THE GERONTOLOGICAL SOCIETY OF AMERICA®

Journals of Gerontology: Psychological Sciences
cite as: *J Gerontol B Psychol Sci Soc Sci*, 2022, Vol. 77, No. 1, 71–83
doi:10.1093/geronb/gbab051
Advance Access publication March 26, 2021

OXFORD

Research Article

Reaction Time Intraindividual Variability Reveals Inhibitory Deficits in Single- and Multiple-Domain Amnestic Mild Cognitive Impairment

Ricky Chow, BSc,[1,†] Rahel Rabi, PhD,[1,†] Shahier Paracha, BSc,[1] Brandon P. Vasquez, PhD, CPsych,[2,3] Lynn Hasher, PhD,[1,4] Claude Alain, PhD,[1,4] and Nicole D. Anderson, PhD, CPsych[1,4,5,*]

[1]Rotman Research Institute, Baycrest Centre, Toronto, Ontario, Canada. [2]Neuropsychology & Cognitive Health, Baycrest Centre, Toronto, Ontario, Canada. [3]Department of Occupational Science & Occupational Therapy, University of Toronto, Ontario, Canada. [4]Department of Psychology, University of Toronto, Ontario, Canada. [5]Department of Psychiatry, University of Toronto, Ontario, Canada.

*Address correspondence to: Nicole D. Anderson, PhD, CPsych, Rotman Research Institute, Baycrest Centre, 3560 Bathurst Street, Toronto, ON M6A 2E1, Canada. E-mail: nanderson@research.baycrest.org
[†]These authors contributed equally to this work.

Received: November 3, 2020; Editorial Decision Date: March 16, 2021

Decision Editor: Alyssa Gamaldo, PhD

Abstract

Objectives: Amnestic mild cognitive impairment (aMCI), a prodromal stage of Alzheimer's disease and other dementias, is characterized by episodic memory impairment. Recent evidence has shown inhibitory control deficits in aMCI, but the extent of these deficits across inhibitory domains (i.e., response inhibition and interference control) and aMCI subtypes (i.e., single vs multiple domain) remains unclear. Few studies have included reaction time intraindividual variability (RT IIV) in these efforts. The aim of this study was to compare response inhibition and interference control between aMCI subtypes using measures of accuracy, mean RT, and RT IIV.

Methods: We report data from 34 individuals with single-domain aMCI (sdaMCI, 66–86 years), 20 individuals with multiple-domain aMCI (mdaMCI, 68–88 years), and 52 healthy controls (HC, 64–88 years) who completed tasks of response inhibition (Go–NoGo) and interference control (Flanker). Group differences in accuracy, mean RT, and RT IIV were examined for both tasks.

Results: Individuals with mdaMCI had higher RT IIV than the other groups on both tasks. In RT IIV, we observed an interference control deficit in mdaMCI and sdaMCI relative to healthy controls, a finding not observed through accuracy or mean RT.

Discussion: RT IIV may detect subtle differences in inhibition deficits between aMCI subtypes that may not be evident with conventional behavioral measures. Findings support the supplementary use of RT IIV when assessing early executive function deficits.

Keywords: Executive functioning, Flanker, Go–NoGo, Inhibitory control, Interference control, Response inhibition

Mild cognitive impairment (MCI) is an intermediate stage between healthy aging and dementia. Individuals with MCI demonstrate a decline in cognitive abilities greater than expected for an individual's age, but are able to maintain functional independence (Petersen, 2004). MCI can be divided into four subtypes based on the presence or absence

of episodic memory impairment (amnestic and nonamnestic subtypes, respectively) and number of impaired cognitive domains (single or multiple domains; Petersen et al., 2009). Amnestic MCI (aMCI) is thought to represent the prodromal phase of dementia due to Alzheimer's disease (AD), although it can progress to other forms of dementia (Petersen et al., 2009). Multiple-domain aMCI (mdaMCI) is of particular interest as it represents a more severe subtype due to the presence of additional cognitive deficits (Petersen et al., 2009), with a twofold greater likelihood of converting to AD compared to single-domain aMCI (sdaMCI) over a 7-year time period (Golob et al., 2007). Given the high prevalence of AD, it is important to characterize cognitive impairments that distinguish mdaMCI and sdaMCI subtypes from healthy older adults. One potential tool is reaction time intraindividual variability (RT IIV), that is, within-person variability in performance across trials, which is thought to be indicative of executive attention ability (Vasquez et al., 2016; West et al., 2002). As limited research has explored intraindividual variability between aMCI subtypes in tasks of inhibitory control, the primary goal of this study is to compare RT IIV between individuals with sdaMCI, individuals with mdaMCI, and healthy controls (HC) on two inhibition measures. To our knowledge, this is the first study to systematically examine two types of inhibitory control between aMCI subtypes using a measure of intraindividual variability.

Greater RT IIV is correlated with cognitive decline and greater neurological impairment resulting in executive functioning deficits (MacDonald et al., 2006). RT IIV can distinguish individuals with early stage AD from healthy older adults in simple and choice RT tasks (Christ et al., 2018). RT IIV is more strongly associated with neuropsychological measures of executive functioning (including inhibition) compared to other cognitive domains, such as memory or processing speed (Vasquez et al., 2018). Previous studies have found greater RT IIV in individuals with aMCI than healthy controls in simple RT tasks (Christensen et al., 2005; Strauss et al., 2007). Furthermore, past studies have found greater RT IIV in the mdaMCI subtype than the sdaMCI subtype and healthy controls on simple/choice RT tasks and visual search tasks (McLaughlin et al., 2010; Strauss et al., 2007). RT IIV has also been associated with inhibition failure in adults with attention-deficit hyperactivity disorder (Borella et al., 2013) and healthy older adults (Joly-Burra et al., 2018). Individuals with early stage AD have also demonstrated higher RT IIV in Simon and Stroop inhibition tasks relative to healthy older adults (Jackson et al., 2012). Similarly, higher RT IIV was found in inhibition tasks (set-shifting and Simon tasks) for individuals with mdaMCI than individuals with sdaMCI or healthy controls (Strauss et al., 2007).

Although episodic memory deficits are the hallmark of aMCI, deficits in executive functioning, including inhibitory control, are also prevalent (Johns et al., 2012; Rabi et al., 2020). Inhibitory control, a core component of executive functioning, is the ability to suppress irrelevant information and restrain inappropriate prepotent responses (Diamond, 2013; Hasher et al., 1999). A recent meta-analysis by Rabi et al. (2020) including 2,184 individuals with aMCI and 3,049 healthy controls found aMCI-related deficits of moderate effect sizes (Hedge's g = –0.73) across inhibitory control domains including response inhibition and interference control.

Response inhibition is the ability to withhold a response according to task-relevant information (Simmonds et al., 2008), and is often measured with the Go–NoGo task (Mesulam, 1985). Studies have found impaired response inhibition in aMCI (Mudar et al., 2016; Nguyen et al., 2017; Zheng et al., 2012, 2014), with moderate effect sizes (Hedge's g = –0.71) across studies (Rabi et al., 2020). To our knowledge, research examining response inhibition between aMCI subtypes is limited to two studies by Cid-Fernández et al. (2017a, 2017b). They used a Go–NoGo task with an additional selective attention component and found lower Go accuracy in the mdaMCI group relative to sdaMCI and healthy control groups, and longer Go RTs relative to healthy controls, but did not evaluate group differences in response inhibition deficits (i.e., Go vs NoGo accuracy).

Interference control refers to the ability to inhibit irrelevant information present in the target or environment, and has been measured by the Flanker task (Eriksen & Eriksen, 1974), the Simon task (Simon & Wolf, 1963), and the Stroop task (Stroop, 1935). Several studies have found impaired interference control in aMCI (Bélanger & Belleville, 2009; Bélanger et al., 2010; Borella et al., 2017; Borsa et al., 2018; Duong et al., 2006; Pereiro et al., 2014; Van Dam et al., 2013; Villeneuve et al., 2009; Wylie et al., 2007; Zhang et al., 2015), with moderate effect sizes (Hedges' g = –0.74) across studies (Rabi et al., 2020). Comparing aMCI subtypes, Pereiro et al. (2014) found a greater Simon effect in accuracy in individuals with mdaMCI compared to those with sdaMCI or healthy controls. To our knowledge, only one other study (Strauss et al., 2007) has compared RT IIV between aMCI subtypes on an inhibition task (Simon task), but only evaluated overall mean RT and RT IIV rather than group by condition interactions needed to identify group differences in inhibition deficits. We are not aware of any studies comparing aMCI subtypes on other tests of interference control.

The aim of the present study was to compare inhibitory control deficits between individuals with sdaMCI, mdaMCI, and healthy controls using accuracy, mean RT, and RT IIV in two domains of inhibitory control: response inhibition with a Go–NoGo task, and interference control with a Flanker task. We expected individuals with mdaMCI to show greater RT IIV on all task conditions than individuals with sdaMCI and healthy controls. Furthermore, we expected the mdaMCI group to demonstrate greater deficits than the sdaMCI and healthy control groups across all measures.

Method

Participants

Target sample size was based on the Go–NoGo commission error rate of Cid-Fernández et al. (2017a). Using G*Power (Faul et al., 2007), as few as 16 participants per group would be sufficient to detect a significant group main effect comparing healthy controls, individuals with sdaMCI, and individuals with mdaMCI, with an effect size of $f = 0.59$, $\alpha = 0.05$, and $1 - \beta = 0.95$. However, as we were interested in assessing mean RT and RT IIV in addition to accuracy metrics, we aimed to recruit 20–30 per group. Participant recruitment took place from January 2017 to March 2020 until it was stopped due to coronavirus disease 2019, but we had already surpassed this target by that point.

Participants were recruited if they were native English speakers or learned English before the age of 5, had normal or corrected-to-normal vision, and reported no significant hearing loss, no history of learning disabilities, stroke, transient ischemic attack, traumatic brain injury with loss of consciousness greater than 5 min, substance abuse disorder, brain abnormalities, intracranial surgery, or any other diagnosis of major neurological or psychiatric disorder. Participants were excluded if they had a history of myocardial infarction, coronary artery disease, or bypass surgery. Participants were also excluded if they were taking medications known to affect cognitive functioning, including antidepressants, anticonvulsants, neuroleptics, or recreational drugs either currently or within the year prior to testing. Participants were excluded if they scored below the cutoff on the Telephone Interview for Cognitive Status—Modified. Finally, to control for time-of-day effects on cognitive performance (e.g., Hasher et al., 1999), all participants were required to be of morning chronotype, as categorized by the Morningness–Eveningness Questionnaire (Horne & Ostberg, 1976).

Fifty-four healthy controls, 37 people with sdaMCI, and 22 people with mdaMCI were recruited for the study. Participants were diagnosed by a registered neuropsychologist (N. D. Anderson) using Petersen's (2004) criteria, specifically (a) memory complaint (reported by self and/or reliable informant), (b) objective memory impairment verified by neuropsychological assessment, and (c) maintenance of a functional level of independence in daily activities. Impairment was defined as an age-corrected scaled score 1.5 *SD*s below their estimated intellectual functioning on two or more tests within a cognitive domain. Data were excluded from analysis for one healthy control and two participants with sdaMCI who did not complete the inhibition tasks, and two participants with mdaMCI who received a diagnosis of another neurological disorder after testing. To control for influences of sleep loss on inhibition (Sagaspe et al., 2012), data were excluded from one healthy control who received inadequate sleep the night before testing. Our final sample consisted of 52 healthy controls (64–88 years, 25 females), 34 individuals with sdaMCI (66–86 years, 20 females), and 20 individuals with mdaMCI (68–88 years, six females). The groups did not statistically differ in age, $F(2, 103) = 2.97$, $p = .056$, $\eta_p^2 = 0.055$, sex, $\chi^2(2, N = 106) = 4.191$, $p = .123$, or education, $F(2, 103) = 1.69$, $p = .189$, $\eta_p^2 = 0.032$. Individuals were recruited from the Rotman Research Institute research participant pool, the Baycrest Centre memory clinic, and through local advertisements and community talks. The study protocol was approved by the Research Ethics Board of the Rotman Research Institute at Baycrest Centre. Informed written consent was obtained from all participants.

Neuropsychological Assessment

Neuropsychological assessments took place during an individual's optimal time of day (i.e., morning). The Montreal Cognitive Assessment was administered to assess global cognitive ability. The Shipley's Institute of Living Scale II was administered to estimate crystallized intelligence, and the Wechsler Adult Intelligence Scale (WAIS) Matrix Reasoning to estimate fluid intelligence. Processing speed was assessed with the WAIS Digit Symbol Coding subtest, the Delis–Kaplan Executive Function System (D-KEFS) Trail Making Test (Number and Letter subtests), and D-KEFS Color–Word Interference Test (CWIT) Color Naming and Word Reading subtests. Memory was assessed through the California Verbal Learning Test II, Incidental and Free Recall subsections of the Digit Symbol Coding Test, Verbal Paired Associates, and Visual Paired Associates subtests from the Wechsler Memory Scale—Revised. FAS and Animal fluency tests assessed phonemic and semantic fluency, respectively, and the short form of the Boston Naming Test was administered as a language/naming measure. Executive functioning measures included the Wisconsin Card Sorting Test, Alpha Span Test, the D-KEFS Trail Making Test Number–Letter Switching Subtest, and D-KEFS CWIT Inhibition subtest.

To assess sleep quality, participants completed the Epworth Sleepiness Scale and Pittsburgh Sleep Quality Index. Participants also completed the Hospital Anxiety and Depression Scale. The Memory Assessment Clinics Self-Rating Scale was administered to assess subjective memory concern. Self-reported functional independence was assessed with the Basic Activities of Daily Living Scale and the Instrumental Activities of Daily Living Scale, and verified among individuals with an sdaMCI or mdaMCI profile through the Functional Assessment Questionnaire by a reliable third-party informant. Demographic, neuropsychological, and clinical data for each group are displayed in Table 1.

Procedure

All participants performed both inhibition tasks on a separate day than the neuropsychological assessment to prevent fatigue. We were interested in time-of-day effects on inhibitory control; thus, participants were randomized to

complete the inhibition tasks either in the morning (i.e., optimal time of day for older adults, between 09:00 a.m. and 12:00 p.m.), or in the afternoon (i.e., nonoptimal time of day, between 03:00 p.m. and 06:00 p.m.). As preliminary analyses did not reveal any time-of-day effects on task performance, we therefore collapsed across this variable. The order of inhibition tasks was counterbalanced across participants, and no participant was familiar with either task. Both tasks were performed seated in a sound-attenuated booth 60 cm in front of a computer monitor with a visual angle of 2.9° for the Go–NoGo task, and 3.8° for the Flanker task. Electroencephalography data were acquired during these tasks; these data will be reported elsewhere.

The Go–NoGo task comprised four stimuli created from two shapes (triangles or rectangles) in two different colors (white or pink) to reduce stimulus repetition effects. For each trial, one shape was presented centered on a black background of a computer screen for 186 ms followed by a blank screen interstimulus interval lasting 1,500, 2,000, or 2,500 ms to prevent expectancy effects. Participants were randomized to whether white or pink stimuli (regardless of shape) signified a standard or deviant trial to control for stimulus saliency. Participants were instructed to press the spacebar on a computer keyboard in response to standard trials as quickly and accurately as possible (75% probability) and to withhold responding to deviant trials (25% probability). The response time window was 1,000 ms from stimulus onset. The paradigm consisted of 576 trials (432 Go and 144 NoGo trials) in total, separated into three blocks of 192 trials each. A practice block of 20 trials was used to familiarize participants with the task. The task took approximately 25 min. Figure 1A displays the sequence of events for each trial.

For the Flanker task, stimuli were presented centered on a computer monitor. The task comprised three different arrays made of five symbols, with each array comprising a centered arrowhead pointing either left or right, and two flanker symbols on either side. The flankers were Congruent (i.e., > > > > >), Incongruent (i.e., > > < > >), or Neutral (i.e., = = > = =) with respect to the central arrowhead. For each trial, a stimulus array was presented on a white background for 300 ms followed by a fixed interstimulus interval of 2,000 ms with a central fixation cross. Participants were instructed to press an arrow key on a standard keyboard in response to the direction of the central arrowhead (left arrow with left index finger, right arrow with right index finger) as quickly and accurately as possible. The response time window was 2300 ms from stimulus onset. The paradigm consisted of 306 trials in total (102 trials per condition) separated into three blocks of 102 trials each with randomized trial order. A practice block of 17 trials was used to familiarize participants with the task. The task took approximately 15 min. Figure 1B displays the sequence of events for each trial.

Stimuli for both tasks were displayed using E-Prime version 1.2 (Psychology Software Tools, Inc.). Participants did not receive any feedback on their performance during the tasks.

Data Preparation

Go–NoGo mean accuracy values were calculated from hits and correct rejections. Go–NoGo mean RT and RT IIV values were calculated only from hits. For the Flanker task, accuracy and mean RT values were calculated for each of the Congruent, Incongruent, and Neutral conditions, and trials without a response were discarded from calculation. For both tasks, the first trial in each block was omitted to accommodate for task warm-up effects, and trials with a response time less than 200 ms were removed. These removed on average 0.74% (*SD* = 0.16%) of trials in the Go–NoGo task, which did not vary by group, $F(2, 103) = 0.84$, $p = .436$, $\eta_p^2 = 0.016$, and 0.04% (*SD* = 0.15%) of trials in the Flanker task, with more trials trimmed in the mdaMCI group (0.16%) than sdaMCI or healthy control groups (0.01% for both), $F(2, 103) = 9.09$, $p = .001$, $\eta_p^2 = 0.150$. Incorrect trials and any trials beyond 3 *SD*s of the participants' mean in each condition were additionally removed from calculations of mean RT. This removed on average 1.14% (*SD* = 0.58%) of trials per participant in the Go–NoGo task, which did not differ by group, $F(2, 103) = 0.01$, $p = .989$, $\eta_p^2 < 0.001$, and 1.31% (*SD* = 0.69%) of trials per participant in the Flanker task, which did not differ by group, $F(2, 103) = 0.41$, $p = .665$, $\eta_p^2 = 0.008$. RT IIV was measured using intraindividual standard deviation (ISD) of RTs (Hultsch & MacDonald, 2004). Each participant's RT data retained after trimming were submitted to a multiple regression model that included block number, trial number within the block, and the block by trial number interaction as independent variables and RT as the dependent variable to account for practice and fatigue effects. This method yields residuals around each participant's mean RT. For each participant, the standard deviation of the unstandardized residuals was calculated to yield ISD values.

Data Analysis

Dependent measures were subjected to Bayesian analyses of covariance (ANCOVAs) with age, sex, and education as covariates using JASP software (Version 0.14.1) with default prior probabilities. This approach compares the marginal likelihood of the data under null (i.e., no effect or interaction) and alternative (i.e., an effect/interaction) models and allows one to state the weight of evidence in favor of one over another. Advantages and specific parameters of the Bayesian approach, including the use of default priors, are discussed in Rouder et al. (2012). We followed prior literature (e.g., Goghari & Lawlor-Savage, 2017) in denoting a Bayes factor (B_{10}) greater than 3 as providing support for the alternative hypothesis (i.e., 3:1 odds in favor of the alternative), and a B_{10} greater than

Table 1. Demographic, Neuropsychological, and Clinical Data for Healthy Controls (HC), HC, sdaMCI, and mdaMCI Groups

	HC (n = 52)		sdaMCI (n = 34)		mdaMCI (n = 20)	
Variable	Raw	Scaled	Raw	Scaled	Raw	Scaled
Demographics						
Age (years)	75.19 (6.40)	—	76.41 (6.42)	—	79.15 (5.57)	—
Education (years)	16.50 (2.83)	—	15.59 (2.86)	—	15.35 (2.80)	—
Sex (F:M)	25:27	—	20:14	—	6:14	—
MoCA[a,b]	26.90 (2.38)	—	23.12 (2.17)	—	21.80 (3.37)	—
TICS-M[b]	37.19 (3.02)	—	33.18 (2.85)	—	32.45 (3.39)	—
MEQ	65.81 (4.68)	—	64.06 (5.07)	—	63.35 (4.22)	—
Estimates of IQ						
WAIS-III Matrix Reasoning[b]	24.25 (4.74)	14.42 (2.41)	22.24 (5.79)	13.68 (2.80)	19.15 (5.55)	12.55 (2.54)
Shipley Vocabulary	35.83 (3.34)	12.48 (2.75)	34.32 (4.01)	11.35 (3.07)	34.45 (3.49)	11.35 (2.78)
Memory						
CVLT-II Learning[a,b]	49.71 (12.11)	13.43 (2.84)	27.70 (6.85)	6.06 (2.71)	22.25 (10.74)	5.10 (2.75)
CVLT-II Short Delay FR[a,b]	10.39 (3.42)	12.31 (3.17)	2.91 (2.49)	4.47 (2.98)	2.00 (2.58)	3.30 (3.21)
CVLT-II Long Delay FR[a,b]	10.67 (3.45)	11.61 (2.86)	3.22 (2.50)	4.44 (2.95)	2.05 (2.27)	3.53 (2.55)
WMS-R Visual PA I[a–c]	12.14 (3.44)	11.90 (2.57)	8.97 (3.96)	9.94 (2.42)	5.80 (3.30)	7.80 (1.99)
WMS-R Visual PA II[a–c]	5.08 (1.37)	12.00 (1.60)	3.65 (1.82)	10.44 (2.30)	2.20 (1.67)	9.00 (1.95)
WMS-R Verbal PA I[a,b]	16.43 (3.23)	10.25 (2.41)	10.35 (3.56)	5.68 (2.64)	9.75 (4.46)	5.60 (2.98)
WMS-R Verbal PA II[a,b]	6.96 (1.09)	11.92 (2.16)	4.65 (1.89)	8.62 (2.98)	4.25 (1.97)	8.15 (3.25)
WAIS-III Digit Symbol IL-FR[a,b]	7.50 (1.13)	10.46 (1.16)	5.26 (1.80)	8.09 (2.75)	4.25 (2.22)	7.00 (3.42)
WAIS-III Digit Symbol IL-PR[a,b]	12.65 (4.17)	10.58 (1.19)	5.03 (4.73)	7.09 (3.32)	2.90 (3.60)	5.80 (3.79)
Language						
BNT-15[b]	53.84 (4.81)	10.96 (3.00)	51.35 (6.38)	10.06 (2.83)	46.40 (10.50)	8.75 (3.84)
Phonemic Fluency (FAS)[b]	49.23 (13.12)	12.00 (3.38)	43.26 (10.60)	10.74 (2.91)	34.40 (10.10)	8.60 (2.80)
Semantic Fluency (Animals)[a,b]	18.50 (4.83)	10.31 (3.29)	14.21 (4.05)	7.44 (2.77)	11.45 (3.76)	5.70 (2.94)
Executive Functioning and Processing Speed						
WAIS-III Digit Symbol[b,c]	61.77 (14.67)	12.96 (2.96)	54.91 (13.58)	11.56 (2.58)	40.30 (15.08)	9.30 (2.99)
D-KEFS Trails Numbers[b,c]	38.57 (13.19)	12.87 (2.23)	46.76 (17.00)	12.00 (3.04)	61.40 (32.92)	10.00 (4.05)
D-KEFS Trails Letters[b,c]	38.52 (12.16)	12.79 (1.64)	47.26 (15.47)	11.82 (2.38)	66.53 (36.14)	9.89 (3.86)
D-KEFS Trails N-L Switch[b,c]	94.82 (40.61)	12.31 (2.44)	109.75 (40.58)	11.74 (2.96)	211.97 (60.31)	4.60 (3.70)
D-KEFS Color[b,c]	30.59 (5.34)	11.50 (2.06)	31.79 (5.72)	11.15 (2.49)	40.79 (10.14)	7.63 (3.68)
D-KEFS Word[b,c]	22.91 (4.93)	11.54 (2.50)	22.89 (4.75)	11.55 (2.53)	29.12 (6.92)	8.58 (2.91)
D-KEFS Inhibition[b,c]	57.69 (12.44)	12.98 (1.73)	65.79 (17.23)	12.03 (2.19)	96.55 (38.38)	8.47 (4.31)
Alpha Span[a,b]	28.88 (10.82)	10.61 (3.35)	21.58 (7.17)	8.73 (3.02)	19.30 (7.36)	7.70 (2.52)
WCST Categories	4.90 (1.79)	—	4.41 (2.09)	—	2.60 (2.41)	—
WCST Perseverative Errors %[b,c]	14.25 (10.06)	13.18 (4.34)	18.21 (10.09)	11.79 (3.85)	32.35 (15.63)	7.95 (3.39)
Questionnaires						
HADS Anxiety	4.58 (2.88)	—	5.79 (3.84)	—	5.25 (4.22)	—
HADS Depression	2.40 (1.95)	—	3.36 (2.67)	—	3.35 (2.39)	—
EPW	7.06 (3.04)	—	5.94 (3.46)	—	5.00 (4.19)	—
PSQI	5.96 (2.98)	—	5.47 (2.62)	—	4.89 (3.34)	—
MAC Abilities[a,b]	69.49 (9.56)	10.84 (2.33)	58.71 (8.57)	8.00 (2.13)	59.70 (10.77)	8.30 (2.77)
FAQ[c]	—	—	1.39 (1.82)	—	3.00 (2.58)	—

Notes: Data are means (*SD*s) except for sex. aMCI = amnestic mild cognitive impairment; BNT = Boston Naming Test; CVLT = California Verbal Learning Test; D-KEFS = Delis–Kaplan Executive Functioning System; EPW = Epworth Sleepiness Scale; FAQ = Functional Assessment Questionnaire; FAS = phonemic fluency to the letters F, A, and S; FR = Free Recall; HADS = Hospital Anxiety and Depression Scale; HC = healthy control; IL = Incidental Learning; MAC = Memory Assessment Clinics Self-Rating Scale; mdaMCI = multiple-domain aMCI; MEQ = Morningness–Eveningness Questionnaire; MoCA = Montreal Cognitive Assessment (raw score out of 30); N-L = Number-Letter; PA = Paired Associates; PR = Paired Recall; PSQI = Pittsburgh Sleep Quality Index; sdaMCI = single-domain aMCI; TICS-M = modified Telephone Interview of Cognitive Status (raw score out of 50); WAIS = Wechsler Adult Intelligence Scale; WCST = Wisconsin Card Sorting Test; WMS-R = Wechsler Memory Scale-Revised. For normed assessments, tests of significance were run on scaled scores.

[a]HC ≠ sdaMCI.

[b]HC ≠ mdaMCI.

[c]sdaMCI ≠ mdaMCI.

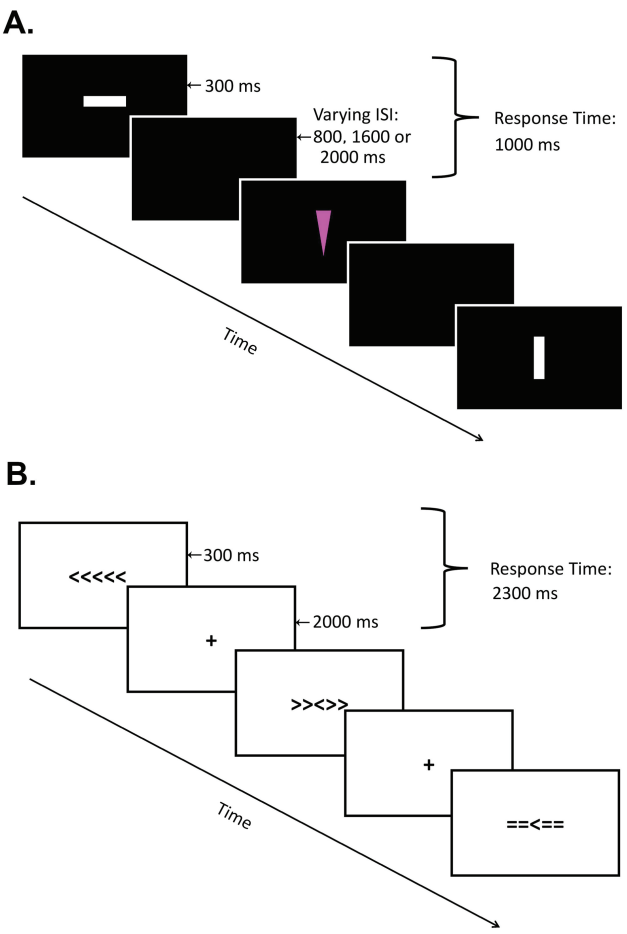

Figure 1. Visual representation of (A) Go–NoGo Task and (B) Flanker Task. Full color version is available within the online issue.

20 as indicative of strong evidence for the alternative. Conversely, B_{10} less than 0.33 indicates support for the null hypothesis (3:1 odds in favor of the null) and B_{10} less than 0.05 indicates strong support for the null.

Accuracy values from the Go–NoGo task were subjected to a mixed ANCOVA with Group (healthy control, sdaMCI, mdaMCI) as a between-subjects factor and Condition (Go, NoGo) as a within-subjects factor. Participants' mean RT and RT IIV values from Go trials were subjected to a one-way ANCOVA with Group (healthy control, sdaMCI, mdaMCI) as a between-subjects factor. For the Flanker task, accuracy, mean RT, and RT IIV values were subjected to a mixed ANCOVA with Group (healthy control, sdaMCI, mdaMCI) as a between-subjects factor and Condition (Congruent, Incongruent, Neutral) as a within-subjects factor. For main effects, the null model included the covariates only and the alternative model also included the main effect of interest. For interactions, the null model contained the covariates and all main effects while the alternative model also included the interaction of interest. Post hoc pairwise comparisons based on the default *t* test with a Cauchy prior were run when B_{10} for main effects exceeded 3. Post hoc Bayesian univariate ANCOVAs were run for two Flanker interference effects, defined as the difference between Incongruent and Congruent (Incongruent–Congruent effect), and between Incongruent and Neutral (Incongruent–Neutral effect) when B_{10} for Group by Condition interactions exceeded 3.

Results

Neuropsychological Performance

The mdaMCI and sdaMCI groups demonstrated impairments on tests of memory and semantic fluency relative to HC as expected (Murphy et al., 2006). The mdaMCI group demonstrated additional impairments on tests of executive functioning and processing speed relative to sdaMCI and HC groups. The mdaMCI group also performed worse on tests of naming, phonemic fluency, and visuospatial reasoning than the HC group.

Go–NoGo Task

Table 2 shows a summary of results for omnibus and post hoc statistics for both tasks. Figure 2 shows accuracy, mean RT, and RT IIV on the Go–NoGo task. As expected, the accuracy analysis revealed strong evidence for greater accuracy on Go than NoGo trials. However, there was no evidence for a Group main effect or Group by Condition interaction in accuracy. The analyses for mean RT and RT IIV on Go trials revealed evidence for Group main effects. Pairwise comparisons revealed evidence for slower mean RTs and elevated RT IIV in the mdaMCI group compared to sdaMCI or HC groups, as well as support for a null difference in mean RTs and RT IIV between the sdaMCI and HC groups. Inclusion of data from one HC participant excluded due to inadequate sleep the night before testing did not change the pattern of findings. To summarize, the mdaMCI group performed with slower and more variable RTs than their sdaMCI and HC counterparts, but no response inhibition deficits were apparent in sdaMCI or mdaMCI groups.

Flanker Task

Figure 3 shows accuracy, mean RT, and RT IIV on the Flanker task. As expected, the analysis revealed strong evidence for Condition main effects. Pairwise comparisons revealed strong evidence for greater accuracy, faster mean RT, and lower RT IIV on Congruent and Neutral trials relative to Incongruent trials, as well as support for null differences between Congruent and Neutral trials on all three metrics. The analyses also revealed evidence for Group main effects for all three metrics. Post hoc pairwise comparisons revealed strong evidence for lower accuracy, slower mean RT, and elevated RT IIV on all task conditions in the mdaMCI group compared to sdaMCI or HC groups, whereas there was evidence for a null Group difference on all three metrics between sdaMCI and HC groups.

Table 2. Summary of Bayes Factors for Go–NoGo and Flanker Tasks.

Effect	Omnibus B_{10}	Post hoc comparison	Post hoc B_{10}
Go–NoGo Accuracy			
Group	0.78		
Condition[a]	1.06×10^{19}		
Group × Condition	2.25		
Go Mean RT			
Group[a]	4.60	mdaMCI > sdaMCI[a]	3.10
		mdaMCI > HC[a]	7.93
		sdaMCI = HC[b]	0.25
Go RT IIV			
Group[a]	4,355.78	mdaMCI > sdaMCI[a]	1,119.10
		mdaMCI > HC[a]	1,887.79
		sdaMCI = HC[b]	0.28
Flanker Accuracy			
Group[a]	48.18	mdaMCI < sdaMCI[a]	573.06
		mdaMCI < HC[a]	1,615.98
		sdaMCI = HC[b]	0.15
Condition[a]	4.72×10^{27}	Con > Inc[a]	5.35×10^{13}
		Neu > Inc[a]	5.22×10^{13}
		Con = Neu[b]	0.21
Group × Condition[a]	24.46	Inc–Con	0.54
		Inc–Neu	1.59
Flanker Mean RT			
Group[a]	8.55	mdaMCI > sdaMCI[a]	79.344
		mdaMCI > HC[a]	189.078
		sdaMCI = HC[b]	0.139
Condition[a]	3.75×10^{55}	Inc > Con[a]	8.90×10^{27}
		Inc > Neu[a]	1.03×10^{31}
		Con = Neu[b]	0.13
Group × Condition[b]	0.24		
Flanker RT IIV			
Group[a]	1014.46	mdaMCI > sdaMCI[a]	2.00×10^{6}
		mdaMCI > HC[a]	1.85×10^{9}
		sdaMCI = HC[b]	0.164
Condition[a]	8163.31	Inc > Con[a]	87.42
		Inc > Neu[a]	739.26
		Con = Neu[b]	0.12
Group × Condition[a]	17.75	Inc–Con	0.44
		Inc–Neu[a]	23.38
		mdaMCI = sdaMCI	0.38
		mdaMCI > HC[a]	27.62
		sdaMCI > HC[a]	265.73

Notes: B_{10} = Bayes factor for evidence in favor of alternative versus null hypothesis; Con = Congruent; HC = healthy control; Inc = Incongruent; IIV = intraindividual variability; mdaMCI = multiple-domain aMCI; Neu = Neutral; RT = reaction time; sdaMCI = single-domain aMCI.
[a]Indicates evidence for the alternative hypothesis.
[b]Indicates evidence for the null hypothesis.

The analysis also revealed strong evidence for a Group by Condition interaction in accuracy, but post hoc univariate ANCOVAs revealed no evidence for Group main effects for both the Incongruent–Congruent and the Incongruent–Neutral differences. Evidence for null Group by Condition interactions was supported for mean RT. In terms of RT IIV, the analysis revealed strong evidence for a Group by Condition interaction. Post hoc univariate ANCOVAs revealed no evidence for a Group main effect for the Incongruent–Congruent difference, but strong evidence for a Group main effect for the Incongruent–Neutral difference. Pairwise comparisons revealed strong evidence for elevated Incongruent–Neutral Flanker effects in both mdaMCI and sdaMCI groups relative to the HC group. Inclusion of data from one HC participant excluded due to inadequate sleep the night before testing did not change the

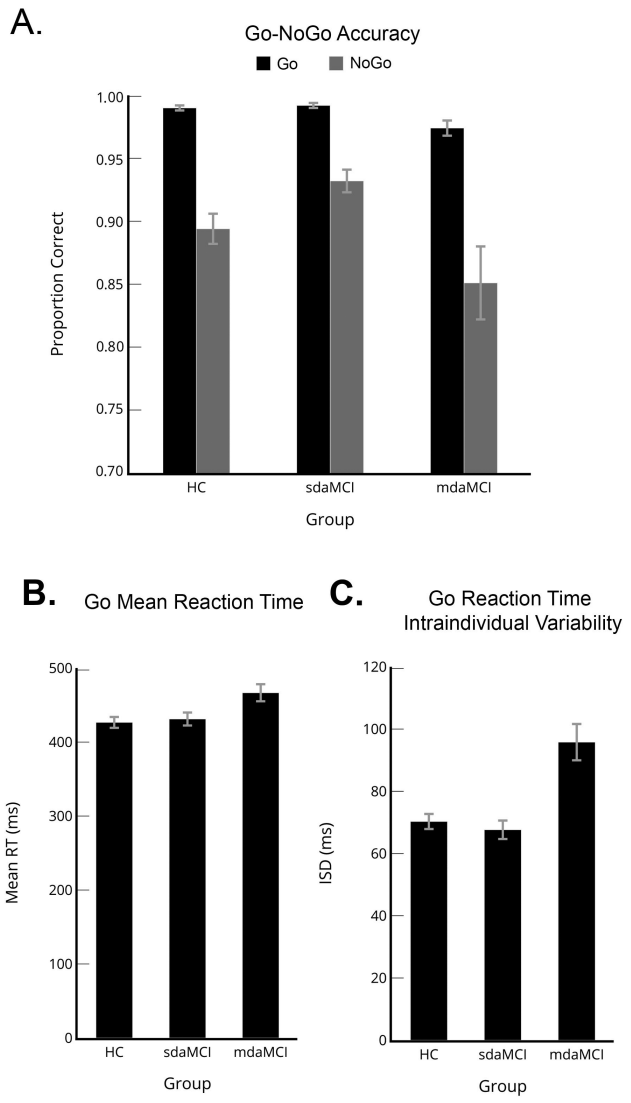

Figure 2. Performance on the Go–NoGo Task by group and condition for measures of (A) accuracy, (B) mean RT, and (C) RT IIV. Error bars represent standard error, and the *y*-axis scale is truncated to aid in visualizing the Go–NoGo effect. IIV = intraindividual variability; RT = reaction time.

pattern of findings. To summarize, the mdaMCI group performed with lower accuracy, and slower and more variable RTs relative to sdaMCI and HC groups. Although interference control deficits were not observed in accuracy or mean RT, RT IIV revealed interference control deficits in both mdaMCI and sdaMCI groups relative to the HC group.

Discussion

To our knowledge, this is the first study to systematically examine inhibitory control between aMCI subtypes using a measure of intraindividual variability. As expected, RT IIV was greater in all task conditions in individuals with mdaMCI relative to individuals with sdaMCI and healthy controls. In terms of inhibitory deficits, RT IIV revealed

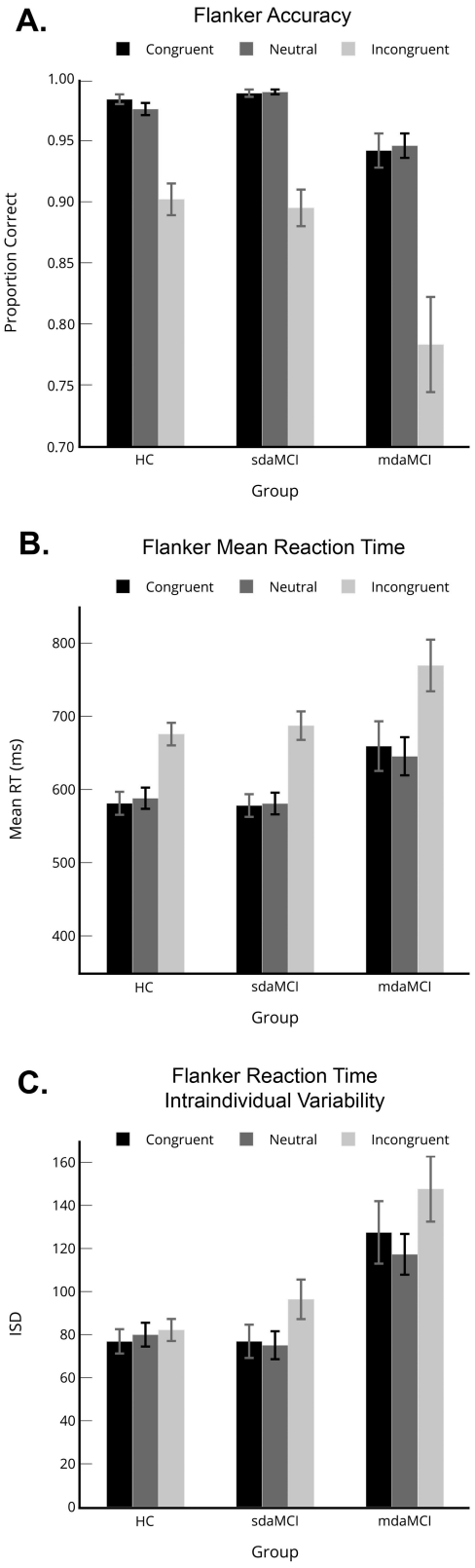

Figure 3. Performance on Flanker Task by group and condition for measures of (A) accuracy, (B) mean RT, and (C) RT IIV. Error bars represent standard error, and the *y*-axis scale is truncated to aid in visualizing Incongruent–Congruent and Incongruent–Neutral Flanker effects. IIV = intraindividual variability; RT = reaction time.

interference control deficits in individuals with mdaMCI relative to healthy controls. Notably, our findings also demonstrated deficits in interference control among individuals with sdaMCI relative to healthy controls; these findings were apparent in RT IIV but not when examining measures of accuracy or mean RT.

Response Inhibition

In the present study, there was no evidence of response inhibition deficits in sdaMCI or mdaMCI. To our knowledge, this is the first study to examine response inhibition deficits between aMCI subtypes (i.e., comparing Go vs NoGo). Past research has demonstrated response inhibition deficits in individuals with aMCI combined across subtypes (e.g., Mudar et al., 2016, Zheng et al., 2014) with the exception of one study (Zhang et al., 2007). The studies that did explore response inhibition between aMCI subtypes (Cid-Fernández et al., 2017a, 2017b) did not evaluate whether groups performed disproportionately worse in the NoGo than Go conditions, so it is uncertain whether poorer performance is attributed to deficits in inhibition or information processing. Future work is needed to determine whether response inhibition is indeed compromised in mdaMCI and sdaMCI relative to healthy aging.

Similar to past research, the mdaMCI group performed with overall slower processing speed (longer Go mean RTs) than the other groups. These mean RT effects may arise from compromised information processing in mdaMCI in evaluating whether a particular stimulus indicates a Go or NoGo trial. These effects have been similarly demonstrated in individuals with aMCI of unspecified subtype relative to healthy controls (Cid-Fernández et al., 2014; López Zunini et al., 2016), and specifically in individuals with mdaMCI relative to those with sdaMCI and healthy controls (Cid-Fernández et al., 2017a, 2017b). Furthermore, our findings in Go RT IIV suggests greater attentional inefficiency in the mdaMCI group relative to sdaMCI or healthy control groups in a task condition without an inhibitory component. These findings replicate previous work using RT IIV in simple RT tasks (McLaughlin et al., 2010; Strauss et al., 2007).

Interference Control

As expected, the mdaMCI group performed less accurately and with slower processing speed on all Flanker task conditions than sdaMCI and healthy control groups. Similar to the Go–NoGo task, these effects in accuracy and mean RT may arise from compromised stimulus evaluation or information processing in mdaMCI. Similar findings have been demonstrated in individuals with aMCI combined across subtype (Bélanger & Belleville, 2009; Wang et al., 2013), and in individuals with mdaMCI compared to those with sdaMCI or healthy controls in Simon tasks (Pereiro et al., 2014; Strauss et al., 2007). The mdaMCI group also showed elevated RT IIV in all task conditions relative to the sdaMCI or healthy control groups, suggesting overall greater attentional inefficiency. This is consistent with previous findings using the Simon task (Strauss et al., 2007) and a visuospatial attention task (McLaughlin et al., 2010).

Individuals with mdaMCI had greater RT IIV than healthy controls on Incongruent trials than Neutral trials, suggesting an interference control deficit in mdaMCI. Prior research using measures of accuracy and mean RT has found similar interference control deficits in individuals with aMCI combined across subtype (e.g., Bélanger & Belleville, 2009, Zhang et al., 2015), with the exception of some studies using Stroop (Puente et al., 2014; Zhang et al., 2007; Zheng et al., 2012) and Flanker tasks (Fernández et al., 2011; Lv et al., 2010). These studies with null group findings may arise from the heterogeneity of interference control deficits between aMCI subtypes. The literature examining interference control between aMCI subtypes has also used accuracy and mean RT and, to our knowledge, is limited to the Simon task where Pereiro et al. (2014) demonstrated a greater interference effect for accuracy in the mdaMCI group than the sdaMCI and healthy control groups. Our findings extend this work to a different task (Flanker) and to a sensitive measure of attentional inefficiency (RT IIV). Notably, our findings in RT IIV revealed a greater Flanker interference effect in the sdaMCI group relative to healthy controls as well. As far as we are aware, the present study is the first to demonstrate interference control deficits in both sdaMCI and mdaMCI using a measure of intraindividual variability. To our knowledge, only one other study with seven participants per group revealed a greater Flanker interference effect in accuracy for individuals with sdaMCI than healthy controls (Borsa et al., 2018). Our data highlight the presence of interference control deficits in not only mdaMCI, but in sdaMCI as well, a finding apparent through RT IIV but not through conventional measures of accuracy or mean RT.

Theoretical Implications

Given that RT IIV is particularly sensitive to frontal dysfunction (Hultsch & MacDonald, 2004), our findings advance current knowledge of aMCI by suggesting changes in higher-order frontal lobe functioning even in early stages of pathology. Indeed, the meta-analysis by Rabi et al. (2020) suggests that, accounting for processing speed, response inhibition and interference control are compromised in aMCI relative to healthy aging. Furthermore, neuroimaging studies have demonstrated reduced integrity of frontal brain areas underlying inhibition, such as the anterior cingulate cortex, in individuals with aMCI (Borsa et al., 2018; Van Dam et al., 2013). Our findings extend this work by providing converging evidence for attentional inefficiency in aMCI and

demonstrate compromised interference control in both aMCI subtypes relative to healthy aging. Our RT IIV findings in sdaMCI are especially noteworthy given that impairments in executive functioning are not detectable in this population with neuropsychological tests or traditional metrics of accuracy and mean RT. These findings suggest that even in the early stage of aMCI, subtle deficits in frontal functioning may be present.

Additionally, our findings contribute to the converging literature showing that RT IIV is a more informative metric of frontal lobe functioning than conventional measures of accuracy and mean RT, possibly by capturing differences in attentional integrity. When intraindividual variability represents systematic rather than random fluctuations, accuracy and mean RT may provide skewed estimates of performance (Hultsch & MacDonald, 2004; Stuss & Binns, 2008). Thus, RT IIV has potential to reveal subtle differences that may not be apparent with conventional measures when groups systematically vary in attentional efficiency (MacDonald et al., 2009; Murtha et al., 2002), which may be a key distinguishing factor between aMCI and healthy aging as demonstrated by the present findings. Prior research has found RT IIV to uniquely improve group differentiation of multiple-domain MCI subtypes from a combined group of individuals with single-domain MCI and healthy controls above mean RT (Strauss et al., 2007). Furthermore, both mean RT and RT IIV on a simple RT task differed between the mdaMCI group and healthy controls, whereas only RT IIV (and not mean RT) differed between the sdaMCI group and healthy controls (Strauss et al., 2007). These findings bear similarity to those of the present study, where conventional measures of accuracy and mean RT appeared to mask interference control deficits in sdaMCI that were evident in RT IIV. Given that this research had mainly focused on simple RT and visual search tasks, our RT IIV findings thus extend this work to the domain of inhibition.

Clinical Implications

Inhibitory control is reported to be the most frequently impaired executive domain in aMCI regardless of subtype (Johns et al., 2012). Currently, Go–NoGo and Flanker tasks are not standardized for clinical assessments with older adults; thus, inhibition impairments may go undetected in individuals with aMCI (Rabi et al., 2020). A more sensitive measure of executive functioning, such as RT IIV from inhibition tasks, may improve diagnostic power when used in supplementation to neuropsychological test batteries. Future research should explore the added classification utility of RT IIV metrics on inhibition tasks between aMCI subtypes and healthy controls. Furthermore, our present findings suggest individuals with aMCI regardless of subtype may benefit from interventions in executive attention, in addition to early interventions for memory impairments, to preserve independent functioning.

Limitations

The number of people we recruited differed between groups; deficits in response inhibition may have reached significance with more participants, particularly with mdaMCI. Additionally, RT IIV has limited utility in capturing response inhibition deficits since these paradigms require a null response. Thus, mean RT and RT IIV measures from Go trials cannot provide inferences of response inhibition. Finally, as inhibitory deficits in aMCI are exacerbated by cardiovascular burden (Villeneuve et al., 2009), our exclusion criteria comprised vascular diseases and risk factors. We suspect these deficits would be more prevalent had we included these conditions, particularly since the likelihood of cardiovascular burden is higher in mdaMCI than sdaMCI (Villeneuve et al., 2009).

Conclusion

The present study utilized RT IIV in addition to accuracy and mean RT to characterize deficits in two domains of inhibitory control in sdaMCI and mdaMCI. Although prior studies using accuracy and mean RT have shown response inhibition and interference control deficits in aMCI, few have compared these deficits between aMCI subtypes. Through RT IIV, the present study revealed interference control deficits in mdaMCI as well as sdaMCI compared with healthy controls. Our findings support the utility of intraindividual variability measures alongside conventional behavioral measures in assessing early executive function deficits.

Funding

This work was supported by the Natural Sciences and Engineering Council of Canada (grant number RGPIN-2017–06057 to N. D. Anderson); and the Alzheimer Society of Canada to C. Alain. R. Rabi was funded by a postdoctoral fellowship from Natural Sciences and Engineering Council of Canada and the Alzheimer Society of Canada.

Conflict of Interest

The authors declare no conflicts of interest.

Acknowledgments

We thank Elizabeth Baker-Sullivan, Haley Gabel, Farnosh Hakimy, Zakia Hussain, Brook Koblinsky, Thaneya Kuganesan, Cherie Lin, Kaljani Mahalingam, Karishma

Ramdeo, Brahm Sanger, Serah Seo, Parinaz Soghrati, Parnian Tajbakhsh, Kevin Tang, and Amy Zhao for assistance in participant recruitment, data collection, and data preparation, with special thanks to Mariam Sidrak and Dr. Stephen Rhodes. We thank Drs. Morris Freedman, Theone Paterson, Angela Troyer, Paul Verhoeff, and Uri Wolf of Baycrest Centre for aiding in participant recruitment. We thank all participants for their involvement in this study. This study was not preregistered.

Data Availability

Data can be made available upon reasonable request and in accordance with applicable laws. For further information about accessibility of data, please contact the corresponding author.

References

Bélanger, S., & Belleville, S. (2009). Semantic inhibition impairment in mild cognitive impairment: A distinctive feature of upcoming cognitive decline? *Neuropsychology*, **23**(5), 592–606. doi:10.1037/a0016152

Bélanger, S., Belleville, S., & Gauthier, S. (2010). Inhibition impairments in Alzheimer's disease, mild cognitive impairment and healthy aging: Effect of congruency proportion in a Stroop task. *Neuropsychologia*, **48**(2), 581–590. doi:10.1016/j.neuropsychologia.2009.10.021

Borella, E., Carretti, B., Mitolo, M., Zavagnin, M., Caffarra, P., Mammarella, N., Fairfield, B., Gamboz, N., & Piras, F. (2017). Characterizing cognitive inhibitory deficits in mild cognitive impairment. *Psychiatry Research*, **251**, 342–348. doi:10.1016/j.psychres.2016.12.037

Borella, E., de Ribaupierre, A., Cornoldi, C., & Chicherio, C. (2013). Beyond interference control impairment in ADHD: Evidence from increased intraindividual variability in the color-stroop test. *Child Neuropsychology*, **19**(5), 495–515. doi:10.1080/09297049.2012.696603

Borsa, V. M., Della Rosa, P. A., Catricalà, E., Canini, M., Iadanza, A., Falini, A., Abutalebi, J., & Iannaccone, S. (2018). Interference and conflict monitoring in individuals with amnestic mild cognitive impairment: A structural study of the anterior cingulate cortex. *Journal of Neuropsychology*, **12**(1), 23–40. doi:10.1111/jnp.12105

Christ, B. U., Combrinck, M. I., & Thomas, K. G. F. (2018). Both reaction time and accuracy measures of intraindividual variability predict cognitive performance in Alzheimer's disease. *Frontiers in Human Neuroscience*, **12**, 124. doi:10.3389/fnhum.2018.00124

Christensen, H., Dear, K. B., Anstey, K. J., Parslow, R. A., Sachdev, P., & Jorm, A. F. (2005). Within-occasion intraindividual variability and preclinical diagnostic status: Is intraindividual variability an indicator of mild cognitive impairment? *Neuropsychology*, **19**(3), 309–317. doi:10.1037/0894-4105.19.3.309

Cid-Fernández, S., Lindín, M., & Díaz, F. (2014). Effects of amnestic mild cognitive impairment on n2 and p3 go/nogo ERP components. *Journal of Alzheimer's Disease*, **38**(2), 295–306. doi:10.3233/JAD-130677

Cid-Fernández, S., Lindín, M., & Díaz, F. (2017a). Neurocognitive and behavioral indexes for identifying the amnestic subtypes of mild cognitive impairment. *Journal of Alzheimer's Disease*, **60**(2), 633–649. doi:10.3233/JAD-170369

Cid-Fernández, S., Lindín, M., & Díaz, F. (2017b). Stimulus-locked lateralized readiness potential and performance: Useful markers for differentiating between amnestic subtypes of mild cognitive impairment. *The Journal of Prevention of Alzheimer's Disease*, **4**(1), 21–28. doi:10.14283/jpad.2016.88

Diamond, A. (2013). Executive functions. *Annual Review of Psychology*, **64**, 135–168. doi:10.1146/annurev-psych-113011-143750

Duong, A., Whitehead, V., Hanratty, K., & Chertkow, H. (2006). The nature of lexico-semantic processing deficits in mild cognitive impairment. *Neuropsychologia*, **44**(10), 1928–1935. doi:10.1016/j.neuropsychologia.2006.01.034

Eriksen, B. A., & Eriksen, C. W. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. *Perception & Psychophysics*, **16**(1), 143–149. doi:10.3758/BF03203267

Faul, F., Erdfelder, E., Lang, A. G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, **39**(2), 175–191. doi:10.3758/bf03193146

Fernández, P. J., Campoy, G., García Santos, J. M., Antequera, M. M., García-Sevilla, J., Castillo, A., Antúnez, C., & Fuentes, L. J. (2011). Is there a specific pattern of attention deficit in mild cognitive impairment with subcortical vascular features? Evidence from the attention network test. *Dementia and Geriatric Cognitive Disorders*, **31**(4), 268–275. doi:10.1159/000327165

Goghari, V. M., & Lawlor-Savage, L. (2017). Comparison of cognitive change after working memory training and logic and planning training in healthy older adults. *Frontiers in Aging Neuroscience*, **9**, 39. doi:10.3389/fnagi.2017.00039

Golob, E. J., Irimajiri, R., & Starr, A. (2007). Auditory cortical activity in amnestic mild cognitive impairment: Relationship to subtype and conversion to dementia. *Brain*, **130**(Pt 3), 740–752. doi:10.1093/brain/awl375

Hasher, L., Zacks, R. T., & May, C. P. (1999). Inhibitory control, circadian arousal, and age. In D. Gopher & A. Koriat (Eds.), *Attention and performance XVII* (pp. 653-675). Cambridge, MA: MIT Press.

Horne, J. A., & Ostberg, O. (1976). A self-assessment questionnaire to determine morningness–eveningness in human circadian rhythms. *International Journal of Chronobiology*, **4**(2), 97–110.

Hultsch, D. F., & MacDonald, S. W. S. (2004). Intra-individual variability in performance as a theoretical window onto cognitive aging. In R. Dixon, L. Backman, & L.-G. Nilsson (Eds.), *New frontiers in cognitive aging* (pp. 65–88). Oxford University Press. doi:10.1093/acprof:oso/9780198525691.003.0004

Jackson, J. D., Balota, D. A., Duchek, J. M., & Head, D. (2012). White matter integrity and reaction time intraindividual variability in healthy aging and early-stage Alzheimer disease. *Neuropsychologia*, **50**(3), 357–366. doi:10.1016/j.neuropsychologia.2011.11.024

Johns, E. K., Phillips, N. A., Belleville, S., Goupil, D., Babins, L., Kelner, N., Ska, B., Gilbert, B., Massoud, F., de Boysson, C., Duncan, H. D., & Chertkow, H. (2012). The profile of executive functioning in amnestic mild cognitive impairment:

Disproportionate deficits in inhibitory control. *Journal of the International Neuropsychological Society*, **18**(3), 541–555. doi:10.1017/S1355617712000069

Joly-Burra, E., Van der Linden, M., & Ghisletta, P. (2018). Intraindividual variability in inhibition and prospective memory in healthy older adults: Insights from response regularity and rapidity. *Journal of Intelligence*, **6**(1), 13. doi:10.3390/jintelligence6010013

López Zunini, R. A., Knoefel, F., Lord, C., Breau, M., Sweet, L., Goubran, R., & Taler, V. (2016). P300 amplitude alterations during inhibitory control in persons with mild cognitive impairment. *Brain Research*, **1646**, 241–248. doi:10.1016/j.brainres.2016.06.005

Lv, S., Wang, X., Cui, Y., Jin, J., Sun, Y., Tang, Y., Bai, Y., Wang, Y., & Zhou, L. (2010). Application of attention network test and demographic information to detect mild cognitive impairment via combining feature selection with support vector machine. *Computer Methods and Programs in Biomedicine*, **97**(1), 11–18. doi:10.1016/j.cmpb.2009.05.003

MacDonald, S. W., Li, S. C., & Bäckman, L. (2009). Neural underpinnings of within-person variability in cognitive functioning. *Psychology and Aging*, **24**(4), 792–808. doi:10.1037/a0017798

MacDonald, S. W., Nyberg, L., & Bäckman, L. (2006). Intraindividual variability in behavior: Links to brain structure, neurotransmission and neuronal activity. *Trends in Neurosciences*, **29**(8), 474–480. doi:10.1016/j.tins.2006.06.011

McLaughlin, P. M., Borrie, M. J., & Murtha, S. J. (2010). Shifting efficacy, distribution of attention and controlled processing in two subtypes of mild cognitive impairment: Response time performance and intraindividual variability on a visual search task. *Neurocase*, **16**(5), 408–417. doi:10.1080/13554791003620306

Mesulam, M. M. (Ed.). (1985). *Principles of behavioral neurology (no. 26)*. Oxford University Press.

Mudar, R. A., Chiang, H. S., Eroh, J., Nguyen, L. T., Maguire, M. J., Spence, J. S., Kung, F., Kraut, M. A., & Hart, J. (2016). The effects of amnestic mild cognitive impairment on go/nogo semantic categorization task performance and event-related potentials. *Journal of Alzheimer's Disease*, **50**(2), 577–590. doi:10.3233/JAD-150586

Murphy, K. J., Rich, J. B., & Troyer, A. K. (2006). Verbal fluency patterns in amnestic mild cognitive impairment are characteristic of Alzheimer's type dementia. *Journal of the International Neuropsychological Society*, **12**(4), 570–574. doi:10.1017/s1355617706060590

Murtha, S., Cismaru, R., Waechter, R., & Chertkow, H. (2002). Increased variability accompanies frontal lobe damage in dementia. *Journal of the International Neuropsychological Society*, **8**(3), 360–372. doi:10.1017/s1355617702813170

Nguyen, L. T., Mudar, R. A., Chiang, H. S., Schneider, J. M., Maguire, M. J., Kraut, M. A., & Hart, J., Jr. (2017). Theta and alpha alterations in amnestic mild cognitive impairment in semantic Go/NoGo tasks. *Frontiers in Aging Neuroscience*, **9**, 160. doi:10.3389/fnagi.2017.00160

Pereiro, A. X., Juncos-Rabadán, O., & Facal, D. (2014). Attentional control in amnestic MCI subtypes: Insights from a Simon task. *Neuropsychology*, **28**(2), 261–272. doi:10.1037/neu0000047

Petersen, R. C. (2004). Mild cognitive impairment as a diagnostic entity. *Journal of Internal Medicine*, **256**(3), 183–194. doi:10.1111/j.1365-2796.2004.01388.x

Petersen, R. C., Roberts, R. O., Knopman, D. S., Boeve, B. F., Geda, Y. E., Ivnik, R. J., Smith, G. E., & Jack, C. R., Jr. (2009). Mild cognitive impairment: Ten years later. *Archives of Neurology*, **66**(12), 1447–1455. doi:10.1001/archneurol.2009.266

Puente, A. N., Faraco, C., Terry, D. P., Brown, C., & Miller, L. S. (2014). Minimal functional brain differences between older adults with and without mild cognitive impairment during the stroop. *Neuropsychology, Development, and Cognition. Section B, Aging, Neuropsychology and Cognition*, **21**(3), 346–369. doi:10.1080/13825585.2013.824065

Rabi, R., Vasquez, B. P., Alain, C., Hasher, L., Belleville, S., & Anderson, N. D. (2020). Inhibitory control deficits in individuals with amnestic mild cognitive impairment: A meta-analysis. *Neuropsychology Review*, **30**(1), 97–125. doi:10.1007/s11065-020-09428-6

Rouder, J. N., Morey, R. D., Speckman, P. L., & Province, J. M. (2012). Default Bayes factors for ANOVA designs. *Journal of Mathematical Psychology*, **56**(5), 356–374. doi: 10.1016/j.jmp.2012.08.001

Sagaspe, P., Taillard, J., Amiéva, H., Beck, A., Rascol, O., Dartigues, J. F., Capelli, A., & Philip, P. (2012). Influence of age, circadian and homeostatic processes on inhibitory motor control: A Go/Nogo task study. *PLoS One*, **7**(6), e39410. doi:10.1371/journal.pone.0039410

Simmonds, D. J., Pekar, J. J., & Mostofsky, S. H. (2008). Meta-analysis of Go/No-go tasks demonstrating that fMRI activation associated with response inhibition is task-dependent. *Neuropsychologia*, **46**(1), 224–232. doi:10.1016/j.neuropsychologia.2007.07.015

Simon, J. R., & Wolf, J. D. (1963). Choice reaction time as a function of angular stimulus–response correspondence and age. *Ergonomics*, **6**(1), 99–105. doi:10.1080/00140136308930679

Strauss, E., Bielak, A. A., Bunce, D., Hunter, M. A., & Hultsch, D. F. (2007). Within-person variability in response speed as an indicator of cognitive impairment in older adults. *Aging, Neuropsychology, and Cognition*, **14**, 608–630. doi:10.1080/13825580600932419

Stroop, J. R. (1935). Studies of interference in serial verbal reactions. *Journal of Experimental Psychology*, **18**(6), 643–662. doi:10.1037/h0054651

Stuss, D. T., & Binns, M. A. (2008). The patient as a moving target: The importance to rehabilitation of understanding variability. In D. T. Stuss, G. Winocur, & I. H. Robertson (Eds.), *Cognitive neurorehabilitation* (2nd ed., pp. 39–61). Cambridge University Press. doi:10.1017/CBO9781316529898.005

Van Dam, N. T., Sano, M., Mitsis, E. M., Grossman, H. T., Gu, X., Park, Y., Hof, P. R., & Fan, J. (2013). Functional neural correlates of attentional deficits in amnestic mild cognitive impairment. *PLoS One*, **8**(1), e54035. doi:10.1371/journal.pone.0054035

Vasquez, B. P., Binns, M. A., & Anderson, N. D. (2016). Staying on task: Age-related changes in the relationship between executive functioning and response time consistency. *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences*, **71**(2), 189–200. doi:10.1093/geronb/gbu140

Vasquez, B. P., Binns, M. A., & Anderson, N. D. (2018). Response time consistency is an indicator of executive control rather than global cognitive ability. *Journal of the International Neuropsychological Society*, **24**(5), 456–465. doi:10.1017/S1355617717001266

Villeneuve, S., Belleville, S., Massoud, F., Bocti, C., & Gauthier, S. (2009). Impact of vascular risk factors and diseases on cognition in persons with mild cognitive impairment. *Dementia and Geriatric Cognitive Disorders*, **27**(4), 375–381. doi:10.1159/000209965

Wang, P., Zhang, X., Liu, Y., Liu, S., Zhou, B., Zhang, Z., Yao, H., Zhang, X., & Jiang, T. (2013). Perceptual and response interference in Alzheimer's disease and mild cognitive impairment. *Clinical Neurophysiology*, **124**(12), 2389–2396. doi:10.1016/j.clinph.2013.05.014

West, R., Murphy, K. J., Armilio, M. L., Craik, F. I., & Stuss, D. T. (2002). Lapses of intention and performance variability reveal age-related increases in fluctuations of executive control. *Brain and Cognition*, **49**(3), 402–419. doi:10.1006/brcg.2001.1507

Wylie, S. A., Ridderinkhof, K. R., Eckerle, M. K., & Manning, C. A. (2007). Inefficient response inhibition in individuals with mild cognitive impairment. *Neuropsychologia*, **45**(7), 1408–1419. doi:10.1016/j.neuropsychologia.2006.11.003

Zhang, Y., Han, B., Verhaeghen, P., & Nilsson, L. G. (2007). Executive functioning in older adults with mild cognitive impairment: MCI has effects on planning, but not on inhibition. *Neuropsychology, Development, and Cognition. Section B, Aging, Neuropsychology and Cognition*, **14**(6), 557–570. doi:10.1080/13825580600788118

Zhang, Z., Zheng, H., Liang, K., Wang, H., Kong, S., Hu, J., Wu, F., & Sun, G. (2015). Functional degeneration in dorsal and ventral attention systems in amnestic mild cognitive impairment and Alzheimer's disease: An fMRI study. *Neuroscience Letters*, **585**, 160–165. doi:10.1016/j.neulet.2014.11.050

Zheng, D., Dong, X., Sun, H., Xu, Y., Ma, Y., & Wang, X. (2012). The overall impairment of core executive function components in patients with amnestic mild cognitive impairment: A cross-sectional study. *BMC Neurology*, **12**, 138. doi:10.1186/1471-2377-12-138

Zheng, D., Sun, H., Dong, X., Liu, B., Xu, Y., Chen, S., Song, L., Zhang, H., & Wang, X. (2014). Executive dysfunction and gray matter atrophy in amnestic mild cognitive impairment. *Neurobiology of Aging*, **35**(3), 548–555. doi:10.1016/j.neurobiolaging.2013.09.007