRT Plasticity) Level-2

$$\beta_{0i} = \gamma_{00} + \gamma_{01}\,(\text{Age}) + \gamma_{02}\,(\text{Education}) + \gamma_{03}\,(\text{CRT Plasticity}) + u_{0i} \quad \textbf{(2)}$$

$$\beta_{1i} = \gamma_{10} + \gamma_{11}\,(\text{Age}) + \gamma_{12}\,(\text{Education}) + \gamma_{13}\,(\text{CRT Plasticity}) + u_{1i} \quad \textbf{(3)}$$

Results of the Model 4 (CRT Plasticity) and Model 5 (BRT Plasticity) analyses are presented in an aggregate format in Table 12. Consistent with the previous HLM analyses (Models 1-3), significant differences in baseline intercepts (γ_{00}) were observed for each of the five cognitive tasks for both Models 4 and 5 (see Table 12 for γ_{00} and *p*-values). Baseline age differences (γ_{01}) exhibited select effects on cognitive performance (i.e., the average difference in performance associated with a 1-unit increase in age older than 75 years) for both the CRT Plasticity and BRT Plasticity models. For Model 4 (CRT Plasticity), age differences were significant for all cognitive tasks except Vocabulary (Digit Symbol $\gamma_{01} = -0.81$, $p_{\text{diff}} < .001$; Letter Series $\gamma_{01} = -0.33$, $p_{\text{diff}} < .001$; Word Recall $\gamma_{01} = -0.18$, $p_{\text{diff}} < .001$; Verbal Fluency $\gamma_{01} = -0.11$, $p_{\text{diff}} < .05$). In Model 5 (BRT Plasticity), age differences were significant for Digit Symbol ($\gamma_{01} = -0.68$, $p_{\text{diff}} < .001$),

Letter Series (γ_{01} = -0.26, p_{diff} <.001), and Word Recall (γ_{01} = -0.13, p_{diff} <.01). Significant education differences (γ_{02}) were found in baseline cognitive performance, with high education (i.e., > 12 years) conferring improvements in each of the five cognitive tasks for both CRT Plasticity and BRT Plasticity models (see Table 12 for γ_{02} and *p*-values). In Model 4 (CRT Plasticity), significant differences were only observed for Digit Symbol (γ_{03} = 0.16, p_{diff} <.01) baseline performance (i.e., with each 1-unit increase in CRT plasticity, the average 75 year-old transcribed 0.16 more symbols on the Digit Symbol Substitution task). In Model 5, positive significant differences were found for BRT Plasticity on all cognitive measures except Vocabulary (Digit Symbol γ_{03} = 0.06, p_{diff} <.001; Letter Series γ_{03} = 0.03, p_{diff} <.001; Word Recall γ_{03} = 0.02, p_{diff} <.001; Verbal Fluency γ_{03} = 0.02, p_{diff} <.05). Therefore, in both Models 4 and 5, increased cognitive plasticity (especially BRT plasticity) resulted in increased performance at baseline for most cognitive measures.

Limited significant effects on rates of cognitive change (β_{1i}) were found for Models 4 and 5 (see Table 12). Age was the only predictor that resulted in significant effects, and this moderating effect was selective for specific cognitive tasks. For both plasticity models, each additional year in study and each additional year older beyond 75 years (γ_{11}) significantly moderated rates of change, in a negative direction, on Digit Symbol (CRT Plasticity Model: γ_{11} = -0.04, p_{diff} <.05; BRT Plasticity Model: γ_{11} = -0.04, p_{diff} <.05), Word Recall (CRT Plasticity Model: γ_{11} = -0.04, p_{diff} <.001; BRT Plasticity Model: γ_{11} = -0.03, p_{diff} <.01), and Verbal Fluency (CRT Plasticity Model: γ_{11} = -0.02, p_{diff} <.05; BRT Plasticity Model: γ_{11} = -0.03, p_{diff} <.05). Neither CRT nor BRT plasticity

predictors exerted significant moderating effects on rates of cognitive change independent of chronological age or years of education.

The random effects components for Models 4 and 5 indicate that significant variance remains to be explained for both individual differences in starting points (u_{0i}; Intercept) and rate of cognitive change (u_{1i}; Slope) for all cognitive measures, except Letter Series (see Table 12). This suggests significant variance remains to be explained by other Level-1 and Level-2 predictors not explored in the current study.

Table 12) Models 4 & 5: Multilevel Models of Cognitive Change as a Function of Time in Study, Age, Education, & Cognitive Plasticity

		Digit Symbol	Letter Series	Word Recall	Verbal Fluency	Vocabulary
Fixed Effects: Coefficient (SE)						
Initial Status **(β_{0i})**						
Model 4: CRT Plasticity	Intercept (γ_{00})	37.42 (0.98)***	6.97 (0.47)***	14.70 (0.44)***	10.59 (0.58***	27.92 (0.49)***
	Age (γ_{01})	-0.81 (0.08)***	-0.33 (0.04)***	-0.18 (0.04)***	-0.11 (0.05)*	-0.04 (0.04)
	Education (γ_{02})	5.43 (1.13)***	2.50 (0.55)***	2.52 (0.51)***	3.69 (0.67)***	2.75 (0.56)***
	CRT Plasticity (γ_{03})	0.16 (0.06)**	0.05 (0.03)	0.01 (0.03)	-0.00 (0.04)	-0.00 (0.03)
Model 5: BRT Plasticity	Intercept (γ_{00})	37.50 (0.95)***	7.04 (0.45)***	14.76 (0.43)***	10.65 (0.57)***	27.96 (0.49)***
	Age (γ_{01})	-0.68 (0.08)***	-0.26 (0.04)***	-0.13 (0.04)**	-0.06 (0.05)	-0.01 (0.04)
	Education (γ_{02})	5.49 (1.09)***	2.49 (0.52)***	2.50 (0.50)***	3.66 (0.66)***	2.73 (0.56)***
	BRT Plasticity (γ_{03})	0.06 (0.01)***	0.03 (0.00)***	0.02 (0.00)***	0.02 (0.01)*	0.01 (0.01)
Rate of Change **(β_{1i})**						
Model 4: CRT Plasticity	Intercept (γ_{10})	0.37 (0.22)	0.00 (0.07)	0.09 (0.10)	-0.01 (0.13)	-0.01 (0.06)
	Age (γ_{11})	-0.04 (0.02)*	-0.01 (0.01)	-0.04 (0.01)***	-0.02 (0.01)*	-0.01 (0.01)
	Education (γ_{12})	-0.34 (0.25)	-0.06 (0.08)	-0.15 (0.12)	-0.01 (0.15)	0.01 (0.07)
	CRT Plasticity (γ_{13})	-0.01 (0.01)	0.00 (0.00)	-0.00 (0.01)	-0.00 (0.01)	0.00 (0.00)
Model 5: BRT Plasticity	Intercept (γ_{10})	0.37 (0.22)	0.00 (0.07)	0.09 (0.10)	-0.01 (0.13)	-0.01 (0.06)
	Age (γ_{11})	-0.04 (0.02)*	-0.01 (0.01)	-0.03 (0.01)**	-0.03 (0.01)*	-0.01 (0.01)
	Education (γ_{12})	-0.35 (0.25)	-0.06 (0.08)	-0.15 (0.12)	-0.01 (0.15)	0.01 (0.07)
	BRT Plasticity (γ_{13})	-0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	-0.00 (0.00)	0.00 (0.00)
Random Effects: Variance Component (SD)						
Model 4: CRT Plasticity	Initial Status (u_{0i})	51.91 (7.20)***	13.36 (3.66)***	10.56 (3.25)***	17.47 (4.18)***	15.08 (3.88)***
	Rate of Change (u_{1i})	0.64 (0.80)***	0.00 (0.07)	0.20 (0.44)***	0.16 (0.41)*	0.01 (0.11)**
	Level 1 Residual (e_{it})	24.27 (4.92)	3.50 (1.87)	4.87 (2.21)	9.27 (3.04)	2.42 (1.55)
Model 5: BRT Plasticity	Initial Status (u_{0i})	46.83 (6.84)***	11.77 (3.43)***	9.97 (3.16)***	17.02 (4.13)***	14.90 (3.86)***
	Rate of Change (u_{1i})	0.63 (0.80)***	0.00 (0.06)	0.19 (0.44)***	0.16 (0.40)*	0.02 (0.13)**
	Level 1 Residual (e_{it})	24.28 (4.93)	3.50 (1.87)	4.87 (2.21)	9.27 (3.05)	2.41 (1.55)

NOTE: For all multilevel analyses, Age was centered at 75 years and Education was categorized as > or ≤ 12 years of formal education
CRT = 4-Choice RT; BRT = 1-Back 4-Choice RT; SE = Standard Error; SD = Standard Deviation; * $p<0.05$; ** $p<0.01$; *** $p<0.001$

Discussion

A primary goal of aging research is to evaluate whether current outcomes (e.g., cognitive performance, functional abilities) can be predicted by specific preceding factors (e.g., expertise, physical activity, social engagement, nutrition). Studies of this nature are particularly valuable in establishing theoretical models of aging processes, for developing methodological approaches for the study of age-related change, and for advancing our understanding of the clinical characterization of adult development across the lifespan.

The current study investigated three primary research questions using data derived from Project MIND: **1)** Does baseline intraindividual variability predict long-term (5 year) cognitive function; **2)** Does baseline cognitive plasticity predict long-term (5 year) cognitive function; and **3)** Do specific factors (age, education, intraindividual variability, cognitive plasticity) predict long-term rates of cognitive change, and do the observed patterns vary as a function of domain.

Variability & Plasticity as Predictors of Cognitive Function

To investigate the relationship between baseline intraindividual variability and cognitive plasticity as predictors of subsequent (Year 6) cognitive function, six unique hierarchical multiple regression models, varying in sequential blocked entry, were generated for each of the five cognitive outcome measures (Digit Symbol, Letter Series, Word Recall, Verbal Fluency, Vocabulary). The relative contributions of demographic variables (age, education) were assessed for each model, with intraindividual variability (CRT ISD, BRT ISD) and cognitive plasticity (CRT plasticity, BRT plasticity) then added into each model (individually at first and then in multivariate models), varying the order of entry for ISD and plasticity.

Consistent with expectations, an individual's initial level of intraindividual variability in performing the RT tasks significantly predicted subsequent cognitive function for all five cognitive measures (Table 9). This pattern exhibited an inverse relationship, with increased baseline variability resulting in decreased cognitive performance over time. This trend was observed for both CRT and BRT indices of intraindividual variability (i.e., low and high cognitive load). Overall, intraindividual variability significantly accounted for additional unique variance, regardless of order of entry into the univariate and multivariate hierarchical regression models. The predictive relationship of intraindividual variability at baseline generally followed a "cognitive processes to products" continuum (Hultsch, Hertzog, Small, McDonald-Miszczak, & Dixon, 1992), with increased prediction for cognitive measures of processing speed (Digit Symbol) and fluid reasoning (Letter Series), followed by episodic memory (Word Recall), verbal ability (Verbal Fluency), and crystallized ability (Vocabulary).

Cognitive plasticity also emerged as a predictor of long term cognitive function, although its effects were limited and selective (see Table 9). With the exception of Word Recall, CRT plasticity did not significantly account for unique variance above and beyond demographic variables (age, education) and intraindividual variability (CRT ISD) as a predictor. In contrast, the more cognitively demanding BRT plasticity index (i.e., increased working memory and attentional control; West, Armilio, Craik, & Stuss, 2002), accounted for a significant proportion of additional explained variance for each cognitive measures, except Verbal Fluency. This unique prediction of BRT plasticity was further moderated by the order of entry into the models, accounting for a greater proportion of variance when entered prior to the intraindividual variability predictors.

Variability & Plasticity as Predictors of Cognitive Change

To examine whether specific predictors (age, education, intraindividual variability, cognitive plasticity) selectively moderate longitudinal rates of cognitive change (baseline through Year 6), two-level multilevel models were developed. Five unique models were used to examine mean intraindividual change, as well as interindividual (between-person) differences in intraindividual (within-person) change on each of the five cognitive outcome measures.

An initial multilevel model was conducted to determine if significant differences exist between demographic variables as predictors of cognitive change. Significant age and education differences were found at baseline for all tasks, except Vocabulary, with increased age and lower education (≤ 12 years of formal education) associated with poorer cognitive performance. Small, non-significant rates of change were observed for each of the cognitive tasks, indicating relatively stable cognitive function across 5 years for the study sample as a whole. However, there were significant age-related differences in average rates of change. With each additional year in study and each additional year older beyond 75 years, the average participant's rate of change significantly decreased on each of the five cognitive tasks. These findings suggest that the initial positive slopes observed on more executive cognitive tasks (Digit Symbol, Letter Series, Word Recall) gave way to declines in cognitive performance with increasing age. There were no significant effects of education as a moderator of rates of change on any of the cognitive tasks. Significant individual differences in starting points for cognitive performance at baseline, and significant between-person differences in rates of intraindividual change were found for all tasks, except Letter Series. This lack of significant variance in rates of

change for Letter Series may be reflective of the more fluid nature of the task and its considerable cognitive difficulty. That is, all individuals exhibited decline on the Letter Series task with advancing age, regardless of cognitive performance starting point.

Additional multilevel models were developed to examine intraindividual variability as a predictor of longitudinal rates of change. In both the CRT ISD and BRT ISD models, age emerged as a significant predictor of cognitive change for Letter Series, Word Recall, and Verbal Fluency (i.e., with increasing age, rates of cognitive change for each of these tasks decreased). Intraindividual variability was found to selectively moderate rates of change, independent of all other predictors in the model, for Word Recall (CRT ISD and BRT ISD) and Vocabulary (CRT ISD only). Cognitive plasticity was examined as a predictor of rates of cognitive change using similar multilevel models. Neither CRT plasticity nor BRT plasticity were found to significantly predict rates of change across 5 years on any of the cognitive outcome tasks. Only age emerged as a predictor in the plasticity models, significantly moderating rates of change in a negative direction for Digit Symbol, Word Recall, and Verbal Fluency.

Support for Variability & Plasticity as Predictors

Most contemporary theories of adult development recognize the considerable inter- and intra-individual heterogeneity in trajectories of cognitive and functional change across the lifespan (Figure 1). Li and colleagues (2004) proposed a model in which several types of variability are associated with different stages of skill acquisition (see Figure 5). These stages follow a continuum from initial learning through to acquired functioning. In general, as expertise increases, variability of performance decreases. This

model implies that variability associated with the early acquisition of a skill is potentially quite different than the variability observed about the average performance once asymptote of the skill has been reached. Therefore, there are likely different types of *intraindividual variations* associated with different phases of learning. For example, greater fluctuations during the acquisition phase may reflect diversity processes (e.g., novel exploratory behaviour and strategy use), adaptive shifts in performance (e.g., reactive shifts in response to external stimuli or internal states), or functional plasticity (e.g., training gains). Long-term fluctuations are hypothesized to reflect a lack of processing robustness and maladaptive functioning. A recent model of adult cognitive plasticity, the mismatch model (Lövdén et al., 2010), fits this typical learning curve of initially rapid but then diminishing increases in performance approaching an asymptotic level. The mismatch model suggests that an individual's functional supply initially responds to increased environmental demands with various compensatory processes (e.g., increased attentional control, inhibitory processes, exploratory strategies, goal-maintenance), and later, when supply meets demands, further impetus for cognitive change is lost. From this perspective, levels of cognitive performance that are stable over some time scale (e.g., minutes, weeks, years) can be viewed as dynamic equilibrium states of reactions to changes based on initial mismatch between supply and demand. In this sense, an individual's unique range of flexibility (i.e., adaptive neural, cognitive, and behavioural functioning) determines their capacity for reactive changes in plasticity in interaction with environmental stimuli.

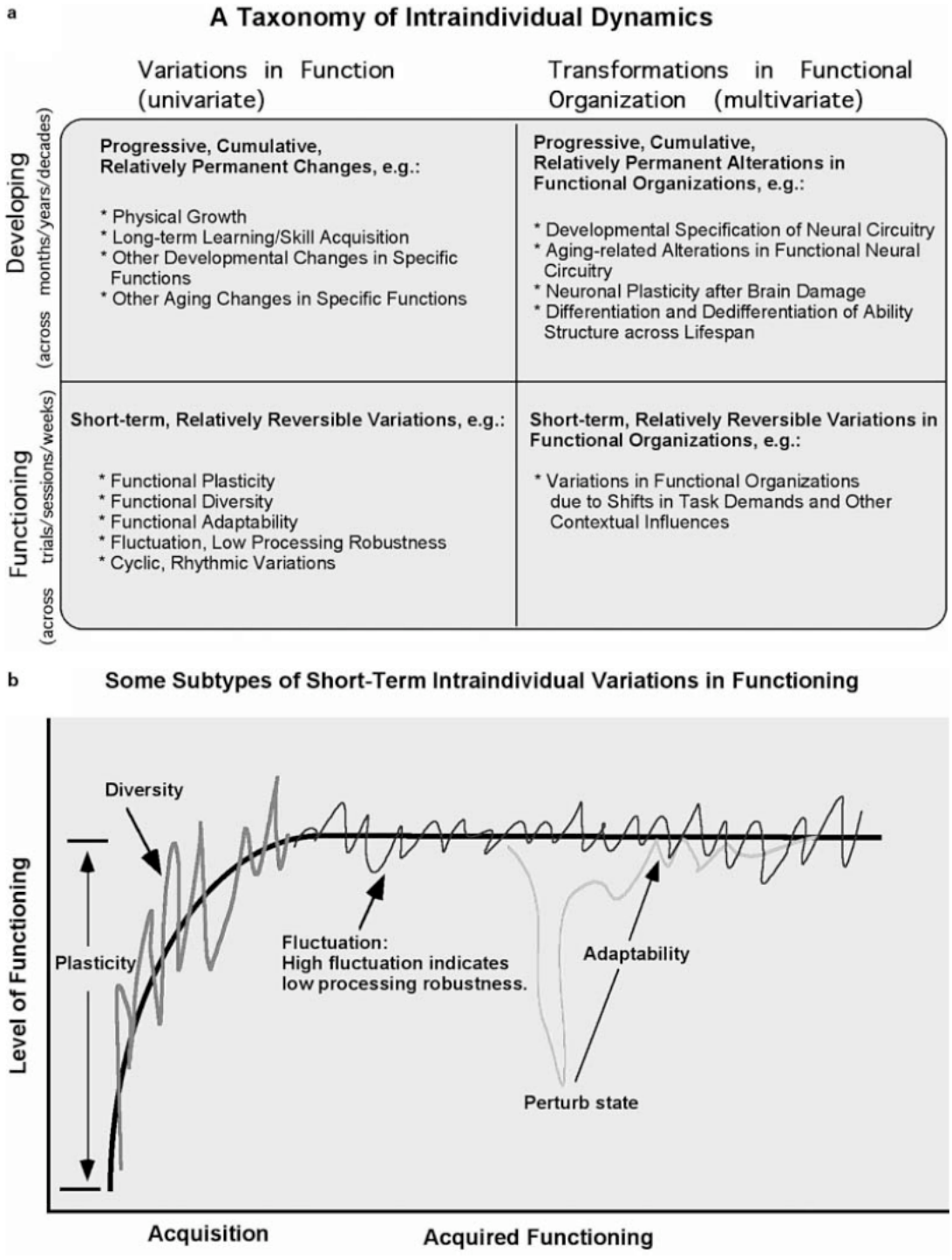

Figure 5) Subtypes of short-term intraindividual variations in functioning.

(Li, S.-C., Huxhold, O., & Schmiedek, F., 2004)

In the current study, we examined intraindividual variability and cognitive plasticity as predictors of cognitive function and rates of change, and to my knowledge this is the first study to concurrently investigate this relationship. In essence, we conceptualized the mismatch model of plasticity to actively contribute to the acquisition and diversity phase (pre-asymptotic) of the Li et al. (2004) multidimensional variability model, while processes involved in intraindividual variability are engaged in the acquired functioning phase (post-asymptotic; see Figure 5). Small to large correlations between indices of plasticity and variability were found in the current study, suggesting unique but related relationships exist between these constructs (Table 2). Overall, measures of intraindividual variability (CRT ISD, BRT ISD) reliably and consistently predicted subsequent cognitive function and rates of change across multiple cognitive domains, whereas measures of cognitive plasticity (CRT plasticity, BRT plasticity) selectively predicted long term cognitive function, but not trajectories of cognitive change.

A key proposition within the framework of the mismatch model is that some unknown duration of the supply-demand mismatch must be reached for a system to abandon its current dynamic equilibrium and adopt a state of plastic change. This "sluggish" capacity for reactive change is likely a protective feature of an efficient neurobiological system. Always responding to supply-demand mismatches with plastic changes would be functionally and economically maladaptive. The mismatch model proposes that the phase of development of a plastic response must be longer than the time it takes to induce the initial and primary plasticity-inducing change in demand or supply. If this developmental phase is not prolonged or the primary plastic changes are not sufficiently repeated, the required supply-demand mismatch will not be achieved. The

mismatch model also suggests that an individual's present level of functioning (i.e., range of cognitive performance) determines the magnitude of the supply-demand mismatch in interaction with environmental stimuli (i.e., task difficulty). Therefore, if a system can effortlessly respond to challenges with existing resources it will not experience the required supply-demand mismatch. It is possible that the basic cognitive RT tasks used in the current study (CRT, BRT) did not induce sufficient mismatch to elicit strong predictive associations for the high-functioning, well-educated, healthy Project MIND participants. Performance accuracy for both the CRT and BRT tasks was extremely high, even for the old-old (> 75 years), therefore the environmental demands (i.e., task difficulty) may not have been sufficient to achieve the required mismatch and overcome the participants' "sluggish" capacity for reactive (plastic) change. Moreover, it may be that the number of RT trials (n = 60) was not enough to induce the primary plasticity-inducing changes in demand. Even with these experimental constraints, BRT plasticity emerged as a unique predictor of long-term cognitive function for a range of domains including perceptual speed, fluid reasoning, episodic memory, and crystallized verbal knowledge (Table 9).

Intraindividual variability, as measured by an individual's baseline performance on either of the RT tasks (CRT ISD, BRT ISD), was found to be a robust predictor of subsequent cognitive function (across cognitive domains), and a significant predictor of rates of change for episodic memory (Word Recall) and verbal knowledge (Vocabulary). These findings are consistent with expectations and prior research demonstrating that intraindividual variability in performance is a stable, endogenous characteristic, associated with the aging process, and predictive of longitudinal cognitive, behavioural,

and neurological functioning (Bielak et al., 2010a; Burton et al., 2006; Dixon et al., 2007; Hultsch et al., 2000, 2002; MacDonald et al., 2003, 2006, 2008).

Evidence for the stability of intraindividual variability has shown that the amount of fluctuation in performance on a particular task at one point in time is positively correlated with the amount of variability on that task at a later point in time (Allaire & Marsiske, 2005; Fuentes et al., 2001; Hultsch et al., 2000, 2002; Rabbitt et al., 2001). Additionally, individuals who are more variable across trials on one RT task, are also more variable trial-to-trial on other RT tasks, lending support for intraindividual variability as an endogenous mechanism present during the performance of each cognitive task (Fuentes et al., 2001; Hultsch et al., 2000, 2002). For example, Hultsch and colleagues (2002) found greater variability in performance on four different RT tasks was associated with lower scores on tasks assessing perceptual speed, working memory, episodic memory, and crystallized abilities. Additionally, increased intraindividual variability in RT performance has been shown to be predictive of poorer everyday problem solving abilities (Burton et al., 2009), and adaptive lifestyle behaviours (Bielak et al., 2007). Intraindividual variability at baseline testing has also been shown to be predictive of rates of attrition. MacDonald and colleagues (2003, 2008) investigated attrition in a 6-year longitudinal study and found significant differences between participants who remained from those who dropped out for several RT tasks (simple, lexical decision, and semantic decision). Individuals who dropped out following initial baseline testing displayed greater intraindividual variability in performance compared to participants who remained throughout the duration of the study. This increased risk of

attrition was shown to reflect underlying health-related factors (e.g., disease progression, age-associated impairments) and predicted impending death up to 15 years in advance.

Additional evidence for the predictive utility of intraindividual variability as a stable endogenous trait comes from studies of the neurological correlates of variability. A number of studies have demonstrated increased performance variability in individuals at risk for neurodegenerative diseases. Hultsch and colleagues (2000) investigated intraindividual variability across trials and occasions for RT and memory tasks in three groups of individuals: healthy older adults, older adults with arthritis, and individuals with mild dementia. They found significantly increased intraindividual variability in the group with mild dementia relative to the two neurologically intact groups regardless of physical health status (i.e., healthy vs. arthritis), suggesting variability was a result of endogenous neurological conditions, rather than exogenous somatic conditions (e.g., arthritis). Similar findings were reported by Strauss et al. (2002), who found individuals with dementia were more variable in their physical functioning as well as cognitive performance. Burton and colleagues (2006) investigated intraindividual variability in individuals with confirmed Parkinson's disease (PD), Alzheimer's disease (AD), and older adults with no neurological condition. Consistent with previous research, both disease groups were more variable on a series of RT tasks relative to healthy adults, with the AD individuals displaying significantly greater levels of variability compared to the PD group. Additional evidence for intraindividual variability as a proxy of neurological integrity comes from studies demonstrating increased variability for individuals with Frontotemporal Dementia (FTD; Murtha, Cismaru, Waechter, & Chertkow, 2002) and Dementia with Lewy Bodies (DLB; Walker et al., 2000), compared to those with AD and

Vascular Dementia (VaD). Intraindividual variability has also been investigated as an early indicator of incipient neurodegenerative disease in individuals with Mild Cognitive Impairment (MCI)/Cognitive Impairment No Dementia (CIND). Overall, these studies have found that older adults at risk for cognitive impairment display greater levels of intraindividual variability compared to healthy matched individuals (Christensen et al., 2005; Dixon et al., 2007; Strauss et al., 2007).

Although the exact neural correlates and underlying processes of increased intraindividual variability remain unknown, evidence from the cognitive neuroscience literature has proposed several possible mechanisms. In a recent review by MacDonald and colleagues (2006), it was shown that intraindividual variability for a range of behaviours can have multiple origins including changes in grey matter density, disconnectivity in associative pathways (caused by white matter demyelinization), and neuromodulatory dysfunction (e.g., altered dopamine regulation). Increased intraindividual variability has also been found to be correlated with a number of frontal brain regions (Bellgrove et al., 2004; MacDonald et al., 2006), which is consistent with the compensatory "scaffolding" processes involved in the STAC model of aging and cognition (see Figure 2; Cabeza, 2002; Park & Reuter-Lorenz, 2009).

Intraindividual variability has also been shown to be associated with normative aging processes across the lifespan (Anstey, Dear, Christensen, & Jorm, 2005; Bunce, MacDonald, & Hultsch, 2004; MacDonald, Hultsch, & Bunce, 2006; Nesselroade & Salthouse, 2004). Hultsch and colleagues (2002) compared younger adults aged 17 to 36 years with three groups of older adults: young-old (54-64 years), mid-old (65-74 years), and old-old (75-94 years). The participants completed 4 RT tasks of varying difficulty

(simple RT, choice RT, lexical decision RT, semantic decision RT), and for all tasks older adults displayed significantly more trial-to-trial intraindividual variability in performance compared to the younger adults (particularly for those in old-old (> 75 years) age range). Importantly, age differences in intraindividual variability have been found to be most apparent on speeded tasks that challenge cognitive functioning, such as those that place large demands on executive functioning and working memory. For example, Dixon and colleagues (2007) found significant age differences on 3 related RT tasks (simple RT, choice RT, and 1-back choice RT), but the greatest age effects occurred on the 1-back choice RT which required participants to ignore the present stimulus and instead respond to the target stimulus presented on the previous trial. Similar findings have been found for neurological conditions (e.g., MCI/CIND, dementia) where the greatest distinctions among groups were on cognitively complex RT tasks (Hultsch et al., 2000; Murtha et al., 2002; Strauss et al., 2007). However, these findings do not suggest that more cognitively complex tasks simply exacerbate the effects of reduced psychomotor and perceptual functioning in older individuals. Bunce and MacDonald (2004; 2007) have demonstrated that increased intraindividual variability in older adulthood is not in fact due to slower motor processing, but rather caused by increased attentional and cognitive demands.

Cognitive Load Hypothesis

Examining the relationship between intraindividual variability and cognitive plasticity as predictors, as a function of degree of task complexity (or cognitive load), is an important and related question for the current study. Specifically, it was expected that tasks requiring greater executive control processes (e.g., working memory, attentional

control, updating, goal-maintenance, inhibition), would be associated with increased performance variability and greater potential for cognitive plasticity (Shammi et al., 1998; Stuss et al., 2003; West et al., 2002). In terms of cognitive plasticity, only the more cognitively complex RT task (1-back 4-choice RT; BRT) emerged in the present study as a predictor of long term (6 year) cognitive function, exhibiting significant associations with measures of processing speed (Digit Symbol), fluid reasoning (Letter Series), episodic memory (Word Recall), and verbal ability (Vocabulary). In contrast, intraindividual variability measure of baseline performance were found to be significant predictors of subsequent cognitive function for both the basic (4-choice RT; CRT) and complex (1-back 4-choice RT; BRT) reaction time tasks. These associations were present across each of the five cognitive domains assessed as outcome measures. However, select effects for prediction of rates of cognitive change were observed for both CRT ISD and BRT ISD, with significant associations found only on tasks of episodic memory (Word Recall) and verbal ability (Vocabulary).

A number of explanations have been proposed that may account for these select findings of increased cognitive load and its relationship to cognitive function. For example, West and colleagues (2001) have advocated for the frontal lobe hypothesis of cognitive aging, and proposed that age-related deficits in the functioning of the prefrontal cortex (PFC) results in decreased stability of executive control, which leads to greater intraindividual variability (West et al., 2002). According to this view of cognitive aging, decreased stability of executive control is associated with an increase in lapses of "intention." These lapses, when they occur, result in very long RT latencies and increase the variability of an individual's performance. West and colleagues (2002) further

proposed that because intentional lapses lead to reaction times that are much longer than an individual's modal RT, they cause older adults' RT distributions to show much greater positive skew than those of younger adults. A similar explanation by Bunce and colleagues (1993) has suggested that aging is associated with an increase in “attentional blocks,” and these blocks are also hypothesized to result in extended RTs. As with intentional lapses, attentional blocks predict both increased intraindividual variability and greater positive skew in the RT distributions of older adults. Therefore, within-task variability can be viewed as a breakdown in an attentional control system that maintains the goals of a task across time and controls competing cognitive processes and pathways.

Recent neuroimaging studies also provide support for intraindividual variability and the frontal lobe hypothesis of cognitive aging. For example, Bunce and colleagues (2007) found white matter hyperintensities (WMH; i.e., white matter lesions that affect the efficiency of neuronal conduction) to be significantly correlated with intraindividual variability on speeded cognitive tasks. Importantly, this relationship was unique to WMHs in the frontal lobes, demonstrating the influential role of these key neural pathways in the regulation of cognitive performance. Additionally, Stuss and colleagues (2003) found that individuals with focal frontal lesions (due to acquired acute disorders such as infarction, haemorrhage, benign tumor, or traumatic brain injury (TBI)) displayed increased intraindividual variability in task performance on simple and complex RT tasks relative to individuals with temporal or parietal lesions. The findings reviewed here are consistent with the possibility that increased variability, either in the form of maladaptive intraindividual variability or adaptive cognitive plasticity, may reflect a sensitive marker of general central nervous system integrity (MacDonald et al., 2006).

Limitations & Future Directions

Although the results of the current study add to the extant knowledge of intraindividual variability and cognitive plasticity, they must be considered alongside a number of limitations. First, it is important to note the relatively homogenous composition of the study sample. The majority of participants were healthy, highly educated, and of Caucasian descent. The selectiveness of the sample likely resulted in an over-estimation of various participant characteristics relative to the average older adult in the Canadian population, and therefore limits the generalizability of the study findings. However, despite these limitations, we still observed significant trends in age differences, intraindividual variability, and cognitive plasticity as predictors of long term cognitive function, likely under-estimating their relative importance in the more heterogeneous general population. Therefore, replication of the current study in a more diverse and less healthy sample will potentially demonstrate even stronger predictive effects.

Another limitation of the current work is that we did not include an assessment of cognitive strategy adopted by the participants. It is reasonable to speculate that some of the variance in intraindividual variability and cognitive plasticity on the RT tasks reflects individual differences in the generation and active engagement of specific cognitive strategies. Future research will benefit from including assessments of participants' strategy use to determine if in fact varying degrees of successful task exploration are related to intraindividual variability and cognitive plasticity performance. In addition, there are likely personality and motivational differences between participants, which may be related to the results of the current investigation. For example, in a series of studies by Duchek (2007) and Tse (2010), participants (including healthy younger adults, healthy

older adults, and clinically confirmed mild-AD adults) were administered three executive attention RT tasks (Stroop, Simon, Switching tasks) along with cognitive measures and a standard personality inventory (NEO-FFI). The results indicate that higher levels of neuroticism and lower levels conscientiousness in the mild-AD individuals relative to the healthy older adults, accounted for unique variance in discriminating these two groups above and beyond standard neuropsychological tests. This finding is consistent with the claim that differences in these personality traits may serve as a "non-cognitive" indicator of the early onset of cognitive impairments (Wilson et al., 2003, 2007).

An important avenue for future research will be the investigation of long-term change in intraindividual variability and cognitive plasticity, with longitudinal change in cognition. For example, using multilevel modeling techniques, MacDonald and colleagues (2003) found significant associations between 6-year change in intraindividual variability and 6-year change in cognitive test scores. On occasions where individuals were more variable in their RT performance, they also tended to score lower on cognitive tasks completed at that wave of testing, independent of the average linear trend across time. Importantly, the significant covariation relationship was invariant across age groups, indicating that the amount of cognitive decline per unit increase in inconsistency did not vary as a function of age. Lövdén, Li, Shing, and Lindenberger (2007) conducted a similar study with a population of very old individuals (70-102 years) across a 13-year timeline. Using latent growth curve modeling, Lövdén et al. (2007) found similar results to that of MacDonald and colleagues (2003), with individuals across the age range becoming more inconsistent over time.

Another important follow up analysis of the current study will be to more systematically investigate the impact of increased cognitive load on intraindividual variability and cognitive plasticity as predictors of cognitive function. The current study examined two related, but distinct, RT tasks (4-choice RT, 1-back 4-choice RT). By increasing the cognitive complexity to a more executively demanding task (e.g., Task-Switching RT task) the mismatch model of cognitive plasticity and the frontal lobe hypothesis of cognitive aging may be more fully explored.

Finally, future analyses should investigate the potential influence of unique moderators of intraindividual variability, cognitive plasticity, and cognitive function. For example, chronic health conditions and medications are important factors that should be considered in the study of older adults. Specifically, cerebrovascular conditions (e.g., hypertension, diabetes, coronary heart disease) should be explored as moderators of cognitive function. Prior research has demonstrated significant associations between vascular risk factors, increased performance variability (Hultsch et al., 2000), and progression to dementia (Hsiung et al., 2006; Rockwood et al., 2007; Solfrizzi et al., 2004). Therefore, we can reasonably predict that older individuals with a high number of comorbid chronic health conditions (especially vascular conditions) and medications use (e.g., statins), will exhibit increased variability (Hardy, 2009) and decreased cognitive performance over time (Brady, Sprio, Gaziano, 2008).

Conclusion

In the current study, individual differences in intraindividual variability and cognitive plasticity were investigated as predictors of subsequent cognitive function and long term change. In recent years, an increased research emphasis on multidimensional and multidirectional trajectories of change has emerged in the cognitive aging literature. However, few studies have systematically investigated the dynamics of longitudinal change in the context of variability and plasticity. The current investigation represents a significant contribution to this area of aging research and establishes a meaningful relationship between these factors as predictors of cognitive change. Studies of this nature are particularly valuable in establishing theoretical models of aging processes, for developing methodological approaches for the study of age-related change, and for advancing our understanding of the clinical characterization of adult development across the lifespan. The identification of proxies of neurological integrity and preclinical markers of underlying pathologies (e.g., MCI/CIND, dementia) represents an important practical area of research, and continued investigation of intraindividual variability and cognitive plasticity may ultimately facilitate the development of sensitive diagnostic tools for the identification of individuals at risk for cognitive impairment.

References

Albert, M. S., Jones, K., Savage, C. R., Berkman, L., Seeman, T., Blazer, D., & Rowe, J. W. (1995). Predictors of cognitive change in older persons: MacArthur Studies of Successful Aging. *Psychology and Aging, 10*, 578–589.

Allaire, J. C., & Marsiske, M. (2005). Intraindividual variability may not always indicate vulnerability in elders' cognitive performance. *Psychology and Aging, 20, 390-401.*

Anstey, K., & Christensen, H. (2000). Education, Activity, Health, blood pressure and apolipoprotein e as predictors of cognitive change in old age: a review. *Gerontology, 46*,163–177.

Anstey, K. J., Dear, K., Christensen, H., & Jorm, A. F. (2005). Biomarkers, health, lifestyle, and demographic variables as correlates of reaction time performance in early, middle, and late adulthood. *The Quarterly Journal of Experimental Psychology*, *58A*, 5-21.

Anstey, K. J., Mack, H. A., Christensen, H., Li, S.-C., Reglade-Meslin, C., Maller, J., & Sachdev, P. (2007). Corpus callosum size, reaction time speed, and variability in mild cognitive disorders and in a normative sample. *Neuropsychologia, 45,* 1911-1920.

Bäckman, L., & Dixon, R. A. (1992). Psychological compensation: A theoretical framework. *Psychological Bulletin, 112,* 259-283.

Bäckman, L., Jones, S., Berger, A. K., Laukka, E. J., & Small, B. J. (2005). Cognitive impairment in preclinical Alzheimer's disease: A meta-analysis. *Neuropsychology, 19*, 520-531.

Bäckman, L., Jones, S., Small, B. J., Guero-Torres, H., & Fratiglioni, L. (2003). Rate of cognitive decline in preclinical Alzheimer's disease: the role of comorbidity. *Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 58,* 228-236.

Bäckman, L., Small, B. J., Wahlin, A., & Larsson, M. (2000). Cognitive functioning in very old age. In F.I.M. Craik & T. A. Salthouse (Eds.), *Handbook of aging and cognition* (2nd ed., pp. 499-558). Mahwah, NJ: Lawrence Erlbaum Associates.

Baltes, P. B., (1987). Theoretical propositions of life-span developmental psychology: On the dynamics between growth and decline. *Developmental Psychology, 23,* 611-626.

Baltes, P. B., Ditman-Kohli, F., & Dixon, R. (1984). New perspectives on the development of intelligence in adulthood: Toward a dual-process conception and a model of selective optimization with compensation. In P. B. Baltes, & O. G. Brim (Eds.), *Life-span development and behavior* (pp. 33-76). New York, NY: Academic Press.

Baltes, M., Kuhl, K. P., & Sowarka, D. (1992). Testing for limits of cognitive reserve capacity: A promising strategy for early diagnosis of dementia? *Journal of Gerontology, 47,* 165-167.

Baltes, P. B., Staudinger, U. M., & Lindenberger, U. (1999). Lifespan psychology: Theory and application to intellectual functioning. *Annual Review of Psychology, 50*, 471–507.

Baltes, P. B., & Singer, T. (2001). Plasticity and the ageing mind: An exemplar of the bio-cultural orchestration of brain and behaviour. *European Review, 1*, 59–76.

Baltes, P., & Willis, S. (1982). Plasticity and enhancement of intellectual functioning in old age: Penn State's adult development and enrichment project (ADEPT). In F. I. M. Craik & S. E. Trehud (Eds.), *Aging and cognitive processes* (pp. 353–389). New York, NY: Plenum Press.

Bellgrove, M. A., Hester, R., & Garavan, H. (2004). The functional neuroanatomical correlates of response variability: evidence from a response inhibition task. *Neuropsychologia, 42,* 1910-1916.

Bielak, A. M., Hughes, T. F., Small, B. J., & Dixon, R. A. (2007). It's never too late to engage in lifestyle activities: Significant concurrent but not change relationships between lifestyle activities and cognitive speed. *Journal of Gerontology: Psychological Sciences, 62(B),* P331-P339.

Bielak, A. M., Hultsch, D. F., Strauss, E., MacDonald, S. W. S., & Hunter, M. A. (2010a). Intraindividual variability is related to cognitive change in older adults: Evidence for within-person coupling. *Psychology and Aging, 25,* 575-586.

Bielak, A. M., Hultsch, D. F., Strauss, E., MacDonald, S. W. S., & Hunter, M. A. (2010b). Intraindividual variability in reaction time predicts cognitive outcomes 5 years later. *Neuropsychology, (in press)*.

Black, J.E., Isaacs, K. R., Anderson, B. J., Alcantara, A. A., & Greenough, W.T. (1990). Learning causes synaptogenesis, whereas motor activity causes angiogenesis, in cerebellar cortex of adult rats. *Proceedings of the National Academy of Sciences. 87*, 5568–5572.

Blair, J. R., & Spreen, O. (1989). Predicting premorbid IQ: A revision of the National Adult Reading Test. *The Clinical Neuropsychologist, 3,* 129-136.

Brady, C. B., Spiro, A. 3rd , & Gaziano, J. M. (2005). Effects of age and hypertension status on cognition: the Veterans Affairs Normative Aging Study. *Neuropsychology, 19,*770-777.

Bunce, D., Anstey, K., J., Christensen, H., Dear, K., Wen, W., & Sachdev, P. (2007). White matter hyperintensities and within-person variability in community-dwelling adults aged 60-64 years. *Neuropsychologia, 45,* 2009-2015.

Bunce, D., MacDonald, S. W. S., & Hultsch, D. F. (2004). Inconsistency in serial choice decision and motor reaction time dissociate in younger and older adults. *Brain and Cognition, 56*, 320-327.

Bunce, D. J., Warr, P., & Cochrane, T. (1993). Blocks in choice responding as a function of age and physical fitness. *Psychology and Aging, 8,* 26–33.

Burton, C. L., Strauss, E., Hultsch, D. F., & Hunter, M. A. (2009). The relationship between everyday problem solving and inconsistency in reaction time in older adults. *Aging, Neuropsychology, and Cognition, 16,* 607-632.

Burton, C. L., Strauss, E., Hultsch, D. F., Moll, A., & Hunter, M. A. (2006). Intraindividual variability as a marker of neurological dysfunction: A comparison of Alzheimer's disease and Parkinson's disease. *Journal of Clinical and Experimental Neuropsychology, 28,* 67-83.

Cabeza R. (2002). Hemispheric asymmetry reduction in old adults: the HAROLD model. *Psychology and Aging, 17*, 85–100.

Calero, M. D., & Navarro, E. (2004). Relationship between plasticity, mild cognitive impairment and cognitive decline. *Archives of Clinical Neuropsychology*, *19*, 653–660.

Calero, M. D., & Navarro, E. (2007). Cognitive plasticity as a modulating variable on the effects of memory training in elderly person. *Archives of Clinical Neuropsychology, 22*, 63-72.

Carro, E., Trejo, L. J., Busiguina, S., & Torres-Aleman, I. (2001). Circulating insulin-like growth factor 1 mediates the protective effects of physical exercise against brain insults of different etiology and anatomy. *Journal of Neuroscience, 21,* 5678-5684.

Chertkow, H.M. (2000). Mild Cognitive Impairment. *Current Opinion in Neurology*, *15,* 401–407.

Christensen, H., Dear, K. B. G., Anstey, K. J., Parslow, R. A., Sachdev, P., & Jorm, A. F. (2005). Within-occasion intraindividual variability and preclinical diagnostic

status: Is intraindividaul variability an indicator of mild cognitive impairment? *Neuropsychology, 19,* 309-317.

Christensen, H, Korten, A.E, Jorm AF, Henderson AS, Jacomb PA, Rodgers B. (1997). Education and decline in cognitive performance: compensatory but not protective. *International Journal of Geriatric Psychiatry, 12,* 323–330.

Christensen, H., Mackinnon, A., Jorm, A., Henderson, A., Scott, R., Korten, A. (1994). Age differences and interindividual variation in cognition in community-dwelling elderly. *PsychologicalAging 9*, 381–390.

Chu, B. C., Millis, S., Rango-Lasprilla, J. C., Hanks, R., Novack, T., & Hart, T. (2007). Measuring recovery in new learning and memory following traumatic brain injury: A mixed-effects modeling approach. *Journal of Clinical and Experimental Neuropsychology, 29,* 617-625.

Cohen, J. (1977). *Statistical power analysis for the behavioural sciences.* New York, N.Y.: Academic Press.

Colcombe, S. J., & Kramer, A. F. (2003). Fitness effects on the cognitive function of older adults: a meta-analytic study. *Psychological Science, 14,* 125-130.

Colcombe, S. J., Kramer, A. F., Erickson, K. I., Scalf, P., McAuley, E., Cohen, N. J., Webb, A., Jerome, G. J., Marquez, D. X., & Elavsky, S. (2004). Cardiovascular fitness, cortical plasticity, and aging. *Proceedings of the National Academy of Sciences, 101*, 3316-3321.

Cotman, C. W., & Berchtold, N. C. (2002). Exercise: a behavioural intervention to enhance brain health and plasticity. *Trends in Neuroscience, 25,* 295-301.

DeFrias, C. M., Lövdén, M., Lindenberger, U., & Nilsson, L.-G. (2007). Revisiting the defifferentiation hypothesis with longitudinal multi-cohort data. *Intelligence, 35,* 381-392.

Deary, I. J., & Der, G. (2005). Reaction time, age, and cognitive ability: Longitudinal findings from age 16 to 63 years in representative population samples. *Aging, Neuropsychology, and Cognition, 12,* 187-215.

Der, G., & Deary, I. J. (2006). Age and sex differences in reaction time in adulthood: Results from the United Kingdom Health and Lifestyle Survey. *Psychology and Aging, 21,* 62-73.

Dixon, R. A., Garrett, D. D., Lentz, T. L., MacDonald, S. W. S., Strauss, E., Hultsch, D. F. (2007). Neurocognitive markers of cognitive impairment: Exploring the roles of speed and inconsistency. *Neuropsychology, 21,* 381-399.

Ekstrom, R. B., French, J. W., Harman, H. H., & Dermen, D. (1976). *Manual for kit of factor-referenced cognitive tests*. Princeton, NJ: Educational Testing Service.

Fernandez-Ballesteros, R., Zamarron, M. D., Tarraga, L., Moya, R., & Iniguez, J. (2003). Cognitive plasticity in healthy, Mild Cognitive Impairment (MCI) subjects and Alzheimer's Disease patients: a research project in Spain. *European Psychologist*, *8,* 148–159.

Folstein, M., Folstein, S., & McHugh, S. (1975). Mini-Mental State: A practical method for grading the cognitive status of patients for the clinician. *Journal of Psychiatric Research, 12,* 189-198.

Freund, A. M., and Baltes, P. B. (2000). The orchestration of selection, optimization, and compensation: an action-theoretical conceptualization of a theory of developmental regulation. In W. J. Perrig and A. Grob, (Eds.), *Control of human behavior, mental processes, and consciousness*. (pp. 35-58). Mahwah, N.J.: Erlbaum.

Fuentes, K., Hunter, M. A., Strauss, E., & Hultsch, D. F. (2001). Intraindividual variability in cognitive performance in persons with chronic fatigue syndrome. *The Clinical Neuropsychologist, 15,* 210-227.

Hardy, J. (2009). The amyloid hypothesis for Alzheimer's disease: a critical reappraisal. *Journal of Neurochemisty, 4,* 1129-1134.

Hertzog, C., Kramer, A. F., Wilson, R. S., & Lindenberger, U. (2009). Enrichment effects on adult cognitive development: Can the functional capacity of older adults be preserved and enhanced? *Psychological Science in the Public Interest, 9,* 1-65.

Hsiung, G.-Y., Donald, A., Grand, J., Black, S. E., Bouchard, R. W., Gauthier, S. G., Loy-English, I., Hogan, D. B., Kertesz, A., Rockwood, K., & Feldman, H. H. (2006). Outcomes of cognitively impaired not demented at 2 years in the Canadian Cohort Study of Cognitive Impairment and Related Dementias (ACCORD). *Dementia & Geriatric Cognitive Disorder, 22,* 413-420.

Hultsch, D. F., Hertzog, C., & Dixon, R. A. (1990). Ability correlates of memory performance in adulthood and aging. *Psychology and Aging, 5,* 356-368.

Hultsch, D. F., Hertzog, C., Small, B. J., & Dixon, R. A. (1999). Use it or lose it: Engaged lifestyle as a buffer of cognitive decline in aging? *Psychology and Aging*, 14, 245-263.

Hultsch, D. F., Hertzog, C., Small, B. J., McDonald-Miszczak, L., & Dixon, R. A. (1992). Short-term longitudinal change in cognitive performance in later life. *Psychology and Aging*, 7, 571-584.

Hultsch, D. F., & MacDonald, S. W. S. (2004). Intraindividual variability in performance as a theoretical window onto cognitive aging. In R. A. Dixon, L. Bäckman, & L.-G. Nilsson (Eds.), *New Frontiers in cognitive agin* (pp. 65-88). Oxford, UK: Oxford University Press.

Hultsch, D. F., MacDonald, S. W., Hunter, M. A., Levy-Bencheton, J., & Strauss, E. (2000). Intraindividual variability in cognitive performance in older adults: comparison of adults with mild dementia, adults with arthritis, and healthy adults. *Neuropsychology, 14,* 588-598.

Hultsch, D. F., MacDonald, S. W. S., & Dixon, R. A. (2002). Variability in reaction time performance of younger and older adults. *Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 57,* 101-115.

Hultsch, D. F., Strauss, E., Hunter, M. A., & MacDonald, S. W. S. (2008). Intraindividual variability, cognition, and aging. In F.I.M. Craik & T.A. Salthouse (Eds.), *The Handbook of Aging and Cognition* (3rd ed., pp. 491-556). New York, NY: Psychology Press.

Kempermann, G., Kuhn, H. G., & Gage, F. H. (1997). More hippocampal neurons in adult mice living in an enriched environment. *Nature, 386,* 493–495.

Kramer, A. F., Bhere, L., Colcombe, S. J., Dong, W., & Greenough, W. T. (2004). Environmental influences on cognitive and brain plasticity during aging. *Journals of Gerontology, Series A: Biological Sciences and Medical Sciences, 59,* 940-957.

Li, S.-C. (2003). Biocultural orchestration of developmental plasticity across levels: The interplay of biology and culture in shaping the mind and behavior across the life span. *Psychological Bulletin, 129,* 171-194.

Li, S.-C., Aggen, S. H., Nesselroade, J. R., & Baltes, P. B. (2001). Short-term fluctuations in elderly people's sensorimotor functioning predicts text and spatial memory performance: The MacArthur Successful Aging Studies. *Gerontology, 47,* 100-116.

Li, S.-C., Huxhold, O., & Schmiedek, F. (2004). Aging and attenuated processing robustness: Evidence from cognitive and sensorimotor functioning. *Gerontology, 50,* 28-34.

Li, S.-C., Lindenberger, U., Hommel, B., Aschersleben, G., Prinz, W., & Baltes, P. B. (2004). Transformations in the couplings among intellectual abilities and consituent cognitive processes across the life span. *Psychological Science, 15,* 155-163.

Li, S.-C., Lindenberger, U., & Sikstrom, S. (2001). Aging cognition: From neuromodulation to representation. *Trends in Cognitive Science, 5, 479-486.*

Lindenberger, U., & Ghisletta, P. (2009). Cognitive and sensory declines in old age: Gauging the evidence for a common cause. *Psychology and Aging, 24,* 1-16.

Lövdén, M., Bäckman, L., Lindenberger, U., Schaefer, S., & Schmiedek, F. (2010). A theoretical framework for the study of adult cognitive plasticity. *Psychological Bulletin, 136,* 659-676.

Lövdén, M., Li, S.-C., Shing, Y.L., & Lindenberger, U. (2007). Within-person trial-to-trial variability precedes and predicts cognitive decline in old and very old age: Longitudinal data from the Berlin Aging Study. *Neuropsychologia, 45,* 2827-2838.

Lustig, C., Shah, P., Seidler, R., & Reuter-Lorenz, P. (2009). Aging, training, and the brain: A review and future directions. *Neuropsychology Review, 19,* 504-522.

Lyketsos, C. G., Chen L. S., & Anthony, J. C. (1999). Cognitive decline in adulthood: an 11.5-year follow-up of the Baltimore Epidemiological Catchment Area Study. *American Journal of Psychiatry, 156*, 58–65.

MacDonald, S. W. S., Cervenka, S., Farde, L., Nyberg, L., & Bäckman, L. (2009). Extrastriatal dopamine D2 receptor binding modulates intraindividual variability in episodic recognition and executive functioning. *Neruopsychologica, 47,* 2299-2304.

MacDonald, S. W. S., Hultsch, D. F., & Bunce, D. (2006). Intraindividual variability in vigilance performance: Does degrading visual stimuli mimic age-related "neural noise"? *Journal of Clinical and Experimental Neuropsychology*, *28*, 655-675.

MacDonald, S. W. S., Hultsch, D. F., & Dixon, R. A. (2003). Performance variability is related to change in cognition: Evidence from the Victoria Longitudinal Study. *Psychology and Aging, 18,* 510-523.

MacDonald, S. W. S., Hultsch, D. F., & Dixon, R. A. (2008). Predicting impending death: Inconsistency in speed is a selective and early marker. *Psychology and Aging, 23,* 595-607.

MacDonald, S. W. S., Nyberg, L., & Bäckman, L. (2006). Intra-individual variability in behavior: Links to brain structure, neurotransmission and neuronal activity. *Trends in Neurosciences, 29,* 474-480.

MacDonald, S. W. S., Nyberg, L., Sandblom, J., Fischer, H. & Bäckman, L. (2008). Increased response-time variability is associated with reduced inferior parietal activation during episodic recognition in aging. *Journal of Cognitive Neuroscience, 20,* 779-786.

Murtha, S., Cismaru, R., Waechter, R., & Chertkow, H. (2002). Increased variability accompanies frontal lobe damage in dementia. *Journal of the International Neuropsychological Society, 8,* 360-372.

Nesselroade, J. R. (1991). The warp and the woof of the developmental fabric. In Roger M. Downs, Lynn S. Liben, & David S. Palermo (Eds.), *Visions of aesthetics, the environment, & development: The legacy of Joachin F. Wohlwill* (pp. 213-240). Hillsdale, NJ: Erlbaum.

Nesselroade, J. R., & Salthouse, T. A. (2004). Methodological and theoretical implications of intraindividual variability in perceptual-motor performance. *Journals of Gerontology, Series B: Psychological Sciences and Social Sciences, 59*, P49-P55.

Park, D. C., & Reuter-Lorenz, P. (2009). The adaptive brain: aging and neurocognitive scaffolding. *Annual Reviews in Psychology, 60,* 173-196.

Rabbitt, P., Osman, P., Moore, B., & Stollery, B. (2001). There are stable individual differences in performance variability, both from moment to moment and from day to day. *Quarterly Journal of Experimental Psychology Section A-Human Experimental Psychology, 54,* 981-1003.

Ram, N., Rabbitt, P., Stollery, B., & Nesselroade, J. R. (2005). Cognitive performance inconsistency: Intraindividual change and variability. *Psychology and Aging, 20,* 623-633.

Raykov, T., Baltes, M., Neher, K., & Sowarka, D. (2002). A comparative study of two psychometric approaches to detect risk status for dementia. *Gerontology*, *48*, 185–193.

Reitan, R. M. & Wolfson, D. (1985). *The Halstead-Reitan Neuropsychological Test Battery*. Tucson, AZ: Neuropsychology Press.

Rey, A. (1964). *L'examen clinique en psychologie* [Clinical assessment in psychology]. Paris: Presses Universitaires de France.

Rockwood, K., Chertkow, H., & Feldman, H.H. (2007). Is mild cognitive impairment a valid target of therapy. *Canadian Journal of Neurological Sciences, 34*, S90-S96.

Rockwood, K., Moorhouse, P. K. , Song, X., MacKnight, C., Gauthier, S., Kertesz, A., Montgomery, P., Black, S., Hogan, D. B. , Guzman, A., Bouchard, R., & Feldman, H. (2007). Disease progression in vascular cognitive impairment: cognitive, functional and behavioural outcomes in the Consortium to Investigate Vascular Impairment of Cognition (CIVIC) cohort study. *Journal of the Neurological Sciences, 252,* 106-112.

Rönnlund, M., & Nilsson, L.-G. (2006). Adult life-span patterns in WAIS-R block design performance: Cross-sectional versus longitudinal age gradients and relations to demographic factors. *Intelligence, 34,* 63-78.

Rönnlund, M., Nyberg, L., Bäckman, L., & Nilsson, L.-G. (2005). Stability, growth, and decline in adult life span development of declarative memory: Cross-sectional and longitudinal data from a population-based study. *Psychology and Aging, 20,* 3-18.

Rosenzweig, M. R., & Bennett, E. L. (1996). Psychobiology of plasticity: effects of training and experience on brain and behavior. *Behavioral Brain Research, 78*, 57–65.

Sattler, J. M., & Ryan, J. J. (1999). *Assessment of children: Revised and updated WAIS-III supplement (3rd ed.).* La Mesa, CA: Sattler.

Schaie, K. W., & Hofer, S. M. (2001). Longitudinal studies in aging research. In J. Birren & K. W. Schaie (Eds.), *Handbook of the Psychology of Aging* (5th ed., pp. 53-77). San Diego, CA: Academic Press.

Schaie, K. W., & Willis, S. L. (1986). Can decline in adult intellectual functioning be reversed? *Developmental Psychology, 22*, 223–232.

Schreiber, M. & Schneider, R. (2007). Cognitive plasticity in people at risk for dementia: Optimizing the testing-the-limits approach. *Aging & Mental Health, 11*, 75-81.

Shammi, P., Bosman, E., & Stuss, D. T. (1998). Aging and variability in performance. *Aging, Neuropsychology, and Cognition, 5,* 1-13.

Singer, J. D. & Willet, J. B. (2003). *Applied longitudinal data analysis: Modeling change and event occurrence*. New York: Oxford University Press.

Sliwinski, M. J., Hofer, S. M., Hall, C., Buschke, H., & Lipton, R. B. (2003). Modeling memory decline in older adults: The importance of preclinical dementia, attrition, and chronological age. *Psychology and Aging, 18,* 658-671.

Solfrizzi, V., Panza, F., Colacicco, A. M., D'Introno, A., Capurso, C., Torres, F., et al. (2004). Vascular risk factors, incidence of MCI, and rates of progression to dementia. *Neurology, 23,* 1882-1891.

Stern, Y. (2002). What is cognitive reserve? Theory and research application of the reserve concept. *Journal of the International Neuropsychological Society, 8*, 448-460.

Strauss, E., Bielak, A. A. M., Bunce, D., Hunter, M. A., & Hultsch, D. F. (2007). Within-person variability in response speed as an indicator of mild cognitive impairment in older adults. *Aging, Neuropsychology, and Cognition, 14,* 608-630.

Strauss, E., MacDonald, S. W. S., Hunter, M., Moll, A., & Hultsch, D. F. (2002). Intraindividual variability in cognitive performance in three groups of older adults: Cross-domain links to physical status and self-perceived affect and beliefs. *Journal of the International Neuropsychological Society*, *8*, 893-906.

Stuss, D. T., Murphy, K. J., Binns, M. A., & Alexander, M. P. (2003). Staying on the job: The frontal lobes control individual performance variability. *Brain*, *126*, 2363-2380.

Thurstone, T. G. (1962). *Primary mental abilities for grades 9-12*. Chicago: Science Research Associates.

Tse, C. S., Balota, D. A., Yap, M. J., Duchek, J. M., & McCabe, D. P. (2010). Efffects of healthy aging and early stage dementia of the Alzheimer's typ on components of response time distributions in three attention tasks. *Neuropsychology, 24, 300-315.*

Walker, M. P., Ayre, G. A., Cummings, J. L., Wesnes, K., McKeith, I. G., O'Brien, J. T. et al. (2000). Quantifying fluctuation in dementia with Lewy bodies, Alzheimer's disease, and vascular dementia. *Neurology*, *54*, 1616-1624.

Wechsler, D. (1981). *Wechsler Adult Intelligence Scale (WAIS) – Revised.* New York, NY: Psychological Corporation.

Wechsler, D. (1997). *WAIS-III Technical Manual.* San Antonio, TX: Psychological Corporation.

West, R. (2001). The transient nature of executive control processes in younger and older adults. *European Journal of Cognitive Psychology, 13,* 91–105.

West, K. J., Armilio, M. L, Craik, F. I. M., & Stuss, D. T. (2002). Lapses of intention and performance variability reveal age-related increases in fluctuations of executive control. *Brain and Cognition, 49,* 402-419.

Wilson, R. S., Beckett, L. A., Barnes, L. L., Schneider, J. A., Bach, J., Evans, D. A. et al. (2002). Individual differences in rates of change in cognitive abilities of older persons. *Psychology and Aging, 17,* 179-193.

Wilson, R. S., Evans, D. A., Bienias, J. L., Mendes de Leon, C. F., Schneider, J. A., & Bennett, D. A. (2003). Proneness to psychological distress is associated with risk of Alzheimer's disease. *Neurology, 61,* 1479–1485.

Wilson, R. S., Schneider, J. A., Arnold, S. E., Bienias, J. L., & Bennett, D. A. (2007). Conscientiousness and the incidence of Alzheimer disease and mild cognitive impairment. *Archives of General Psychiatry, 64,* 1204–1212.

Williams, B. R., Hultsch, D. F., Strauss, E. H., Hunter, M. A., & Tannock, R. (2005). Inconsistency in reaction time across the life span. *Neuropsychology, 19,* 88-96.

Winnock, M., Letenneur, L., Jacqmin-Gadda, H., Dallongeville, J., Amouyel, P., & Dartigues, J. F. (2002). Longitudinal analysis of the effect of apolipoprotein E e4 and education on cognitive performance in elderly subjects: the PAQUID study. *Journal of Neurology, Neurosurgery, & Psychiatry, 72*, 794–797.