Journal of the International Neuropsychological Society (2016), **22**, 453–466.

doi:10.1017/S1355617715001332

Neuropsychological Practice Effects in the Context of Cognitive Decline: Contributions from Learning and Task Novelty

Sommer R. Thorgusen,[1] Yana Suchy,[1] Gordon J. Chelune,[2] AND Brian R. Baucom[1]
[1]University of Utah, Department of Psychology, Salt Lake City, Utah
[2]University of Utah, Department of Neurology, Salt Lake City, Utah

(RECEIVED May 24, 2015; FINAL REVISION December 2, 2015; ACCEPTED December 7, 2015; FIRST PUBLISHED ONLINE January 21, 2016)

Abstract

Objectives: Although cognitive decline is typically associated with decreasing practice effects (PEs) (presumably due to declining memory), some studies show increased PEs with declines in cognition. One explanation for these inconsistencies is that PEs reflect not only memory, but also rebounds from adapting to task novelty (i.e., novelty effect), leading to increased PEs. We examined a theoretical model of relationships among novelty effects, memory, cognitive decline, and within-session PEs. **Methods:** Sixty-six older adults ranging from normal to severely impaired completed measures of memory, novelty effects, and two trials each of *Wechsler Adult Intelligence Scale, 4th Edition* Symbol Search and Coding. Interrelationships among variables were examined using regression analyses. **Results:** PEs for Symbol Search and Coding (a) were related to different proposed PE components (i.e., memory and novelty effects), such that novelty effect predicted Symbol Search PE ($R^2 = .239$, $p < .001$) and memory predicted Coding PE ($R^2 = .089$, $p = .015$), and (b) showed different patterns across stages of cognitive decline, such that the greatest cognitive decline was associated with smallest Coding PE ($R^2 = .125$, $p = .004$), whereas intermediate cognitive decline was associated with the greatest Symbol Search PE ($R^2 = .097$, $p = .040$). The relationship between cognitive decline and PE for Symbol Search was partially mediated by novelty effect among older adults with abnormal cognitive decline (model $R^2 = .286$, $p < .001$). **Conclusions:** These findings (a) suggest that PE is not a unitary construct, (b) offer an explanation for contradictory findings in the literature, and (c) highlight the need for a better understanding of component processes of PE across different neuropsychological measures. (*JINS*, 2016, *22*, 453–466)

Keywords: Cognition, Learning, Memory, Mild cognitive impairment, Cognitive reserve, Models, Theoretical

INTRODUCTION

Practice effects (PEs) are improvements in test performance due to prior test exposure (Beglinger, Tangphao-Daniels, et al., 2005; McCaffrey, Duff, & Westervelt, 2000). PEs are usually conceptualized as a combination of long-term memory (implicit and explicit) and learning of task characteristics, and are well-known confounds of serial assessment (Busch, Chelune, & Suchy, 2006). However, a growing body of literature suggests that PE may have diagnostic utility as a unique cognitive construct. For example, in a meta-analysis of PE, Calamia, Markon, and Tranel (2012) found that PE magnitudes depend not only on logistical factors, such as inter-test interval or use of alternate forms (Beglinger, Gaydos, et al., 2005; Benedict & Zgaljardic, 1998), but also vary by age (Dikmen, Heaton, Grant, & Temkin, 1999) and diagnosis (Basso, Bornstein, & Lang, 1999; Wilson, Watson, Baddeley, Emslie, & Evans, 2000).

Support for diagnostic and prognostic utility of PEs is evident in studies examining PEs among patients with mild cognitive impairment (MCI) and dementia (Duff, 2012; Duff et al., 2007; Duff, Callister, Dennett, & Tometich, 2012; Duff, Chelune, & Dennett, 2012; Machulda et al., 2013). In this research, findings have been somewhat mixed. Some studies show that individuals with dementia and MCI have smaller PEs than healthy peers on measures of category fluency (Cooper et al., 2001; Cooper, Lacritz, Weiner, Rosenberg, & Cullum, 2004), episodic memory (Duff, Chelune, et al., 2012; Schrijnemaekers, de Jager, Hogervorst, & Budge, 2006), and cognitive status (Helkala et al., 2002), presumably due to memory impairments (Jonker, Geerlings, & Schmand, 2000; Mitchell, 2008). By contrast, others have observed *greater* PEs in MCI on measures of verbal and visual explicit memory (Duff et al., 2008) and motor control (Yan & Dick, 2006). Such apparently paradoxical findings call into question the prevailing conceptualization of PE as

Correspondence and reprint requests to: Sommer R. Thorgusen, Department of Psychology, University of Utah, 380 South 1530 East, BEH S Room 502, Salt Lake City, UT 84112. E-mail: somrae@gmail.com

reflecting memory and learning, and suggest that further investigation into the nature of PEs is warranted.

Several explanations have been offered for larger PEs among individuals with MCI, including floor/ceiling effects across patient groups, differential declines in declarative versus procedural learning, or heterogeneity in cognitive status within groups (Duff et al., 2008). Alternatively, PEs may reflect cognitive phenomena beyond memory, such as a *rebound* from initial transient *decrements* in performance caused by poor adaptation to novel task characteristics. That is, when faced with novel tasks, individuals with MCI may initially be overwhelmed by unfamiliar task characteristics, therefore, performing *below* their actual cognitive potential. Once familiar with the task, such individuals exhibit a rebound from this initial performance decrement. This rebound has been termed the "novelty effect" (Suchy, Kraybill, & Franchow, 2011). When this rebound occurs during a second administration of the same task, it clearly contributes to PE. Because the rebound can only be as large as the initial decrement (i.e., the larger the decrement, the larger the rebound), individuals with MCI (who become more overwhelmed by novel tasks) exhibit larger rebound and, therefore, larger PEs.

Although both learning/memory and novelty effect are associated with performance improvements with repeated task exposure, novelty effect differs from memory in that it does *not* reflect acquired knowledge or skills relative to an initial baseline. Rather, novelty-related improvements reflect a *recovery* to baseline from an initial suppression of performance. Because novelty effect can be observed even on tasks that have been previously learned but are presented in novel contexts (Euler, Niermeyer, & Suchy, 2015; Larson & Suchy, 2014; Ouellet, Beauchamp, Owen, & Doyon, 2004), it appears to represent a construct that is distinct from memory. Whereas learning-related improvements reflect better ability to acquire and retain new knowledge or skill, improvements due to novelty effect reflect *poorer* rapid adaptation to novel task demands (e.g., manipulating novel materials or maintaining instructions in working memory).

Recently, we proposed a theoretical model of PE (Figure 1) to explain paradoxical PEs in MCI (Suchy et al., 2011). We conceptualized PEs as consisting of at least two components: (1) memory (both implicit and explicit) and (2) novelty effect. The model posits that memory and novelty effect contribute differentially to PE at different points along the declining trajectory: Whereas the contribution of memory to PE generally *declines* when pathological cognitive change becomes apparent, the contribution of novelty *increases* early in the declining trajectory (possibly *before* pathological detectable memory change), and only later decreases as pathological declines continue. These differential contributions of memory and novelty *jointly* lead to a curvilinear relationship between PE and pathological cognitive decline (see Figure 1). While we have demonstrated larger novelty effect among individuals at preclinical stages of cognitive decline relative to non-declining counterparts (Suchy et al., 2011), the remaining time points on the decline continuum

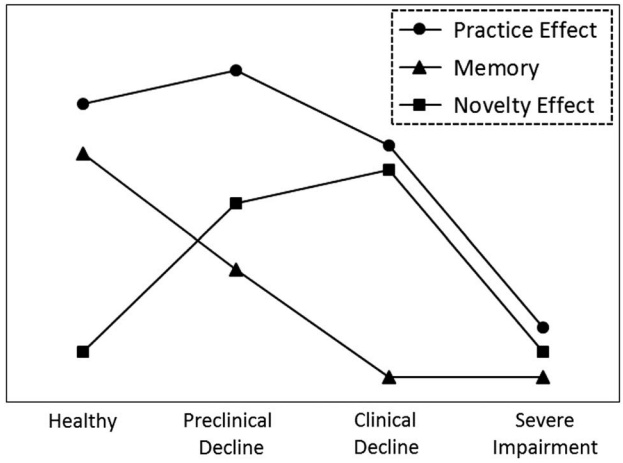

Fig. 1. Theoretical model of components of practice effect across a spectrum of cognitive decline. Adapted from Suchy et al. (2011); copyright 2011 by Cambridge University Press. This figure shows how practice effect (PE) can be conceptualized as the net sum of novelty effect and memory ability. According to the model, the initial increase in novelty effect is of sufficient magnitude to result in an increase in the net PE early on in the neurodegenerative process (i.e., when memory is still relatively preserved). Once a clinically significant level of cognitive decline is reached (i.e., when memory and learning begin to exhibit notable decrement), PE begins to decline, being comprised primarily of novelty effect with little contribution from memory. Finally, as cognitive impairments become more severe, novelty effect also declines because individuals are no longer able to rebound from the deleterious impact of novelty; thus, with minimal to no contributions from memory or novelty effect, PEs also become minimal or even non-existent.

are purely theoretical and are yet to be tested empirically. Furthermore, past research has *not* examined the direct association between novelty effect and PE or the differential contribution of novelty effect and memory along the cognitive decline continuum.

The goal of this study was to examine PEs and their proposed components (i.e., memory and novelty effect) in older adults across a spectrum of cognitive decline with three primary aims. First (Aim 1), we tested the hypothesis that novelty effect and long-term explicit memory *uniquely* contribute to PE as predicted by our model. Second (Aim 2), we tested the hypothesized quadratic relationship between PE and cognitive decline, which predicts greater PE in the context of mild cognitive dysfunction relative to intact cognition or moderate-to-severe impairment. Third (Aim 3), we tested the hypothesis that memory and/or novelty effect would mediate the relationship between PE and cognitive decline.

METHOD

Participants and Recruitment

Participants included 75 adults ages 60 to 89 representing a continuum from healthy to severely impaired cognition.

https://doi.org/10.1017/S1355617715001332 Published online by Cambridge University Press

Table 1. Descriptive statistics for sample

	Total sample (n = 66)		Community (n = 40)	Clinic (n = 26)	Clinic vs. community	
	Range	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*t*(64)	*p*-Value
# Male, female		27, 39	19, 21	8, 18		
Age (years)	60–89	74.62 *(6.62)*	73.33 *(6.47)*	76.62 *(6.48)*	−2.02	.048
Education (years)	11–20	15.41 *(2.76)*	15.63 *(2.73)*	15.08 *(2.81)*	0.79	.434
TICS	21–40	31.48 *(4.25)*	33.35 *(3.35)*	28.62 *(3.93)*	5.24	.000
GDS	0–18	5.32 *(4.90)*	5.13 *(5.18)*	5.62 *(4.51)*	0.40	.694
DRS-2	2–14	8.67 *(3.32)*	10.43 *(2.45)*	5.96 *(2.60)*	7.06	.000
PE_{Coding}	−17–18	5.65 *(6.00)*	7.68 *(4.76)*	2.54 *(6.45)*	3.72	.000
PE_{Search}	−8–11	3.50 *(4.05)*	4.38 *(3.57)*	2.15 *(4.44)*	2.24	.029
Memory	0–15	6.18 *(5.00)*	8.83 *(4.05)*	2.12 *(3.315)*	7.05	.000
Novelty Effect (ms)	−950.5–614.5	71.78 *(274.71)*	106.38 *(198.77)*	18.56 *(360.14)*	1.28	.207
Coding raw Time 1	14–75	47.86 *(12.26)*	50.80 *(11.21)*	43.35 *(12.63)*	2.51	.015
Coding raw Time 2	27–85	53.52 *(13.34)*	58.48 *(11.62)*	45.88 *(12.35)*	4.20	.000
Symbol Search raw Time 1	7–34	23.17 *(6.53)*	25.58 *(6.16)*	19.46 *(5.29)*	4.16	.000
Symbol Search raw Time 2	5–39	26.67 *(7.45)*	29.95 *(6.19)*	21.62 *(6.39)*	5.28	.000
Coding scaled Time 1	3–16	10.20 *(2.40)*	10.5 *(2.23)*	9.73 *(2.62)*	1.28	.206
Coding scaled Time 2	5–17	11.29 *(2.44)*	12.00 *(2.15)*	10.19 *(2.48)*	3.14	.003
Symbol Search scaled Time 1	3–16	10.42 *(2.63)*	11.18 *(2.43)*	9.27 *(2.54)*	3.06	.003
Symbol Search scaled Time 2	2–18	11.91 *(3.04)*	12.98 *(2.52)*	10.27 *(3.08)*	3.91	.000

Note. TICS = Telephone Interview of Cognitive Status; GDS = Geriatric Depression Scale; DRS-2 = Age and education adjusted scaled scores for the Mattis Dementia Rating Scale, 2nd edition; PE_{Coding} = practice effect calculated as difference between time 2 and time 1 raw scores on WAIS-IV Coding; PE_{Search} = practice effect calculated as difference between time 2 and time 1 raw scores on WAIS-IV Symbol Search; Memory = Rey Auditory Verbal Learning Test delayed recall; Novelty Effect = difference in motor planning times between first and second blocks of a motor learning task.

To ensure a range of cognitive functioning, participants were recruited from both the community (i.e., senior centers (n = 2), assisted living facilities (n = 1), and health fairs (n = 43)] and a clinic at the University of Utah's Center for Alzheimer's Care, Imaging, and Research (n = 29). Participants recruited from the community were an average of 3.3 years younger than those recruited from the clinic (p = .048), but did *not* differ on other demographic variables (see Table 1). Because our model hypothesizes that contributions of memory and novelty effect to PE change across the *early* stages of pathological cognitive decline, individuals exhibiting moderate-to-severe impairment on initial screening were excluded. Additional exclusion criteria were non–right-handedness[1], severe depressive symptoms[2], history of neurological disorder (e.g., stroke, seizures, moderate-to-severe brain injury), and serious psychiatric illness (e.g., psychosis, untreated depression). Of the 98 individuals screened, 82 met screening criteria and 7 withdrew before being scheduled for participation. Of the 75 participants who completed study procedures, two participants were excluded for severe depressive symptoms. Due to an administration error, one of the primary measures [*Wechsler Adult Intelligence Scale, 4th Edition* (WAIS-IV) Coding] was not administered to the first seven study participants; therefore, these participants were removed from analyses. This left a final sample of 66 participants. Demographic characteristics of excluded versus included participants did not differ (ps = .34–.87). Four of the 66 included participants had scores that were potential outliers on a primary measure[3]. The results followed a similar pattern whether those participants were excluded or included in analyses; however, some of the results were reduced to trends, possibly due to low power (see the Results section for details). These cases were retained in the analyses to improve power.

Procedures

The study was approved by the University of Utah Institutional Review Board. Participants were pre-screened for inclusion/exclusion criteria *via* brief telephone interview regarding demographics, self-reported handedness, and medical history. Written informed consent was obtained from participants (and legally authorized representatives, if applicable) before participation. Participants completed an individually administered 2-hr battery of cognitive

[1] Non-right-handedness is associated with anomalous profiles of motor output (Rousson, Gasser, Caflisch, & Jenni, 2009). As one of our measures of interest was a motor programming task, non-right-handedness was added as an exclusion criterion.

[2] Severe depression in older adults is associated with attentional problems, potentially precluding collection of valid and reliable results (Camozzato, de Almeida Fleck, Delgado, & Fagundes Chaves, 2007; Köhler et al., 2010)

[3] Two participants had unusually low scores for the measure of novelty effect, a third had an unusually low score for practice effect on WAIS-IV Coding, and a fourth had an unusually low score for practice effect on WAIS-IV Symbol Search. See Supplementary Figure for pair-wise scatterplots of all primary variables.

https://doi.org/10.1017/S1355617715001332 Published online by Cambridge University Press

Table 2. Bivariate Pearson product correlations among dependent and independent variables ($n = 66$)

	Age	Educ.	GDS†	DRS-2	Memory	Novelty effect†	PE_{Coding}	PE_{Search}	Coding raw 1	Coding raw 2	Search raw 1
Education	.056	—									
GDS†	.156	−.322*	—								
DRS-2	−.116	.116	.096	—							
Memory	−.447**	.161	−.143	.674**	—						
Novelty effect†	−.219	−.008	−.002	.109	.214	—					
PE_{Coding}	−.270*	.039	−.122	.354**	.298*	.029	—				
PE_{Search}	.009	.123	.117	.073	.085	.489**	.005	—			
Coding raw 1	−.302*	.253*	−.194	.349**	.393**	.203	−.055	.261*	—		
Coding raw 2	−.399**	.250*	−.233	.480**	.495**	.199	.399**	.242	.894**	—	
Search raw 1	−.438**	.210	−.104	.523**	.526**	.129	.210	−.066	.572**	.620**	—
Search raw 2	−.379**	.251*	−.027	.498*	.507**	.379**	.187	.486**	.643**	.674**	.840**

*$p < .05$. **$p < .01$. †Lower values reflect better performances.
Note. DRS-2 = Age and education adjusted scaled scores for the Mattis Dementia Rating Scale, 2nd edition; Memory = Rey Auditory Verbal Learning Test delayed recall; Novelty effect = difference in motor planning times between first and second blocks of a motor learning task; PE_{Coding} = practice effect for WAIS-IV Coding; PE_{Search} = practice effect for WAIS-IV Symbol Search; GDS = Geriatric Depression Scale.

tasks, were fully debriefed upon completion, and were compensated $10 per hr.

Measures

Eligibility screening

The *Telephone Interview of Cognitive Status* (TICS; Brandt & Folstein, 2003) was used to screen for cognitive status before enrollment. The TICS includes items similar to the Mini Mental State Exam (MMSE) and correlates highly ($r = .94$) with the MMSE. It also has excellent sensitivity (94%) and specificity (100%) for distinguishing demented from non-demented participants (Brandt, Spencer, & Folstein, 1988). Following Brandt and Folstein (2003) interpretive ranges, a cutoff score of 21 or above was selected with the goal of excluding individuals with moderate-to-severe impairment[4]. Participants were screened for depression using the Geriatric Depression Scale (GDS; Yesavage, 1982), which has good validity and reliability among community-dwelling older adults (Dunn & Sacco, 1989; Yesavage, 1982) and adults with mild to moderate dementia (Feher, Larrabee, & Crook, 1992). We used a cutoff score of 19 or above (indicating severe depressive symptoms).

Cognitive decline

Abnormal cognitive decline was operationalized as deviation from demographically expected performance on the *Mattis Dementia Rating Scale, 2nd Edition* (DRS-2; Mattis, 1988); thus, age and education adjusted scaled scores were used in all analyses. DRS-2 is a screening measure used to assess general cognitive decline and includes items assessing attention, initiation, abstraction, visual-constructional abilities, and memory. As explained in the DRS-2 manual, scaled scores of 11 and above represent "average" (i.e., normatively expected) or higher cognitive functioning while scaled scores of 10 and below represent progressively greater deviation from normative expectations (Mattis, 1988).

Practice effects

PEs were measured using repeated administration of the Symbol Search and Coding subtests of the WAIS-IV (Wechsler, 2008), which are paper and pencil processing speed tasks with scores reflecting the number of items correctly completed within 2 min. These tests were selected because (1) they were *not* designed to assess memory or novelty effect (Wechsler, 2008), and, therefore, would not be expected to confound contributions of memory and novelty effect to PE; (2) they are known to exhibit sizeable practice effects in normative samples as compared to, for example, measures of crystallized intelligence (Estevis, Basso, & Combs, 2012); and (3) they were presumed to assess the same construct regardless of repeated administrations, which is not the case for all cognitive measures. Following recent methods in PE research (Darby, Maruff, Collie, & McStephen, 2002; Duff, Chelune, et al., 2012), the same form of each measure was repeated within-session at 30-min intervals. Participants completed other measures during this interval.

Test–retest reliabilities within our sample were .840 for Symbol Search and .894 for Coding. PEs for each subtest were calculated as the change in raw scores between the first and second administrations (the second score minus the first score). These subtests were originally intended to be combined into a PE composite score to optimize reliability. However, the two PE variables were *not* correlated (see Table 2); therefore, they were examined separately in all analyses.

[4] Despite efforts to screen out participants with greater than mild impairments in cognition using the TICS, several participants performed in the moderately to severely impaired range on further assessment with the Mattis Dementia Rating Scale, 2nd Edition (DRS-2) after scores were corrected for age and education.

https://doi.org/10.1017/S1355617715001332 Published online by Cambridge University Press

Fig. 2. Response console for the Push-Turn-Taptap (PTT) task. Using this response console, participants perform sequences (or permutations) of three specified hand movements. These are (a) pushing the joystick forward, (b) turning the joystick clockwise, and (c) double-tapping on the large white dome button. The task consists of four blocks, with each block requiring that participants learn a new and progressively longer sequence (2 movements through 5 movements). Each block begins with 3 learning trials presented on a computer screen. After the learning trials, the computer screen goes blank and participants continue to perform the sequence from memory until 5 correct consecutive sequences have been executed. A block is terminated if the criterion of 5 correct trials is not accomplished after 10 trials. Mistakes are followed by an audible tone, along with a presentation of the correct sequence on the screen. Although the task consists of four blocks, only the first two blocks are used for the calculation of the novelty effect. Also, although the task automatically tracks speed and accuracy of all movements across all four blocks (allowing assessment of not only motor planning, but also motor sequence learning, motor control, and motor speed), only motor planning has been shown to exhibit the novelty effect in past research. Thus, only the motor planning variable was used in this study.

Memory

The *Rey Auditory Verbal Learning Test* (RAVLT; Schmidt, 1996) is a 15-item list learning and memory task that includes five learning trials and a delayed (20–30 min) recall trial. The RAVLT has good test–retest reliability and validity (Schmidt, 1996). Memory was operationalized as total number of items recalled on the delay trial, to be comparable to the delay used for assessment of PE.

Novelty effect

Following our prior work (Euler et al., 2015; Suchy, Euler, & Eastvold, 2014; Suchy et al., 2011), novelty effect was measured using the *Push-Turn-Taptap (PTT)* task (Suchy & Kraybill, 2007), an electronically administered sequence learning task from the Behavioral Dyscontrol Scale, Electronic Version (BDS-EV; Suchy, Derbidge, & Cope, 2005). Participants perform sequences of three hand movements across four blocks, using a response console (Figure 2). These sequences progressively increase in complexity across these four blocks from two movements (Block 1) to five movements (Block 4). Motor planning latencies (i.e., time elapsed between completion of one sequence and initiation of the next *correct* sequence) on the first block are typically affected by novelty, as they are longer than those on the second block. Novelty effect is operationalized as the difference in these latencies between the second and first blocks. In this sample, the reliability of motor planning latencies was .858.

Statistical Analyses

Data were analyzed in SPSS using ordinary least squares regression. Independent contributions of novelty effect and memory to PE (Aim 1) were examined using hierarchical multiple regressions with PEs on WAIS-IV Symbol Search (PE_{Search}) and Coding (PE_{Coding}) as criterion variables. RAVLT delayed recall and novelty effect were used as predictors at Steps 1 and 2, respectively, and subsequently reversed (i.e., Steps 2 and 1, respectively) to examine unique contributions to PE. To test the hypothesis that the relationship between abnormal cognitive decline and PE is curvilinear (Aim 2), we conducted multiple regressions using PE_{Search} and PE_{Coding} as the criterion variables. Predictors included linear and quadratic terms for DRS-2 scaled scores[5].

To determine whether the relationships between PE and cognitive decline were mediated by learning or novelty effect (Aim 3), we used the MEDCURVE procedure for SPSS (Hayes & Preacher, 2010) to estimate the *total*, *direct*, and *indirect effects*[6] of DRS-2 scores on PEs. The MEDCURVE procedure was designed for path models in which one or more paths is nonlinear and for nonlinear models provides estimates of indirect effects at specific values of an independent variable, called *instantaneous indirect effects*. To test for significance of indirect effects, the MEDCURVE procedure generates bias-corrected bootstrap-confidence intervals (CIs) for the indirect effects; CIs that *do not* include zero indicate significant effects. As recommended by Preacher and Hayes (2004), we used 5000 bootstrap samples to create 95% confidence intervals for estimates of indirect effects. Following recommendations by Hayes (2009), mediation was interpreted when both the *total effect* (i.e., the path from a focal predictor to the criterion variable) and the *indirect effect* (i.e., the path from a focal predictor

[5] As a reminder, we used DRS-2 age and education corrected scaled scores (as opposed to raw scores), as demographically-corrected scores can serve as indicators of cognitive decline (relative to one's own predicted premorbid baseline), whereas raw scores reflect performance relative to the population on the whole and may or may not reflect a change from a premorbid baseline. As recommended by Cohen, Cohen, West, and Aiken (2003), DRS-2 scores were centered at zero before calculating the quadratic term.

[6] Simple mediation analysis partitions the *total effect* of DRS-2 scores on PE (denoted as *c*) into *direct* and *indirect effects*. *Direct effects* include 1) the effect of DRS-2 on the proposed mediator (denoted as *a*), 2) the effect of the mediator on PE (denoted as *b*) and 3) the effect of DRS-2 scores on PE independent of the proposed mediator (denoted as *c'*). The *indirect effect* is the effect of DRS-2 scores on PE that is accounted for by the mediator and for linear mediation models is calculated as the product of *a* and *b*. For nonlinear models, the *indirect effect* is calculated as the product of the first partial derivative of the function of the mediator with respect to DRS-2 scores and the first partial derivative of PE with respect to the mediator. In nonlinear models, the estimate of the *indirect effect* is not constant across levels of the independent variables, thus the MEDCURVE procedure is used to calculate *indirect effects* for specific values of an independent variable, called *instantaneous indirect effects* which are denoted by θx.

https://doi.org/10.1017/S1355617715001332 Published online by Cambridge University Press

Table 3. Novelty effect and memory as predictors of PE on WAIS-IV Coding and Symbol Search tests

Outcome variable	Model	Independent variables in model	$R^2\Delta$	$F\Delta$	df1	df2	p-Value
PE_{Coding}	1_a	Memory	.089	6.224	1	64	.015
	2_a	Novelty effect	.001	.089	1	63	.767
	1_b	Novelty effect	.001	.053	1	64	.819
	2_b	Memory	.089	6.166	1	63	.016
PE_{Search}	1_a	Memory	.007	.466	1	64	.497
	2_a	Novelty effect	.233	19.267	1	63	.000
	1_b	Novelty effect	.239	20.136	1	64	.000
	2_b	Memory	.000	.034	1	63	.855
PE_{Coding} with covariates	1	Age, education	.076	2.590	2	63	.083
	2_a	Memory	.036	2.539	1	62	.116
	3_a	Novelty effect	.003		1	61	.634
	2_b	Novelty effect	.001	.066	1	62	.798
	3_b	Memory	.039	2.669	1	61	.107
PE_{Search} with covariates	1	Age, education	.015	.486	2	63	.618
	2_a	Memory	.006	.364	1	62	.548
	3_a	Novelty effect	.247	20.613	1	61	.000
	2_b	Novelty effect	.253	21.431	1	62	.000
	3_b	Memory	.000	.005	1	61	.942

Δ = change; df = degrees of freedom; PE_{Coding} = practice effect for WAIS-IV Coding; PE_{Search} = practice effect for WAIS-IV Symbol Search; Memory = Rey Auditory Verbal Learning Test delayed recall; Novelty effect = difference in motor planning times between first and second blocks of a motor learning task.

to the mediator to the criterion variable) reached significance. Additional detail about mediation analysis is presented in Appendix B.

RESULTS

Preliminary Analyses

Table 2 shows Pearson product correlations between independent and dependent variables, demographics, and depression symptoms. Pairwise scatterplots for the primary variables of interest are available in Supplementary Materials. PE_{Search} was positively correlated with novelty effect ($r = .489$; $p < .001$), but no other variables. In contrast, PE_{Coding} was positively correlated with RAVLT delayed recall ($r = .298$; $p = .015$) and DRS-2 ($r = .354$; $p = .004$), which were also positively correlated with each other ($r = .674$; $p < .001$). Additionally, age was negatively correlated with PE_{Coding} ($r = -.270$; $p = .028$) and RAVLT delayed recall ($r = -.447$; $p < .001$). As mentioned earlier, PE_{Coding} and PE_{Search} were *not* correlated and thus were examined separately in primary analyses.

Aim 1: Contributions of Learning and Novelty Effect to Practice Effect

As seen in Table 3, RAVLT delayed recall accounted for unique variance in PE_{Coding}, whereas novelty effect accounted for unique variance in PE_{Search}. In sum, consistent with our hypotheses, these results show that memory and novelty effects have unique effects on PE, although, unexpectedly, each contributed to PE on a different measure. As a supplement, we repeated these analyses including both age and education, which are typically considered as covariates of cognitive performance in clinical neuropsychology. Results (see Table 3) followed the same pattern as our principal analyses for PE_{Search}. However, in the analysis of PE_{Coding}, neither novelty effect nor delayed recall were significant predictors after including age and education (age and education themselves did not predict PE_{Coding} either). This is likely due to high intercorrelations among age, delayed recall, and PE_{Coding} (see Table 2) and overlapping variance between age (semipartial $r = -.160$) and delayed recall (semipartial $r = .197$) in predicting PE_{Coding}.

Aim 2: Relationship between Cognitive Decline Status and Practice Effect

Results indicated a positive linear effect of DRS-2 scores on PE_{Coding} (linear term: $b = .640$; $beta = .354$; $t = 3.028$; $p = .004$) with DRS-2 scores accounting for 12.5% of variance in PE_{Coding}. In contrast, DRS-2 scores showed a quadratic relationship with PE_{Search} (quadratic term: $b = -.119$; $beta = -.347$; $t = -2.532$;

https://doi.org/10.1017/S1355617715001332 Published online by Cambridge University Press

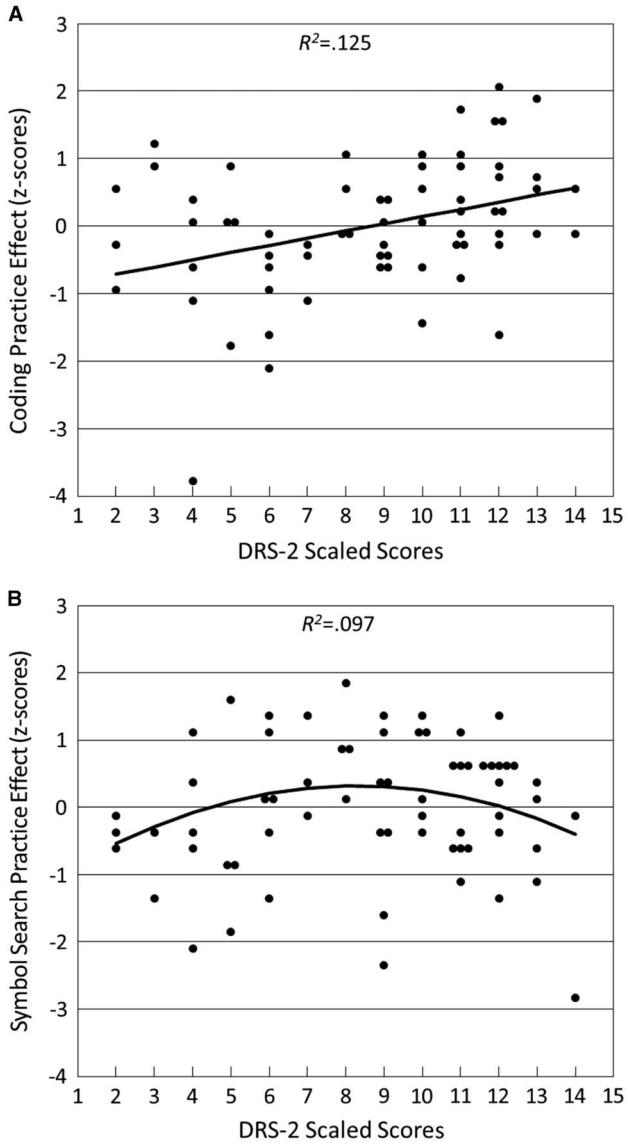

Fig. 3. Scatterplot of practice effects on WAIS-IV Coding (Panel A) and Symbol Search (Panel B) across cognitive decline.

$p = .014$)[7], such that larger PE_{Search} was associated with intermediate DRS-2 scores (i.e., mild impairment, approximate DRS-2 scaled score = 8), whereas smaller PE_{Search} was associated both with highest and lowest DRS-2 scores (see Figure 3B). DRS-2 scores accounted for 9.7% of variance in PE_{Search}. Results followed a similar pattern with age and education included as covariates, indicating that these results cannot be explained by demographic factors.

In sum, consistent with our model, PE_{Search} was a quadratic function of cognitive decline. However, rather than peaking at a preclinical level of decline, PE_{Search} peaked at an approximate DRS-2 scaled score of 8, which is on the cusp of clinical impairment per DRS-2 normative standards (Mattis, 1988). In contrast, the relationship between DRS-2 scores and PE_{Coding} is consistent with the expected linear decrease in PE with cognitive decline.

Aim 3: Mediation Analyses

Because RAVLT delayed recall and novelty effect were differentially related to the two PE variables in Aim 1 analyses, separate mediation analyses were examined for each PE variable. The models in Table 4 were used to estimate *total*, *direct* and *indirect effects* of (1) DRS-2 scores on PE_{Coding} through delayed recall (Table 4; Figure 4A) and (2) DRS-2 scores on PE_{Search} through novelty effect (Table 4; Figure 4B).

Tests of direct effects

As shown in Table 5, DRS-2 scores had a significant linear *total effect* on PE_{Coding} (Model 1; Figure 4A, path *c*) and a significant linear *direct effect* on delayed recall (Model 2; Figure 4A, path *a*), which decreased with declining DRS-2 scores. The *direct effects* of delayed recall (Table 5, Model 3; Figure 4A, path *b*) and DRS-2 scores (Table 5, Model 3; Figure 4A, path *c'*) on PE_{Coding} were not significant. As seen in Table 4 (Analysis A), adding delayed recall as a predictor of PE_{Coding} increased explained variance from 12.5% to 13.2%.

Consistent with Aim 2 results, DRS-2 scores had a significant quadratic *total effect* on PE_{Search} (Table 6, Model 1; Figure 4B, path c_2)[8]. The *direct effects* of DRS-2 scores on novelty (Table 6, Model 2; Figure 4B, paths a_1 and a_2) and PE_{Search} (Table 6, Model 3; Figure 4B, path c'_2) were not significant. Novelty effect had a positive linear *direct effect* on PE_{Search} (Table 6, Model 3; Figure 4B, path *b*). Additionally, adding novelty effect to the model, increased explained variance in PE_{Search} from 9.7% to 28.6% (see Table 4, Analysis B). Results for path models of both PE_{Coding} and PE_{Search} followed a similar pattern when covariates were included. Together these results are generally consistent with the Suchy et al. (2011) theoretical model.

Tests of indirect effects

The estimate of the *indirect effect* of DRS-2 scores on PE_{Coding} was not significant (*indirect effect* = .132; 95% CI = −.153 to .437), which may have been partly due to high correlation between DRS-2 scaled scores and delayed recall ($r = .674$; $p < .001$), resulting in minimal unique variance in PE_{Coding} explained by delayed recall (semipartial $r = .080$). Next we examined novelty effect as a mediator of the effect of DRS-2 scores on PE_{Search}. As shown in Figure 5, novelty effect partially mediated the relationship between PE_{Search}

[7] When potential outliers were excluded from analyses, this result was reduced to a trend (quadratic term: $b = -.087$, *beta* $= -.275$, $t = -1.920$, $p = .060$) and the linear term remained non-significant ($p = .957$).

[8] When potential outliers were excluded, the *total effect* of DRS-2 scores on PE_{Search} was reduced to a trend ($p = .060$). This precludes interpretation of a significant mediation by novelty when potential outliers are excluded despite the fact that *instantaneous indirect effects* of DRS-2 on PE_{Search} through novelty remained significant for DRS-2 scores below 7.

https://doi.org/10.1017/S1355617715001332 Published online by Cambridge University Press

Table 4. Regression results for models used in mediation analyses of cognitive decline on (A) WAIS-IV Coding practice effect through memory and (B) WAIS-IV Symbol Search through novelty effect

Analysis	Model	R^2	F	df1,df2	p-Value
A	(1) $PE_{Coding} = i + c$(DRS-2)	.125	9.170	1,64	.004
	(2) Memory $= i + a$(DRS-2)	.454	53.252	1,64	<.001
	(3) $PE_{Coding} = i + c'$(DRS-2) $+ b$(Memory)	.132	4.779	2,63	.012
B	(1) $PE_{Search} = i + c_1$(DRS-2) $+ c_2$(DRS-2)^2	.097	3.393	2,63	.040
	(2) Novelty $= i + a_1$(DRS-2) $+ a_2$(DRS-2)^2	.048	1.593	2,63	.211
	(3) $PE_{Search} = i + c_1'$ (DRS-2) $+ c_2'$ (DRS-2)$^2 + b$(Novelty)	.286	8.266	3,62	<.001

df = degrees of freedom; PE_{Coding} = practice effect for WAIS-IV Coding; PE_{Search} = practice effect for WAIS-IV Symbol Search; Memory = Rey Auditory Verbal Learning Test delayed recall; Novelty = difference in motor planning times between first and second blocks of a motor learning task; i = intercept; c = total effect of DRS-2 on PE; a = direct effect of DRS-2 on mediator; b = direct effect of mediator on PE independent of DRS-2; c' = direct effect of DRS-2 on PE independent of mediator.

Note. The indirect effect of DRS-2 on PE through the proposed mediator is quantified as the product of a and b. The total effect of DRS-2 on PE is the sum of the direct and indirect effects: $c = ab + c'$. Using this equation, the indirect effect can be calculated as the difference between the total and direct effects of DRS-2 on PE: $ab = c - c'$.

and DRS-2 with significant *instantaneous indirect effects* for DRS-2 scaled scores of 7 and below (impaired status; $\theta_{DRS\text{-}2\ =\ 7} = .126$; 95% CI = .007 to .349). Figure 5 displays *instantaneous indirect effects* for all DRS-2 scores. When covariates were included in the model, the general pattern of results was similar for both PE_{Coding} and PE_{Search}. However, in the latter, mediation by novelty effect occurred only for DRS-2 scores of 6 and below ($\theta_{DRS\text{-}2\ =\ 6} = .188$; 95% CI = .007 to .569).

These results indicate (1) that novelty effect accounted for the effects of DRS-2 scores on PE_{Search} at impaired levels of cognitive functioning, and (2) that these relationships are not due to demographic factors. However, novelty effect did not explain effects of DRS-2 scores on PE_{Search} for cognitively intact participants. Taken together, the mediation analyses suggest that changes in PE with cognitive decline may be attributable to specific cognitive processes that may vary depending on the measures on which PEs are observed.

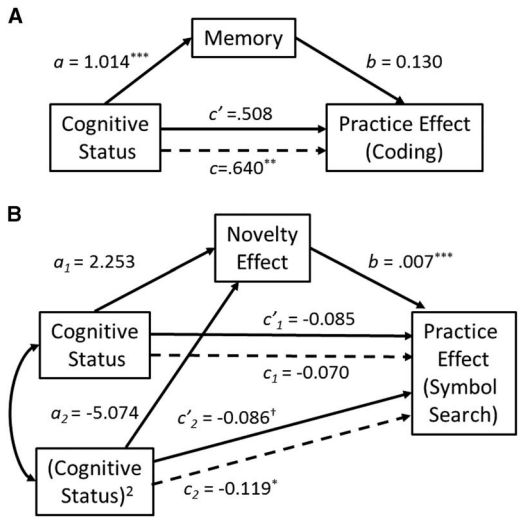

Fig. 4. Path coefficients for mediation models for practice effect on WAIS-IV Coding (A) and Symbol Search (B) tests ($n = 66$). *Note:* Dotted lines indicate the effect of cognitive decline on PE when the mediator is excluded from the model. a, b, c, and c' are unstandardized regression coefficients. The indirect effect of cognitive decline through the proposed mediator is calculated as the product of a and b for linear mediation models and as the product of the partial derivative of the models for paths a and b for nonlinear models. $^{\dagger}p < .10$, $*p < .05$, $**p < .01$, $***p < .001$

DISCUSSION

The key findings of this study were that (1) PE is not a unitary construct and, depending on how it is assessed, it may be explained by memory, novelty effect, or both; (2) the relationship between PE and cognitive decline may be linear for some, and curvilinear for other, measures of PE; and (3) the relationship between cognitive decline and PE on WAIS-IV Symbol Search may be explained by novelty effect, particularly at impaired levels of cognitive functioning. While some aspects of these results were consistent with the original hypotheses and partially supported the theoretical model of PE, others were unexpected. Our results do support contributions of both memory and novelty effect to PE as proposed in the theoretical model. Additionally, our results are consistent with the notion that novelty and cognitive decline may have a nonlinear relationship, and that novelty effect may partially mediate nonlinear changes in PE as a function of cognitive decline. However, contrary to expectation, our two measures of PE were *not* correlated with each other, and, therefore, needed to be analyzed separately. These separate analyses revealed that the two PEs were uniquely related to memory and novelty effect, such that memory predicted PE on WAIS-IV Coding (PE_{Coding}) whereas novelty effect predicted PE on WAIS-IV Symbol Search (PE_{Search}).

Although previous research has shown substantial variability in magnitudes of PE across different cognitive domains (Basso, Carona, Lowery, & Axelrod, 2002; Duff et al., 2010, 2008), the fact that our two indices of PE were uncorrelated is nevertheless unexpected given that they were observed on

https://doi.org/10.1017/S1355617715001332 Published online by Cambridge University Press

Table 5. Mediation analysis for cognitive decline on WAIS-IV Coding practice effect through memory (standard errors in parentheses)

		Model 1			Model 2			Model 3	
Outcome Var. →		PE_{Coding}			Memory			PE_{Coding}	
Predictor		B	*p*		B	*p*		B	*p*
Intercept		.109 (1.958)	.956		−2.610 (1.289)	.047		.448 (2.028)	.826
DRS-2	*c* →	0.640 (0.211)	.004	*a* →	1.014 (0.139)	<.001	*c'* →	0.508 (0.287)	.082
Memory							*b* →	0.130 (0.191)	.498

PE_{Coding} = practice effect on WAIS-IV Coding; DRS-2 = age and education adjusted scaled scores for the Mattis Dementia Rating Scale, 2nd edition; Memory = Rey Auditory Verbal Learning Test delayed recall; *c* = total effect of DRS-2 on PE_{Coding}; *a* = direct effect of DRS-2 on memory; *b* = direct effect of memory on PE_{Coding} independent of DRS-2; *c'* = direct effect of DRS-2 on PE_{Coding} independent of memory.
Note. All coefficients are unstandardized ordinary least squares regression coefficients. Model 1: PE_{Coding} = intercept + *c*(DRS-2) + error. Model 2: Memory = intercept + *a*(DRS-2) + error. Model 3: PE_{Coding} = constant + *c'*(DRS-2) + *b*(Memory) + error.

measures of the *same* cognitive domain. One interpretation of this finding is that each measure draws upon different component processes beyond speed, and these processes are then differentially facilitated by practice. Indeed, memory for number-symbol pairs appears to facilitate performance on WAIS-IV Coding above and beyond speed (Joy, Fein, & Kaplan, 2003; Joy, Fein, Kaplan, & Freedman, 2000; Joy, Kaplan, & Fein, 2004). In contrast, memory processes would offer little support on Symbol Search retest, which may rely more on executive and visual processing (Sweet et al., 2005).

Our findings of unique contributions of cognitive processes to PE and different patterns (i.e., linear *vs*. nonlinear) of PEs with cognitive decline help explain mixed results in the literature regarding PE and cognitive decline (Cooper et al., 2004; Duff et al., 2008; Duff, Chelune, et al., 2012; Yan & Dick, 2006), and suggest that differences in PE between impaired and nonimpaired groups depend on the specific measure used. For example, cognitive impairment is likely associated with smaller PE on tests of memory (Schrijnemaekers et al., 2006; but see Duff et al., 2008 for contradictory results), but larger PE on other measures, such as motor control tasks (e.g., Yan & Dick, 2006). This notion is further supported by the results of our mediation analyses wherein novelty effect partially mediated the effect of cognitive decline on PE_{Search}.

Theoretical Implications

Our finding that PE has diverse cognitive underpinnings is consistent with prior research showing residual PE on

Table 6. Mediation analysis for cognitive decline on WAIS-IV Symbol Search practice effect through novelty effect (standard errors in parentheses)

		Model 1			Model 2			Model 3	
Outcome Var. →		PE_{Search}			Novelty			PE_{Search}	
Predictor		B	*p*-Value		B	*p*-Value		B	*p*-Value
Intercept		4.796 (0.703)	<.001		126.875 (48.893)	.011		3.963 (0.663)	<.001
DRS-2	c_1 →	−0.070 (0.159)	.491	a_1 →	2.253 (11.075)	.839	c_1' →	−0.085 (0.143)	.553
$(DRS\text{-}2)^2$	c_2 →	−0.119 (0.047)	.014	a_2 →	−5.074 (3.279)	.127	c_2' →	−0.086 (0.043)	.050
Novelty							*b* →	0.007 (0.002)	<.001

PE_{Search} = practice effect on WAIS-IV Symbol Search; DRS-2 = age and education adjusted scaled scores for the Mattis Dementia Rating Scale, 2nd edition; Novelty = novelty effect calculated as the difference in motor planning times between first and second blocks of a motor learning tas; *c* = total effect of DRS-2 on PE_{Search}; *a* = direct effect of DRS-2 on novelty; *b* = direct effect of novelty on PE_{Search} independent of DRS-2; *c'* = direct effect of DRS-2 on PE_{Search} independent of novelty.
Note. All coefficients are unstandardized ordinary least squares regression coefficients.Model 1: PE_{Search} = constant + c_1(DRS-2) + $c_2(DRS\text{-}2)^2$ + error. Model 2: Novelty Effect = constant + a_1(DRS-2) + $a_2(DRS\text{-}2)^2$ + error. Model 3: PE_{Search} = constant + c'_1(DRS-2) + $c'_2(DRS\text{-}2)^2$ + *b*(Novelty) + error.

https://doi.org/10.1017/S1355617715001332 Published online by Cambridge University Press

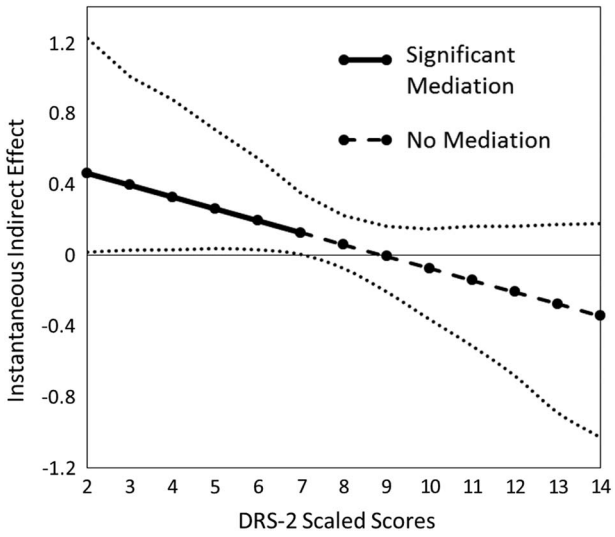

Fig. 5. Instantaneous indirect effects of cognitive status on WAIS-IV Symbol Search practice effect mediated by novelty effect. Dashed lines represent upper and lower confidence intervals for bootstrap-estimated instantaneous direct effects. Confidence intervals that *do not* include zero indicate a significant indirect effect. Significant mediation is depicted by solid bold line.

alternate forms despite changes in test content (Beglinger, Gaydos, et al., 2005; Benedict, 2005; Benedict & Zgaljardic, 1998). These residual PEs could reflect implicit memory processes and other cognitive phenomena, including novelty effects. For example, after observing larger PEs on a visual memory task versus a list-learning task, Benedict and Zgaljardic (1998) noted that in addition to differing in verbal versus nonverbal memory demands, the procedures of the nonverbal memory task were more novel to participants relative to the familiar list-learning procedures.

While the novelty effect appears to be distinguishable from explicit memory, both in this study and in our prior research (Suchy et al., 2011), we currently have a poor conceptual understanding of novelty. It is possible that novelty effect merely reflects implicit/procedural learning, which is dissociable from explicit memory (Squire, 1994) and may be relatively preserved in MCI and early Alzheimer's disease (Akdemir, Cangöz, Örsel, & Selekler, 2007; Gobel et al., 2013). Consequently, MCI patients are able to exhibit the rebound in performance that reflects novelty effect. Alternatively, novelty effect could reflect other cognitive processes, such as controlled attention or strategy selection. While these have not been examined directly, several lines of research (detailed below) offer insights into the possible correlates of novelty effects.

Novelty effect may reflect specific aspects of executive functioning, such as controlled attention, which are involved in set formation or shifting. For example, learning curves research has shown a ubiquitous exponential performance pattern marked by large improvements within the first few trials of a task (Heathcote, Brown, & Mewhort, 2000; Newell & Rosenbloom, 1981), often referred to as a fast-learning stage, which is akin to our definition of novelty effect. This initial learning stage is thought to relate to attention, response selection, and mapping of response to stimuli (Halsband & Lange, 2006). In addition, temporary performance decrements (i.e., slower responses and/or increased errors) are consistently observed in task-switching paradigms (e.g., Biederman, 1972; Rogers & Monsell, 1995) or in response to the reorganization of previously rehearsed task items (Ouellet et al., 2004). Novelty effects may also be related to fluid intelligence as lower fluid intelligence is associated with larger PE (Blalock & McCabe, 2011). Lastly, we recently demonstrated that novel contexts lead not only to behavioral novelty effects, but also to degradation of the EEG-assessed motor readiness potential (Euler et al., 2015), suggesting that the ability to overcome novelty may reflect the efficiency of neuronal synchronization in face of the distracting properties of novel contexts.

Clinical Implications

We recently proposed that novelty effect may represent an early preclinical marker of declining cognitive reserve, the cognitive "buffer" that protects against behavioral manifestations of neurodegenerative disease (Suchy et al., 2011). Cognitive reserve may mask cognitive decline through greater activation or broader recruitment of brain regions to support performance of novel tasks (Eyler, Sherzai, Kaup, & Jeste, 2011; Lenzi et al., 2011). However, activation of broader neural networks may lead to subtle costs early on in task performance; these costs may take the form of delayed re-emergence of motor readiness potentials, which then results in longer latencies before response initiation (Euler et al., 2015). While the present results provide support for the clinical utility of PE (Duff, 2012; Duff et al., 2007; Duff, Callister, et al., 2012; Duff, Chelune, et al., 2012; Machulda et al., 2013) and novelty effect (Suchy et al., 2011), they also demonstrate needs for future research examining PE as a non-unitary construct and tailoring PE assessment to different clinical populations.

Variations in the relationship between PE and cognitive decline across cognitive measures could have implications for interpretation of serial assessments. For example, while large PEs may indicate intact or improved cognitive functioning on some measures (e.g., learning/memory measures), they may represent impairment or an incipient neurodegenerative disorder on measures with more novel task demands. Reliable change indices (RCI) have been developed to address practice-related variance in repeat test performance (Chelune & Franklin, 2003; Duff, 2012); however, RCIs are typically calculated using test–retest data from healthy samples, which may not accurately reflect retest variability in impaired populations.

https://doi.org/10.1017/S1355617715001332 Published online by Cambridge University Press

LIMITATIONS

First, our ability to detect a mediating effect of memory on the relationship between cognitive decline and PE was limited by high correlations between measures of memory and cognitive decline, leading to overlapping variance in prediction of PE_{Coding}. This may relate to the fact that DRS-2 scores are heavily weighted on memory performance and thus correlate highly with memory tests (Smith, Ivnik, Malec, & Kokmen, 1994). Future research should examine these relationships using other indices of cognitive decline, or populations whose cognitive decline is characterized by other changes. It remains to be seen whether different patterns of cognitive decline have differential impact on PE; however, preliminary support for this idea is evident in studies demonstrating that PEs vary across clinical diagnoses (Duff et al., 2007).

Second, cognitive decline was not measured directly, but was estimated using age- and education-adjusted scaled scores. While such scores provide an estimate of deviation from premorbid expectation, low scaled scores may represent longstanding below-average functioning for some participants. Therefore, a direct assessment of cognitive change *via* longitudinal design is warranted.

Lastly, because a large portion of our sample was recruited from a memory disorders clinic, 26 participants (1 healthy, 25 with cognitive decline) had previously completed neuropsychological evaluations, which included the same or similar measures as those used in the current study. Thus, prior exposure could have led to artificially smaller PEs on the WAIS-IV Coding and Symbol Search tests. However, this effect could not explain the pattern of results, as all participants would have experienced equal exposure across *both* tests used for PE calculations.

ACKNOWLEDGMENTS

There are no conflicts of interest to report. This study was financially supported by the University of Utah, Department of Neurology (G.J.C. & Y.S.) and Department of Psychology (S.R.T.).

Supplementary material

To view supplementary material for this article, please visit http://dx.doi.org/10.1017/S1355617715001332

REFERENCES

Akdemir, A., Cangöz, B.T., Örsel, S., & Selekler, K. (2007). A comparison of implicit memory performance in mild cognitive impairment and Alzheimer type dementia patients. *Türk Psikiyatri Dergisi*, *18*(2), 1–10.

Basso, M.R., Bornstein, R.A., & Lang, J.M. (1999). Practice effects on commonly used measures of executive function across twelve months. *The Clinical Neuropsychologist*, *13*(3), 283–292. doi:10.1076/clin.13.3.283.1743

Basso, M.R., Carona, F.D., Lowery, N., & Axelrod, B.N. (2002). Practice effects on the WAIS-III across 3-and 6-month intervals. *The Clinical Neuropsychologist*, *16*(1), 57–63. doi:10.1076/clin.16.1.57.8329

Beglinger, L.J., Gaydos, B., Tangphao-Daniels, O., Duff, K., Kareken, D.A., Crawford, J., … Siemers, E.R. (2005). Practice effects and the use of alternate forms in serial neuropsychological testing. *Archives of Clinical Neuropsychology*, *20*(4), 517–529. doi:10.1016/j.acn.2004.12.003

Beglinger, L.J., Tangphao-Daniels, O., Kareken, D.A., Zhang, L., Mohs, R., & Siemers, E.R. (2005). Neuropsychological test performance in healthy elderly volunteers before and after donepezil administration: A randomized, controlled study. *Journal of Clinical Psychopharmacology*, *25*(2), 159. doi:10.1097/01.jcp.0000155822.51962.b4

Benedict, R.H.B. (2005). Effects of using same- versus alternate-form memory tests during short-interval repeated assessments in multiple sclerosis. *Journal of the International Neuropsychological Society*, *11*(6), 727–736. doi:10.1017/S1355617705050782

Benedict, R.H.B., & Zgaljardic, D.J. (1998). Practice effects during repeated administrations of memory tests with and without alternate forms. *Journal of Clinical and Experimental Neuropsychology*, *20*(3), 339–352. doi:10.1076/jcen.20.3.339.822

Biederman, I. (1972). Human performance in contingent information-processing tasks. *Journal of Experimental Psychology*, *93*(2), 219–238.

Blalock, L.D., & McCabe, D.P. (2011). Proactive interference and practice effects in visuospatial working memory span task performance. *Memory*, *19*(1), 83–91. doi:10.1080/09658211.2010.537035

Brandt, J., & Folstein, M.F. (2003). *TICS, telephone interview for cognitive status: Professional manual*. Odessa, FL: Psychological Assessment Resources.

Brandt, J., Spencer, M., & Folstein, M. (1988). The telephone interview for cognitive status. *Neuropsychiatry, Neuropsychology, & Behavioral Neurology*, *1*(2), 111–117.

Busch, R.M., Chelune, G.J., & Suchy, Y. (2006). Using norms in neuropsychological assessment of the elderly. In D.K. Attix & K.A. Welsh-Bohmer (Eds.), *Geriatric neuropsychology: Assessment and Intervention* (pp. 133–157). New York: Guilford Publications.

Calamia, M., Markon, K., & Tranel, D. (2012). Scoring higher the second time around: Meta-analyses of practice effects in neuropsychological assessment. *The Clinical Neuropsychologist*, *26*(4), 543–570. doi:10.1080/13854046.2012.680913

Camozzato, A., de Almeida Fleck, M.P., Delgado, V., & Fagundes Chaves, M.L. (2007). Education did not interact with major depression on performance of memory tests in acute Southern Brazilian in patients. *Dementia & Neuropsychologia*, *1*(1), 24–31.

Chelune, G.J., & Franklin, R.D. (2003). Assessing reliable neuropsychological change. In R.D. Franklin (Ed.), *Prediction in forensic and neuropsychology: Sound statistical practices* (pp. 115–138). Mahwah, NJ: Lawrence Erlbaum Associates Publishers.

Cohen, J., Cohen, P., West, S.G., & Aiken, L.S. (2003). *Applied multiple regression/correlation analysis for the behavioral sciences* (3rd ed.). Mahwah, NJ: Lawrence Erlbaum Associates Publishers.

Cooper, D.B., Epker, M., Lacritz, L., Weiner, M., Rosenberg, R.N., Honig, L., & Cullum, C.M. (2001). Effects of practice on category fluency in Alzheimer's disease. *The Clinical Neuropsychologist*, *15*(1), 125–128. doi:10.1076/clin.15.1.125.1914

Cooper, D.B., Lacritz, L.H., Weiner, M.F., Rosenberg, R.N., & Cullum, C.M. (2004). Category fluency in mild cognitive impairment: Reduced effect of practice in test-retest conditions. *Alzheimer Disease and Associated Disorders*, *18*, 120–122. doi:10.1097/01.wad.0000127442.15689.92

Darby, D., Maruff, P., Collie, A., & McStephen, M. (2002). Mild cognitive impairment can be detected by multiple assessments in a single day. *Neurology*, *59*(7), 1042–1046. doi:10.1001/archneur.59.6.1042

Dikmen, S.S., Heaton, R.K., Grant, I., & Temkin, N.R. (1999). Test-retest reliability and practice effects of Expanded Halstead–Reitan Neuropsychological Test Battery. *Journal of the International Neuropsychological Society*, *5*(4), 346–356. doi:10.1017/S1355617799544056

Duff, K. (2012). Evidence-based indicators of neuropsychological change in the individual patient: Relevant concepts and methods. *Archives of Clinical Neuropsychology*, *27*(3), 248–261. doi:10.1093/arclin/acr120

Duff, K., Beglinger, L.J., Moser, D.J., Paulsen, J.S., Schultz, S.K., & Arndt, S. (2010). Predicting cognitive change in older adults: The relative contribution of practice effects. *Archives of Clinical Neuropsychology*, *25*(2), 81–88. doi:10.1093/arclin/acp105

Duff, K., Beglinger, L.J., Schultz, S.K., Moser, D.J., McCaffrey, R.J., Haase, R.F., … Paulsen, J.S. (2007). Practice effects in the prediction of long-term cognitive outcome in three patient samples: A novel prognostic index. *Archives of Clinical Neuropsychology*, *22*(1), 15–24. doi:10.1016/j.acn.2006.08.013

Duff, K., Beglinger, L.J., Van Der Heiden, S., Moser, D.J., Arndt, S., Schultz, S.K., & Paulsen, J.S. (2008). Short-term practice effects in amnestic mild cognitive impairment: Implications for diagnosis and treatment. *International Psychogeriatrics*, *20*(5), 986–999. doi:10.1017/S1041610208007254

Duff, K., Callister, C., Dennett, K., & Tometich, D. (2012). Practice effects: A unique cognitive variable. *The Clinical Neuropsychologist*, *26*(7), 1117–1127. doi:10.1080/13854046.2012.722685

Duff, K., Chelune, G., & Dennett, K. (2012). Within-session practice effects in patients referred for suspected dementia. *Dementia and Geriatric Cognitive Disorders*, *33*(4), 245–249. doi:10.1159/000339268

Dunn, V.K., & Sacco, W.P. (1989). Psychometric evaluation of the Geriatric Depression Scale and the Zung Self-Rating Depression Scale using an elderly community sample. *Psychology and Aging*, *4*(1), 125–126.

Estevis, E., Basso, M.R., & Combs, D. (2012). Effects of practice on the Wechsler Adult Intelligence Scale-IV across 3- and 6-month intervals. *The Clinical Neuropsychologist*, *26*(2), 239–254. doi:10.1080/13854046.2012.659219

Euler, M., Niermeyer, M., & Suchy, Y. (2015). Neurocognitive and neurophysiological correlates of motor planning during familiar and novel contexts. *Neuropsychology* [Epub ahead of print] doi:10.1037/neu0000219

Eyler, L.T., Sherzai, A., Kaup, A.R., & Jeste, D.V. (2011). A review of functional brain imaging correlates of successful cognitive aging. *Biological Psychiatry*, *70*(2), 115–122. doi:10.1016/j.biopsych.2010.12.032

Feher, E.P., Larrabee, G.J., & Crook, T.H. (1992). Factors attenuating the validity of the Geriatric Depression Scale in a dementia population. *Journal of the American Geriatrics Society*, *40*(9), 906–909.

Gobel, E.W., Blomeke, K., Zadikoff, C., Simuni, T., Weintraub, S., & Reber, P.J. (2013). Implicit perceptual-motor skill learning in mild cognitive impairment and Parkinson's disease. *Neuropsychology*, *27*(3), 314–321. doi:10.1037/a0032305

Halsband, U., & Lange, R.K. (2006). Motor learning in man: A review of functional and clinical studies. *Journal of Physiology, Paris*, *99*(4–6), 414–424. doi:10.1016/j.jphysparis.2006.03.007

Hayes, A.F. (2009). Beyond Baron and Kenny: Statistical mediation analysis in the new millennium. *Communication Monographs*, *76*(4), 408–420. doi:10.1080/03637750903310360

Hayes, A.F., & Preacher, K.J. (2010). Quantifying and testing indirect effects in simple mediation models when the constituent paths are nonlinear. *Multivariate Behavioral Research*, *45*(4), 627–660. doi:10.1080/00273171.2010.498290

Heathcote, A., Brown, S., & Mewhort, D.J.K. (2000). The power law repealed: The case for an exponential law of practice. *Psychonomic Bulletin & Review*, *7*(2), 185–207.

Helkala, E.L., Kivipelto, M., Hallikainen, M., Alhainen, K., Heinonen, H., Tuomilehto, J., … Nissinen, A. (2002). Usefulness of repeated presentation of Mini-Mental State Examination as a diagnostic procedure–A population-based study. *Acta Neurologica Scandinavica*, *106*(6), 341–346. doi:10.1034/j.1600-0404.2002.01315.x

Jonker, C., Geerlings, M.I., & Schmand, B. (2000). Are memory complaints predictive for dementia? A review of clinical and population-based studies. *International Journal of Geriatric Psychiatry*, *15*(11), 983–991. doi:10.1002/1099-1166(200011)15:11<983::AID-GPS238>3.0.CO;2-5

Joy, S., Fein, D., & Kaplan, E. (2003). Decoding digit symbol: Speed, memory, and visual scanning. *Assessment*, *10*(1), 56–65. doi:10.1177/0095399702250335

Joy, S., Fein, D., Kaplan, E., & Freedman, M. (2000). Speed and memory in WAIS-R-NI Digit Symbol performance among healthy older adults. *Journal of the International Neuropsychological Society*, *6*(7), 770–780. doi:10.1017/S1355617700677044

Joy, S., Kaplan, E., & Fein, D. (2004). Speed and memory in the WAIS-III Digit Symbol–Coding subtest across the adult lifespan. *Archives of Clinical Neuropsychology*, *19*(6), 759–767. doi:10.1016/j.acn.2003.09.009

Köhler, S., van Boxtel, M.P., van Os, J., Thomas, A.J., 'O'Brien, J.T., Jolles, J., … Allardyce, J. (2010). Depressive symptoms and cognitive decline in community-dwelling older adults. *Journal of the American Geriatrics Society*, *58*(5), 873–879. doi:10.1111/j.1532-5415.2010.02807.x

Larson, J.C.G., & Suchy, Y. (2014). The contribution of verbalization to action. *Psychological Research*, 1–19. doi:10.1007/s00426-014-0586-0

Lenzi, D., Serra, L., Perri, R., Pantano, P., Lenzi, G.L., Paulesu, E., … Macaluso, E. (2011). Single domain amnestic MCI: A multiple cognitive domains fMRI investigation. *Neurobiology of Aging*, *32*, 1542–1557. doi:10.1016/j.neurobiolaging.2009.09.006

Machulda, M.M., Pankratz, V.S., Christianson, T.J., Ivnik, R.J., Mielke, M.M., Roberts, R.O., … Petersen, R.C. (2013). Practice effects and longitudinal cognitive change in normal aging vs. incident mild cognitive impairment and dementia in The Mayo Clinic Study of Aging. *The Clinical Neuropsychologist*, *27*(8), 1247–1264. doi:10.1080/13854046.2013.836567

Mattis, S. (1988). *Dementia rating scale: Professional manual*. Odessa, FL: Psychological Assessment Resources.

McCaffrey, R.J., Duff, K., & Westervelt, H.J. (2000). *'Practitioner's guide to evaluating change with neuropsychological assessment instruments*. Dordrecht Netherlands: Kluwer Academic Publishers.

Mitchell, A.J. (2008). The clinical significance of subjective memory complaints in the diagnosis of mild cognitive impairment and dementia: A meta-analysis. *International Journal of Geriatric Psychiatry*, *23*(11), 1191–1202. doi:10.1002/gps.2053

Newell, A., & Rosenbloom, P.S. (1981). Mechanisms of skill acquisition and the law of practice. *Cognitive Skills and Their Acquisition*, 1–55.

Ouellet, M.-C., Beauchamp, M.H., Owen, A.M., & Doyon, J. (2004). Acquiring a cognitive skill with a new repeating version of the Tower of London Task. *Canadian Journal of Experimental Psychology*, *58*(4), 272–288. doi:10.1037/h0087450

Preacher, K.J., & Hayes, A.F. (2004). SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behavior Research Methods, Instruments & Computers*, *36*(4), 717–731. doi:10.3758/BF03206553

Rogers, R.D., & Monsell, S.D. (1995). Costs of a predictable switch between simple cognitive tasks. *Journal of Experimental Psychology. General*, *124*(2), 207. doi:10.1037/0894-4105.20.6.675

Rousson, V., Gasser, T., Caflisch, J., & Jenni, O.G. (2009). Neuromotor performance of normally developing left-handed children and adolescents. *Human Movement Science*, *28*(6), 809–817. doi:10.1016/j.humov.2009.06.001

Schmidt, M. (1996). *Rey auditory verbal learning test: A handbook*. Los Angeles, CA: Western Psychological Services.

Schrijnemaekers, A.M.C., de Jager, C.A., Hogervorst, E., & Budge, M.M. (Writers) (2006). Cases with mild cognitive impairment and Alzheimer's disease fail to benefit from repeated exposure to episodic memory tests as compared with controls. *Journal of Clinical and Experimental Neuropsychology*, *28*, 438–455. doi:10.1080/13803390590935462

Smith, G.E., Ivnik, R.J., Malec, J.F., & Kokmen, E. (1994). Psychometric properties of the Mattis Dementia Rating Scale. *Assessment*, *1*(2), 123–131.

Squire, L.R. (1994). Declarative and nondeclarative memory: Multiple brain systems supporting learning and memory. In D.L. Schacter & E. Tulving (Eds.), *Memory systems 1994* (pp. 203–231). Cambridge, MA: The MIT Press.

Suchy, Y., Derbidge, C., & Cope, C. (2005). Behavioral dyscontrol scale-electronic version: First examination of reliability, validity, and incremental utility. *The Clinical Neuropsychologist*, *19*, 4–26. doi:10.1080/13854040490888585

Suchy, Y., Euler, M., & Eastvold, A. (2014). Exaggerated reaction to novelty as a subclinical consequent of mild traumatic brain injury. *Brain Injury* [Epub ahead of print] doi:10.3109/02699052.2014.888766

Suchy, Y., & Kraybill, M. (2007). The relationship between motor programming and executive abilities: Constructs measured by the Push-Turn-Taptap task from the behavioral dyscontrol scale-electronic version. *Journal of Clinical and Experimental Neuropsychology*, *29*, 648–659. doi:10.1080/13803390600910506

Suchy, Y., Kraybill, M.L., & Franchow, E. (2011). Practice effect and beyond: Reaction to novelty as an independent predictor of cognitive decline among older adults. *Journal of the International Neuropsychological Society*, *17*(1), 101–111. doi:10.1017/S135561771000130X

Sweet, L.H., Paskavitz, J.F., O'Connor, M.J., Browndyke, J.N., Wellen, J.W., & Cohen, R.A. (2005). FMRI correlates of the WAIS-III Symbol Search subtest. *Journal of the International Neuropsychological Society*, *11*(4), 471–476. doi:10.1017/S1355617705050575

Wechsler, D. (2008). *Wechsler Adult Intelligence Scale-Fourth Edition*. San Antonio, TX: Pearson.

Wilson, B.A., Watson, P.C., Baddeley, A.D., Emslie, H., & Evans, J.J. (2000). Improvement or simply practice? The effects of twenty repeated assessments on people with and without brain injury. *Journal of the International Neuropsychological Society*, *6*(04), 469–479. doi:10.1017/S1355617700644053

Yan, J.H., & Dick, M.B. (2006). Practice effects on motor control in healthy seniors and patients with mild cognitive impairment and Alzheimer's disease. *Aging, Neuropsychology, and Cognition*, *13* (3–4), 385–410. doi:10.1080/138255890969609

Yesavage, J.A. (1982). Development and validation of a Geriatric Depression Screening Scale: A preliminary report. *Journal of Psychiatric Research*, *17*(1), 37–49.

APPENDIX A

Detailed Description of Measures

Telephone Interview of Cognitive Status (TICS; Brandt & Folstein, 2003). The TICS is a 10-min cognitive status screening measure with items assessing attention/concentration, orientation, single-trial list learning, serial subtraction, object naming, sentence repetition and simple reasoning. Scores range from 0 to 41 with four suggested interpretive ranges, including nonimpaired (scores 33 and above), ambiguous (26–32), mildly impaired (21–25), and moderately to severely impaired (20 or less).

Mattis Dementia Rating Scale, 2nd Edition (DRS-2; Mattis, 1988). The DRS-2 is a brief paper and pencil screening measure for assessment of general cognitive decline. Test items assess domains of attention, initiation, abstraction, visual-constructional abilities, and verbal and nonverbal memory. The DRS-2 normative sample consists of 623 community-dwelling older adults from the Mayo's Older Americans Normative Studies project (Lucas et al., 1998) who did not have any current medical, neurological, or psychiatric diagnoses that might impact cognitive functioning.

Wechsler Adult Intelligence Scale, 4th Edition (WAIS-IV; Wechsler, 2008) Symbol Search and Coding Subtests. These pencil and paper tasks are measures of information processing speed and make up the Processing Speed Index of the WAIS-IV. Scores for both tests are based on the number of items completed within a 2-min time limit. For each item in the Symbol Search subtest participants were asked to identify one of two abstract symbols among a group of distractor symbols or to mark a box indicating that neither symbol is present. The Symbol Search Raw score is calculated as the number of correct items minus the number of incorrect items completed within the time limit (incomplete items are not scored). The Coding subtest is a symbol digit substitution test in which participants rapidly match an abstract symbol to numbers that are presented in a pseudorandom order. The Coding raw score is calculated as the total number of symbols correctly coded within the time limit.

References

Brandt, J., & Folstein, M. F. (2003). *TICS, telephone interview for cognitive status: Professional manual*. Odessa, FL: Psychological Assessment Resources.

Lucas, J. A., Ivnik, R. J., Smith, G. E., Bohac, D. L., Tangalos, E. G., Kokmen, E., … Petersen, R. C. (1998). Normative data for the Mattis dementia rating scale. *Journal of Clinical and Experimental Neuropsychology*, *20*(4), 536–547.

Mattis, S. (1988). *Dementia rating scale: Professional manual*. Odessa, FL: Psychological Assessment Resources.

Wechsler, D. (2008). *Wechsler Adult Intelligence Scale-Fourth Edition*. San Antonio, TX: Pearson.

APPENDIX B

Explanation of Mediation Analyses

Simple mediation analysis partitions the *total effect* of an independent variable X on a dependent variable Y into two separate components: the direct effect and the indirect effect. The *direct effect* of X represents the effect of X on Y that is independent of the proposed mediator, M. The *indirect effect* is the effect of X on Y that is accounted for by M. These effects are estimated using the following set of regression equations:

$$Y = i_1 + cX \tag{1}$$

$$M = i_2 + aX \tag{2}$$

$$Y = i_3 + bM + c'X \tag{3}$$

where c is an estimate of the *total effect* of X on Y, a is an estimate of the *direct effect* of X on M, b is the *direct effect* of M on Y independent of X, and c' is an estimate of the *direct effect* of X on Y independent of M. The *indirect effect* of X on Y through M is quantified as the product of a and b, which represents the rate at which Y changes as a function of both X and X's effect on M. Thus the *total effect* of X on Y is the sum of the *indirect* and *direct effects*: $c = ab + c'$. Using this equation, one can also calculate the *indirect effect* as the difference between c and c' ($c–c' = ab$). For a detailed explanation of these concepts see Hayes and Preacher (2010).

In contrast to linear mediation models where the indirect effect is constant for all values of X, in nonlinear models the indirect effect changes across values of X. For nonlinear models, the rate at which a change in X changes Y indirectly through changes in M is called an *instantaneous indirect effect* (denoted by θ_x) and represents the simple slope of the quadratic function at a particular value of X. To test for significance of the instantaneous indirect effect in nonlinear models, the MEDCURVE procedure enables computation of θ_x and associated CIs for specified values of X. *Instantaneous indirect effects* are calculated the product of the partial derivative of the direct effect of X on M and the direct effect of M on Y using the following formula:

$$\theta = \left(\frac{\partial M}{\partial X}\right)\left(\frac{\partial Y}{\partial M}\right). \tag{4}$$

The mediation models examined in our study included a simple linear model as depicted in Equations 1–3 above and a nonlinear model in which the functions of Y and M with respect to X were quadratic:

$$Y = i_1 + c_1X + c_2X^2 \tag{5}$$

$$M = i_2 + a_1X + a_2X^2 \tag{6}$$

$$Y = i_3 + bM + c_1'X + c_2'X^2. \tag{7}$$

Applying these models to Equation 4 yields the following formula for the *instantaneous indirect effect,* θ_x:

$$\theta_x = (a_1 + 2a_2X)b \tag{8}$$

We used the MEDCURVE procedure for SPSS developed by Hayes & Preacher (2010) to estimate *total*, *direct*, and *indirect effects* for our hypothesized mediation models. This procedure is applicable to both linear and nonlinear models. The MEDCURVE procedure provides a test of significance for indirect effects by generating bias-corrected bootstrap confidence intervals (CIs) for the indirect effects. The bootstrapping procedure uses sampling with replacement to generate a large number of samples (with n equal to that of the original sample size) from the original data and computes CIs for the indirect effect. CIs that *do not* include zero indicate significant results. The bootstrapping method provides a more accurate test of significance of the indirect effect because it does not assume that the variables are normally distributed and it can be applied to small samples (Preacher & Hayes, 2004).

References

Hayes, A. F., & Preacher, K. J. (2010). Quantifying and testing indirect effects in simple mediation models when the constituent paths are nonlinear. *Multivariate Behavioral Research*, *45*(4), 627–660. doi:10.1080/00273171.2010.498290

Preacher, K. J., & Hayes, A. F. (2004). SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behavior Research Methods, Instruments & Computers*, *36*(4), 717–731. doi:10.3758/BF03206553