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Aerobic fitness and intraindividual reaction time variability in middle and old age

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Abstract

Objective: To examine whether aerobic fitness moderated age differences in within-person reaction time variability (WP variability) and given conceptual linkage involving the frontal cortex, whether effects were mediated by executive function.

Method: Aerobic fitness (estimated VO_{2max}) and within-person RT variability were investigated in 225 healthy, community-dwelling adults aged 50 to 90 years ($M = 63.83$) across four cognitive domains; psychomotor performance, executive function, visual search and recognition.

Results: Significant Age x Aerobic fitness interactions were found in relation to WP variability in three cognitive domains: psychomotor performance (4-choice reaction time), executive function (Flanker and Stroop arrows) and immediate recognition. Lower aerobic fitness was associated with greater RT variability, and this effect increased with age. Additionally, some of these effects were mediated by executive function.

Discussion: The findings suggest that aerobic fitness moderated the association between age and intraindividual RT variability, and that executive function selectively mediated that association. It is possible that aerobic fitness helps attenuate the neurobiological decline that contributes to cognitive deficits in old age, and that within-person variability is a measure that may be particularly sensitive to this effect.

Key terms: age, aerobic fitness, physical activity, cognitive function, reaction time, intraindividual variability

There is accumulating evidence that physical fitness benefits cognition and is protective against dementia in old age (Bielak, Cherbuin, Bunce & Anstey, 2014; Colcombe, Kramer, Erickson, et al., 2004; Flicker, Liu-Ambrose, & Kramer, 2011; van Praag, 2009; Weinstein et al., 2011). Some of the neurobiological mechanisms by which physical fitness may benefit cognition include attenuation of pre-frontal cortex volume atrophy (Colcombe et al., 2006; Weinstein et al., 2011), and increased hippocampal volume (Bugg et al., 2012; Erickson & Kramer, 2009), cerebral blood flow (Ruuskanen & Ruoppila, 1995) and mitochondrial production (Steiner, Murphy, McClellan, Carmichael, & Davis, 2011), together with enhanced efficiency of neurotransmitter synthesis (Dishman et al., 2006). Additionally, physical fitness is associated with greater cardiovascular capacity which aids the efficiency with which oxygen and nutrients are delivered to the brain (Vogiatzis et al., 2011). Increased oxygenation benefits wider cognition because glucose oxidation creates adenosine triphosphate which provides energy for neuronal activity (Huettel, Song & McCarthy, 2004). This may help buffer age-related decline of the frontal brain regions that support executive control (e.g., Kramer, Erickson, & Colcombe, 2006).

Given the foregoing evidence that aerobic/physical fitness positively impacts brain processes and cognitive function, the present paper focuses on a relatively neglected aspect of cognition in this context – within-person (WP) RT variability (also known as “intraindividual variability” and “inconsistency”). WP variability refers to the trial-to-trial variation in RTs over the course of a cognitive task that reflects variability around an individual’s average response time (MacDonald, Hultsch, & Dixon, 2003).

It is thought that WP variability reflects both neurobiological disturbance and age-related compromise to central nervous system integrity (e.g., Hendrickson, 1982, Hultsch et al., 2002, MacDonald, Nyberg, & Bäckman, 2006). The deleterious influence of age-related decline in, and neuropathology or damage to, neuronal processes and structures is evidenced

by increased WP variability in mild dementia (e.g., Bielak, Hultsch, Strauss, MacDonald, & Hunter, 2010), brain injury (e.g., Stuss, Pogue, Buckle, & Bonder, 1994) and normal aging (e.g., Hultsch, MacDonald, & Dixon, 2001). To our knowledge, there is only one study (Bunce, Warr & Cochrane, 1993) that has investigated WP variability (operationalized as intermittently slower responses) in relation to age and fitness, and this used a proxy measure of aerobic fitness (a composite measure derived from body mass, body fat, and lung function), in a working aged population (i.e., 17 to 63 years). In that study, aerobic fitness was found to be associated with fewer slower responses (i.e., lower intraindividual variability) in older adults assessed through a single psychomotor task. Our first objective in the present study, therefore, was to extend that work by examining age and WP variability across a broader range of cognitive domains including psychomotor performance, executive function, visual search and recognition using a sub-maximal measure of aerobic capacity (VO_{2max}). Additionally, we focused on an older age range (50 to 90 years) as although the bulk of the research suggests that aerobic fitness benefits cognition in old age, there is work (Bunce & Murden, 2006) suggesting that those benefits diminish with greater age. Specifically, although older, fitter individuals performed better on an episodic memory task, in absolute terms, those benefits diminished between the ages of 60 and 75 years. Here, we seek to examine this possibility further in the expectation that aerobic fitness would moderate age differences in WP variability but that benefits would diminish with increasing age.

Additionally, as aging is associated with neurobiological decline, particularly in the frontal regions (R. L. West, 1996), and there is evidence suggesting that the benefits of aerobic fitness on cognition in old age are manifest in mental performance supported by those regions (Colcombe & Kramer, 2003; Kramer et al., 2006), our second objective was to investigate whether any Age x Fitness interactions in relation to cognition were mediated by executive control (i.e., supported by the frontal cortex). As WP variability may capture

attentional lapses (Bunce et al., 1993) and, relatedly, fluctuations in executive control (Bunce et al., 2004; R. West et al., 2002), we selected our executive control measures so as to emphasize inhibition. Our rationale here was that this cognitive mechanism may be particularly sensitive to the moment-to-moment variations in mental activity captured by WP variability.

Method

Participants

Two hundred and fifty seven (154 women) community-dwelling persons aged 50 to 90 years were recruited from local health clubs, sport clubs, community groups and the general local community through printed advertisements. Motivated by another study in this sample that investigated age, mental health and cognition (Bauermeister & Bunce, 2014), participants above the “caseness” score of 3 on the General Health Questionnaire-12 (Goldberg, 1978) were excluded from the present sample ($n = 32$) as this may indicate clinical levels of anxiety, depression and social dysphoria. In consequence, 225 (134 women) persons ($M = 63.83$, $SD = 7.51$) participated in the present study. All participants scored > 25 on the Mini-Mental State Examination (MMSE: Folstein, Folstein, & McHugh, 1975) and none had experienced a major neurological disorder as determined by a brief self-report biographical questionnaire. Full scale IQ was estimated using the National Adult Reading Test (NART: Nelson, 1982). The study received ethical approval from the appropriate local Research Ethics Committee.

Aerobic fitness

The Rockport Fitness Walking Test (Kline, Porcari, Hintermeister, Freedson, & Rippe, 1987), a sub-maximal measure of aerobic fitness, provided an estimate of VO_{2max} . Resting pulse was recorded before a 1-mile (1,609 m) walk on a motorized treadmill commenced. Participants were required to walk as fast as possible (walking defined as having foot contact with the treadmill at all times). The treadmill walk was timed and the participant's pulse rate measured again on completion of the 1-mile walk. The estimate of VO_{2max} was computed according to the formula: $132.853 - (0.0769 \times \text{weight}) - (0.3877 \times \text{Age}) + (6.315 \times \text{gender}) - (3.2649 \times \text{time}) - (0.1565 \times \text{heart rate})$ where weight is in pounds (lbs), gender coded as male = 1 and female = 0, time expressed in 1/100 minutes, heart rate in beats/minute, and age in years (Kline et al., 1987). Higher scores derived from this measure indicate higher aerobic fitness ($\text{ml.kg}^{-1}.\text{min}^{-1}$). The mean VO_{2max} value obtained was 25.46 (SD = 15.73). In the present sample, a oneway ANOVA suggested VO_{2max} to decline with age ($F(3,221) = 18.62, p < .01$) and this is confirmed by inspection of means scores for each age decade: Age 50-59 = 34.30 (SD = 8.59); 60-69 = 25.71 (SD = 13.59); 70-79 = 14.59 (SD = 20.11); and 80-90 = 9.86 (SD = 7.01). These values are comparable to normative VO_{2max} values for those age bands reported elsewhere (e.g., Heywood, 2006, MacKenzie, 2001).

Cognitive Tasks

RTs were collected from a battery of cognitive tasks using E-Prime (Psychology Software Tools, 2002). Trials were presented pseudorandomly and practice trials were administered for each task.

Psychomotor Tasks: Three versions of a 48-trial psychomotor task were presented. In the Simple RT task (SRT), participants pressed the space bar when an 'X' appeared in the center of the computer screen (inter-trial intervals varied randomly between 300 and 1,000

ms). In the Two-Choice RT task (2-CRT), participants responded to a single black 25 mm diameter circle presented to the right or left of the screen by pressing one of two keys (left and right) corresponding with the position of the circle (inter-trial interval = 500 ms). In the Four-Choice version of the task (4-CRT), a black circle appeared in any of the four corners of the screen and participants responded by pressing one of four keyboard keys (upper right and left, lower right and left) corresponding to the position of the circle (inter-trial interval = 500 ms).

Executive function: Three tasks emphasizing inhibitory executive control were presented. In a 64-trial version of the Eriksen Flanker task (Eriksen & Schultz, 1979), participants responded to the horizontal direction of a central target arrow while ignoring distractor flanker arrows (2 either side of the target arrow) using designated keyboard keys indicating direction (left and right). The trials were divided equally into congruent (all arrows in same direction) and incongruent (middle arrow opposed direction of flanker arrows) trials. Inter-trial intervals were between 300 and 1,000 ms. A 100-trial spatial Stroop arrow task (Salthouse, Toth, Hancock, & Woodward, 1997) followed where participants responded to the direction of an arrow presented to the left, right or centre of the screen. 40 trials were spatially congruent (arrow pointed in the same direction as its spatial position on the screen), 40 trials were incongruent (arrow pointed in the opposite direction to its spatial position) and 20 trials were neutral (arrow appeared centrally, pointing left or right). An assigned left and right key was used to respond (inter-trial interval = 500 ms). In a 96-trial Stroop word task, participants responded to the presented word ink color (red, blue, yellow and green) and ignored the written word (red, blue, yellow and green) using appropriately colored keys. The trials were equally divided into congruent (word-color match) and incongruent (word-color

not matched) trials. The inter-trial interval was 500ms. For all executive function tasks, data from incongruent trials were used in statistical analyses.

Visual search: A 64-trial simple visual search task with a 6 x 6 array of green letter 'O's was presented. For half of the trials, a green target letter 'Q' was embedded randomly within the array. Designated keyboard keys were pressed to indicate the presence or absence of the Q (inter-trial interval = 500 ms). A complex version of the task then followed. The same block was presented whereby stimuli consisted of both green and red letter 'O's and 'Q's (inter-trial interval = 500 ms). Targets were determined by the conjunction of letter type and color with responses indicating whether the conjunction was present (e.g., green 'Q' in an array of red 'Q's, and red and green 'O's), or absent. Correct responses from target and non-target trials were combined in statistical analyses for both versions of the task.

Recognition: In immediate recognition, 16 target concrete nouns were randomly presented for 2 s (inter-word interval = 500ms). After the completion of a brief distractor task, the 16 target nouns were presented with 16 randomly intermixed distractor nouns. Participants pressed "yes" for a target or "no" for a distractor using designated keyboard keys. Approximately 30 minutes later, having completed several other cognitive tasks, a delayed test of recognition was administered. RTs for correct hits and rejections were combined for statistical analyses for both versions of the task.

Procedure

Participants completed informed consent and a biographical questionnaire. They then underwent MMSE and NART assessments before questionnaire measures for elements of the

study not reported here, were administered. Then participants completed the cognitive tasks and the treadmill walk. The testing session lasted between one and a half to two hours.

Data processing and statistical analysis

For the RT tasks, extremely fast or slow trials were eliminated using a lower boundary of 150ms and an upper boundary of the individual mean RT + 3 SD. Missing data were replaced with the individual's mean RT for that task. Using correct trials only, we computed the intraindividual standard deviation (ISD). Here, we adjusted for age and trial-to-trial variance (using trial number) which may reflect practice or fatigue effects (and their higher-order interaction) using a regression procedure (Hultsch, MacDonald, & Dixon, 2002) that produced residuals statistically independent of differences resulting from age or trial number. The residual scores were converted to t scores ($M = 50$, $SD = 10$) to enable comparisons across the different cognitive tasks. At the sample level, a small amount of missing data ($\leq 1.6\%$) was replaced using the EM algorithm in SPSS version 18 (PASW Statistics for Windows, 2009) taking into account all variables in the study (Shafer & Graham, 2002). To test moderation effects, the age and VO_{2max} variables were centred and the Age x VO_{2max} cross-product interaction term computed.

Results

Bivariate correlations, together with means and standard deviations for the key variables, are presented in Table 1. Consideration of that table indicates that correlations between VO_{2max} , and both age and gender were negative and significant, suggesting older age and being female were associated with lower VO_{2max} . For VO_{2max} and the cognitive variables, all correlations were negative and significant with the exception of visual search measures

which were nonsignificant (although the complex version of the task approached conventional levels of significance; $p = .08$). These correlations suggest higher aerobic fitness was associated with lower WP variability.

A series of hierarchical multiple regression models were used to explore the relationship between age, aerobic fitness and the cognitive variables. As NART scores were significantly associated with several of the cognitive variables, we adjusted for this measure at Step 1 of all of the regression models. At Step 2, the primary effects for chronological age and VO_{2max} were entered, and at Step 3, the Age x VO_{2max} cross-product interaction term was entered. Importantly, if Step 3 added significantly to the variance ($R^2\Delta$) explained in the cognitive variable after taking the primary effects of age and VO_{2max} into account, it would suggest that the strength of the association between age and cognitive performance varied according to VO_{2max} .

The results of the hierarchical regression models are presented in Table 2. Although the primary effects of age and VO_{2max} significantly predicted WP variability for the majority of variables with shared variances ranging between 5% and 22%, consideration of the beta weights suggests this was mainly due to age. However, the important question was whether the influence of fitness varied according to age, tested by entry of the Age x VO_{2max} cross-product interaction term at Step 3. As can be seen in Table 2, for half of the measures (4-CRT, Flanker, Stroop arrows and word tasks, and immediate recognition), entry of this term significantly added to the variance explained in WP variability. For example, for the Stroop word task, $\Delta R^2 = .08$ ($p < .01$). The pattern for this and the other significant interactions is presented in Figure 1. It can be seen that WP variability increased with age, but that the potential influence of VO_{2max} also increased with age. This suggests that increased VO_{2max} is

associated with decreased WP variability and this association becomes more marked in older age.

A further aim of this study was to assess if executive function mediated the significant Age x VO_{2max} interactions obtained for the non-executive control tasks (4-CRT and immediate recognition) in the initial series of models (i.e., mediated-moderation: Baron & Kenny, 1986). Therefore, a composite measure of variability in executive function that combined the Flanker, Stroop arrow and Stroop word tasks was computed using principal component analysis where a single factor was requested and the factor scores saved. The correlations of this measure with age and all of the cognitive variables were positive and significant (all $ps < .01$). The regressions for 4-CRT and immediate recognition were then repeated but having adjusted for this composite measure at Step 1 of the models. Attenuation of the shared variance associated with the significant Age x VO_{2max} interaction terms would suggest that executive function mediated that effect. The outcome of this procedure was that the previously significant Age x VO_{2max} interaction term for immediate recognition became non-significant suggesting that executive function was the mechanism mediating the influence of VO_{2max} on age differences in WP person variability for this variable. The previously significant Age x VO_{2max} interaction for 4-CRT remained significant but was substantially attenuated, $\Delta R^2 = .02$ ($p < .05$).

Finally, the regression analyses were repeated excluding one participant with a MMSE score of 26 as this may be indicative of possible dementia. The majority of results were as in the original analyses, the one exception being the Stroop arrows interaction which became non-significant.

Discussion

This study had several aims. The first was to investigate if aerobic fitness moderated age differences across several cognitive domains. Additionally, following the rationale that WP variability reflects fluctuations in executive control and that this cognitive mechanism has been shown to benefit from aerobic fitness (Colcombe & Kramer, 2003), we investigated whether variability in executive function mediated significant Age x VO_{2max} interactions where they were found. Finally, we extended earlier work (Bunce & Murden, 2006) that showed in absolute terms, that although aerobic fitness continued to benefit cognition in older persons, with increasing age, those benefits diminished. The findings revealed significant Age x VO_{2max} interactions in respect to five cognitive variables, 4-CRT, Flanker, Stroop arrows and word tasks, and immediate recognition. These interactions indicated that lower aerobic fitness was associated with greater WP variability and that this trend became greater with increasing age. Additionally, we found that those effects were mediated by executive control in relation to immediate recognition, and partially mediated for 4-CRT. Finally, unlike the earlier Bunce and Murden (2006) study, we found no evidence that the benefits of fitness on cognition diminished with increasing age.

The findings of the study confirm earlier work (Bunce et al., 1993) that fitness moderates age gradients in WP variability and more broadly benefits cognitive performance in old age (e.g., Bielak et al., 2014; Bunce & Murden, 2006; Colcombe & Kramer, 2003; Colcombe, Kramer, Erickson, et al., 2004). Given the putative benefits of aerobic fitness to frontal lobe structures (Colcombe et al., 2004; Colcombe et al., 2006), and that WP variability is thought to be supported by those structures and reflect fluctuations in attentional and executive control (Bunce et al., 1993, 2004; West et al., 2002), we expected the measure to be particularly sensitive to the effects of aerobic fitness. This expectation was confirmed by the above results. Regarding the neurobiological mechanisms that may account for this finding, higher aerobic fitness is associated with greater cardiovascular capacity which assists

efficient oxygen and nutrient transportation to the brain through increased cerebral blood flow (Vogiatzis et al., 2011). Evidence suggests that the resultant increased oxygenation benefits wider cognition, and in particular the frontal brain regions supporting executive control (e.g., Kramer et al., 2006). Our findings are consistent with this view and suggest that measures of WP variability are sensitive to this effect.

Following the guidelines of Baron and Kenny (1986), we also found that executive control selectively mediated those effects. That is, for immediate recognition but not for the 4-choice psychomotor task, the significant Age x VO_{2max} interaction in the initial model was rendered nonsignificant in the second model having adjusted for the executive control measure. There are two possible explanations for this selective effect. First, immediate recognition relative to psychomotor performance is likely to place greater demands on executive processes. It is possible that the shared variance between these processes and those captured by WP variability may explain the attenuated effects. However, it should also be noted that the effect size for 4-CRT was greater than for immediate recognition, and there was evidence that R^2 was reduced. Clearly though, the mediating influence of our executive control measures were insufficient to fully account for that larger effect on this variable suggests the possibility that there are two pathways of influence on WP variability, direct and indirect.

Contrary to the findings of an earlier study (Bunce & Murden, 2006), we found no evidence that in absolute terms, the benefits of aerobic fitness to cognition diminished with increasing age. Indeed, fitness-related benefits were shown to be maintained as age increased across several measures in our cognitive battery. There are several reasons that may explain this disparity in findings relative to the earlier study that included a single cognitive measure (free recall), narrower age range (60 to 75 years) and a small subsample ($n = 39$) being used in that particular analysis. Here, the age range (50 to 90 years) and sample size ($N = 225$)

were greater, and a much wider battery of measures were used covering several cognitive domains. These features, together with the greater statistical power, are likely to explain the differences between the respective studies.

Given the above, there are also several limitations associated with the present study that we should acknowledge. First, due to the practical constraints of the investigation, the measure of aerobic fitness that we used provided estimates of VO_{2max} obtained from submaximal assessments. Although the Rockport Fitness Walking Test (Kline et al., 1987) gives reliable estimates of maximal oxygen uptake, albeit unlikely, it is possible that different results would have been obtained had VO_{2max} been directly assessed. Additionally, although participants reported being healthy and were all active community-living individuals, they were not formally assessed for age-related neuropathology or dementia. However, all participants scored > 25 on the MMSE and although this measure does not categorically rule out neuropathology, those scores reduce the likelihood that our respondents were in the preclinical phase of dementia. Finally, the study was cross-sectional, and therefore causality between the key variables cannot be inferred.

To conclude, in a sample of 225 community-dwelling, healthy older adults aged 50 to 90 years, we found evidence that aerobic fitness moderated the association between age and WP variability across several cognitive domains. Additionally, we found that executive function selectively mediated those effects. The findings underline the benefits of regular aerobic exercise to cognition in old age, and suggest that public health campaigns to promote physical activity may be particularly beneficial in older populations.

5370 words

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Table 1. Bivariate Correlations Between Aerobic Fitness (VO_{2max}) and WP Variability in Cognitive Variables

	<i>M (SD)</i>	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1 Age	63.83 (7.51)	-														
2 Gender	<i>n</i> = 225 (134 women)	-.202**	-													
3 MMSE	29.23 (.84)	-.150*	.045	-												
4 NART	120.13 (7.37)	-.046	-.112	.146*	-											
5 VO _{2max}	25.46 (15.73)	-.523**	-.182**	.217**	.055	-										
6 SRT	6.76 (3.18)	.316**	.012	-.132*	-.118	-.301**	-									
7 2-CRT	6.63 (2.92)	.307**	-.082	-.113	.000	-.315**	.321**	-								
8 4-CRT	6.95 (2.77)	.305**	-.136*	-.128	-.122	-.238**	.238**	.381**	-							
9 Flanker Arrows	6.25 (6.15)	.351**	.049	-.155*	-.173**	-.355**	.297**	.336**	.449**	-						
10 Stroop Arrow	8.01 (3.14)	.265**	.057	-.207**	-.239**	-.277**	.316**	.323**	.404**	.325**	-					
11 Stroop Word	8.27 (4.61)	.407**	-.071	-.285**	-.066	-.424**	.301**	.306**	.348**	.410**	.346**	-				
12 Visual Search S	6.56 (3.53)	.293**	-.195**	-.103	-.137*	-.150*	.143*	.162*	.281**	.135*	.312**	.324**	-			
13 Visual Search C	7.16 (3.34)	.127	-.059	-.019	-.067	-.116	.040	.014	.112	.052	.232**	.288**	.447**	-		
14 Recognition Imm	8.27 (4.84)	.171*	-.007	-.128	.000	-.220**	.157*	.249**	.163*	.280**	.167*	.200**	.144*	.165*	-	
15 Recognition Del	8.01 (4.64)	.181**	.030	-.008	.038	-.208**	.034	.217**	.168*	.165*	.103	.215**	.091	.134*	.303**	-

Notes: WP variability measured as intraindividual standard deviation (ISD), presented as t-scores; MMSE = Mini Mental State Examination;

NART = National Adult Reading Test; VO_{2max} = aerobic fitness; SRT, 2-CRT, 4-CRT = simple, two-choice and four-choice reaction time respectively; Visual Search S and C = simple and complex visual search, respectively; Recognition Imm and Del = Immediate and delayed recognition, respectively.

**p* < .05; ** *p* < .01

Table 2. Hierarchical Regression Analysis: WP variability in cognitive variables Regressed on Age, Aerobic Fitness (VO_{2max}) and the Age x Aerobic Fitness Cross-Product Interaction Term

	SRT		2-CRT		4-CRT		Flanker Arrows		Stroop Arrow		Stroop Word		Visual Search (Simple)		Visual Search (Complex)		Recognition (Immediate)		Recognition (Delayed)	
Step 1:	β	ΔR^2	β	ΔR^2	β	ΔR^2	β	ΔR^2	β	ΔR^2	β	ΔR^2	β	ΔR^2	β	ΔR^2	β	ΔR^2	β	ΔR^2
NART	-.11	.01	.01	.00	-.08	.02	-.15*	.03**	-.23**	.06**	-.03	.00	-.12	.02*	-.05	.00	.01	.00	.04	.00
Step 2:																				
Age	.24**		.22**		.28**		.25**		.16*		.30**		.29**		.10		.11		.11	
VO_{2max}	-.13	.12**	-.16*	.13**	.09	.10**	-.09	.16**	-.13	.10**	-.09	.22**	.04	.08**	-.01	.02	-.08	.05**	-.14	.06**
Step 3:																				
Age x VO_2	-.10	.01	-.10	.01	-.33**	.08**	-.27**	.06**	-.17*	.02*	-.34**	.08**	-.10	.01	-.13	.01	-.17*	.02*	-.05	.00

Notes: NART = National Adult Reading Test; VO_{2max} = aerobic capacity; SRT = simple reaction time; 2-CRT or 4-CRT = two or four-choice reaction time;

Step 1, df = 1,223; Step 2, df = 2,221; Step 3, df = 1,220.

*p <.05; ** p<.01

