Long-term high-effort endurance exercise in older adults: diminishing returns for cognitive and brain aging

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**Long-Term High-Effort Endurance Exercise in Older Adults: Diminishing Returns
for Cognitive and Brain Aging**

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1 **Abstract**

2 While there is evidence that age-related changes in cognitive performance and brain
3 structure can be offset by increased exercise, little is known about the impact on these of
4 long-term high-effort endurance exercise. In a cross-sectional design with 12-month
5 follow-up, we recruited older adults engaging in high-effort endurance exercise over at
6 least twenty years, and compared their cognitive performance and brain structure with a
7 non-sedentary control group similar in age, sex, education, IQ, and lifestyle factors. Our
8 findings showed no differences on measures of speed of processing, executive function,
9 incidental memory, episodic memory, working memory, or visual search for older adults
10 participating in long-term high-effort endurance exercise, when compared without
11 confounds to non-sedentary peers. On tasks that engaged significant attentional control,
12 subtle differences emerged. On indices of brain structure, long-term exercisers displayed
13 higher white matter axial diffusivity than their age-matched peers, but this did not
14 correlate with indices of cognitive performance.

15 Key terms: Exercise; Aging; Cognition; MRI; Effort

16

1. Introduction

As we age, our cognitive abilities change and older adults have more difficulty than younger adults with tasks that are more complex, effortful, and strategic (for reviews see Luo & Craik, 2008; Salthouse, 2010). Contributing factors likely include slower processing speed (Salthouse, 1996, 2000), reduced attentional processing resources (Craik, 2006; McAvinue et al., 2012), loss of inhibitory functions (Darowski, Helder, Zacks, Hasher, & Hambrick, 2008; Peltsch, Hemraj, Garcia, & Munoz, 2011; Zanto, Rubens, Thangavel, & Gazzaley, 2011), and decline in controlled processing (Coubard et al., 2011).

These changes in cognitive ability accompany well-documented structural changes in the aging brain, specifically, cortical thinning and regional volumetric loss (for a review see Hedden & Gabrieli, 2004), and poorer white matter integrity (for a review see Madden et al., 2012). Volumetric changes in older adults can be detected over as little as 4 months in the hippocampus (Lövdén et al., 2012) and over just 6 months in many other brain regions (Raz et al. 2013), though there are substantive individual differences in trajectory of these age-related structural changes (Bennett, Madden, Vaidya, Howard, & Howard, 2010; Burzynska et al., 2010; Raz et al., 2013; Raz, Ghisletta, Rodrigue, Kennedy, & Lindenberger, 2010; Zhang et al., 2010).

Many factors influence the rate of cognitive and structural brain changes in older adulthood (Richards, Hardy, & Wadsworth, 2003; Salthouse, 2012; Scherder et al., 2013; Sturman et al., 2013; Thomas & O'Brien, 2008), and a particular target of research interest is the effect of exercise.

Notwithstanding the small effect sizes, the protective effects of exercise against age-related cognitive changes have been evidenced in retrospective (Middleton, Barnes, Lui, & Yaffe, 2010), cross-sectional (Benedict et al., 2012; Eskes et al., 2010; Nemati Karimooy, Hosseini, Nemati, & Esmaily, 2011), medium-term (Weuve et al., 2004) and longer-term studies (Barnes, Yaffe, Satariano, & Tager, 2003; Middleton, Mitnitski, Fallah, Kirkland, & Rockwood, 2008). In normal healthy older populations, moderate aerobic exercise programs leading to small improvements in cognitive ability, particularly executive function, have been reported in systematic reviews of interventions from 2 months to 6 years (Angevaren, Aufdemkampe, Verhaar, Aleman, & Vanhees, 2008; Chang, Labban, Gapin, & Etnier, 2012; Colcombe & Kramer, 2003; Etnier et al., 1997; Hindin & Zelinski, 2012; P. J. Smith et al., 2010). However a recent meta-analysis (Young, Angevaren, Rusted, & Tabet, 2015) that scrutinized and screened the data more closely reported little evidence for significant effects of exercise on cognition in older healthy adults.

Exercise also impacts age-related changes in brain structures (for reviews see Bherer, Erickson, & Liu-Ambrose, 2013; Hayes, Hayes, Cadden, & Verfaellie, 2013), with benefits from exercise reported on grey and white matter volume (Colcombe et al., 2003, 2006) and hippocampal volume (Erickson et al., 2009, 2011). The latter reporting that in groups of older adults, higher levels of aerobic fitness correlated both with higher hippocampal volumes and enhanced spatial memory function.

A limited amount of recent research has explored the sustained impact of long-standing exercise regimes, in older athletes. Winker et al. (2010) compared elderly marathon runners and bicyclists against a sedentary control group similar in age, sex, and

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education. From a large battery of cognitive tasks, athletes performed better only in a non-verbal fluency task. Similarly, comparing cognitive performance in a small group of twelve older runners with sedentary older adults similar in age, sex, and education, Tseng, Uh, et al. (2013) reported advantages for their runners only on tasks of category and letter fluency. Structural brain differences were evidenced. Compared to sedentary control volunteers, the older athletes had some regional volumetric advantages in grey and white matter concentrations (Tseng, Gundapuneedi, et al., 2013). They suggested that long-term exercise may preserve white matter integrity from age-related changes.

An issue with many of the aforementioned behavioral and MRI cross-sectional studies is that they compared groups that were not expressly similar on measures of lifestyle, (cognitive activities and social interaction) or diet, which complicates interpretation of the data. In addition, most of the studies either were interventions with sedentary volunteers or used sedentary volunteers as the control group. Comparing groups similar in all key lifestyle measures is necessary to provide an accurate picture of the particular value of long-term exercise. Comparing long-term exercise against non-sedentary control groups is necessary to establish the impact of exercise against a normative “healthy” lifestyle.

Both of these criteria were met in the current study, which compared two older adult populations that were different only in their exercise profiles. The first group, super veteran athletes (“supervets”), comprised individuals whose age qualified them for super veteran categorization by UK Athletics, and who had engaged in long-term (minimum 20 years) high-effort endurance exercise. The second group, non-sedentary control volunteers, was active but not exercising beyond regular levels. The two groups were

1 similar in age, sex, education level, intelligence, depression scores, social network,
2 cognitive activities, adherence to Mediterranean diet, and potential for physical fitness.
3 More importantly, we collected longitudinal measures of cognitive performance and brain
4 structural changes over a 12-month period, so that in our study we can establish not only
5 cross-sectional differences between the groups but also whether age-related changes over
6 12 months differentiate them further.

7 We included a comprehensive battery of cognitive tasks, which have robustly been
8 reported to change with aging and/or correlated with physical fitness or exercise levels.
9 We included speed of processing tasks to explore whether exercise alleviated age-related
10 slower processing speed (Salthouse, 1996, 2000). We included executive function
11 measures since systematic reviews of previous exercise interventions observed
12 differences in executive function (Angevaren et al., 2008; Chang et al., 2012; Colcombe
13 & Kramer, 2003; Etnier et al., 1997; Hindin & Zelinski, 2012; P. J. Smith et al., 2010).

14 We included a prospective memory tasks because the effect of exercise on
15 prospective memory has not been reported yet to our knowledge. Focal and non-focal
16 prospective memory theoretically utilize different cognitive processes for optimal
17 performance (McDaniel & Einstein, 2000); both were included as exercise may affect
18 these processes differently. In attentional control tasks, such as the Stroop task, which
19 involves suppressing attention and switching attention, older adults have been shown to
20 perform worse than younger adults (Coubard et al., 2011), yet also show exercise-related
21 improvement (Winker et al. 2010; Prakash et al., 2011). However, two meta-analyses of
22 exercise intervention RCTs that included standard Stroop tasks as a measure, observed no
23 differences in this task from the exercise interventions (P. J. Smith et al., 2010; Young et

1 al., 2015), and in a recent exercise RCT, only in most difficult modified Stroop condition
 2 did the exercise improve performance (Predovan, Fraser, Renaud, & Bherer, 2012).
 3 Therefore in our study, we included a more difficult Stroop task that included a switching
 4 component (Hutchison, Balota, & Ducheck, 2010), and a sustained attention task to test
 5 control over time.

6 Structurally, well-documented changes occur in the aging brain: cortical thinning
 7 and regional volumetric loss are observed (for reviews see Hedden & Gabrieli, 2004;
 8 Raz, 2000), and white matter integrity deteriorates (for reviews see Gunning-Dixon,
 9 Brickman, Cheng, & Alexopoulos, 2009; Madden et al., 2012; Madden, Bennett, & Song,
 10 2009).

11 Specifically for white matter integrity, it has been observed that mean diffusivity
 12 of water molecules within the white matter (MD) increases with age, while the fractional
 13 anisotropy of that diffusion (FA) decreases. Decline in FA is greater in anterior regions
 14 of the brain than in posterior regions (Madden et al., 2012). More recent studies have
 15 started looking more at the specific diffusivity measures, axial diffusivity (λ_1) and radial
 16 diffusivity (RD). Axial diffusivity has been related to the myelin content of white matter
 17 tissue, while RD has been related to amount of demyelination and is proposed to be a
 18 marker of overall tissue integrity (Klawiter et al., 2011).

19 Volumetrically, in a typical study, Resnick, Pham, Kraut, Zonderman, &
 20 Davatzikos (2003) looking longitudinally at healthy older adults 59-85 observed
 21 significant decline in both grey and white matter volume from their first follow-up of 2
 22 years even in a very healthy subgroup that did not develop any medical conditions or
 23 cognitive impairments during the 4-year period of evaluation. Declines in brain volume

1 can be detected in as little as a year (Erickson et al., 2011; Fjell et al., 2009). In
2 longitudinal studies, volumetric changes can be detected over as little as 4 months in both
3 healthy younger (20-30) and older adults (60-70) in the hippocampus (Lövdén et al.,
4 2012). Raz et al. (2013) in a longitudinal study of healthy younger (20-31) and older
5 adults (65-80) over just 6 months, observed significant decline in volume of lateral
6 prefrontal cortex, hippocampus, caudate nucleus, and cerebellum.

7 Individual differences in trajectory of these brain volume changes vary
8 significantly though, as seen in both Raz et al. (2010) and Raz et al. (2013). Also many
9 factors are likely to influence the rate of structural brain changes in older adulthood
10 (Bickart, Wright, Dautoff, Dickerson, & Barrett, 2011; Kanai, Bahrami, Roylance, &
11 Rees, 2012; Schinka et al., 2010). One such factor is exercise.

12 Exercise may induce positive change in the aging brain or at least decrease the
13 trajectory of decline in key areas (for reviews see Bherer, Erickson, & Liu-Ambrose,
14 2013; Hayes, Hayes, Cadden, & Verfaellie, 2013). To highlight, Erickson et al. (2011)
15 reported an RCT with older adults 55-80 years, observing that a 1-year aerobic exercise
16 intervention increased hippocampal volume, while in their stretching control group
17 hippocampal volume decreased. Greater increases in fitness were correlated with greater
18 increases in hippocampal volume, and there was a positive relationship between higher
19 aerobic fitness levels and spatial memory and between increased hippocampal volume
20 and improved spatial memory. Interestingly, while hippocampal volume declined in the
21 stretching group, higher fitness before the intervention was protective against volume loss
22 and partially attenuated the decline in volume.

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Recent research has explored longer-term benefits of exercise in older athletes. Tseng, Uh, et al. (2013) reported a cross-sectional study that compared a small group of twelve older runners with sedentary older adults also similar in age, sex, and education. VBM measures of brain volume indicated that their older athletes had more grey matter concentrations in right parietal lobe, cuneus, and the culmen of the cerebellum and more white matter concentrations in precuneus, subgyral occipital lobe, and inferior temporal subgyral temporal lobe. Their runners also did better than sedentary older adults in executive function tasks of category fluency and letter fluency. In a similar cohort comparing ten older runners with twelve sedentary older adults, Tseng, Gundapuneedi, et al. (2013) reported their runners had better white matter integrity, as indexed by TBSS (Tract-based spatial statistics, S. M. Smith et al. 2006). In fractional anisotropy (FA) and mean diffusivity (MD) measures, they observed differences in brain regions associated with motor function; front-and-back connections related to visuospatial function, motor control and coordination; and regions associated with memory function. They also observed that runners had lower deep white matter hyperintensity volume. From this evidence, the authors suggested that long-term exercise may preserve white matter integrity from age-related changes. While participants in these older athlete studies were similar in age, sex, and education level, their cross-sectional design precluded unequivocal attribution of the observed differences to the volunteers' exercise regimen.

The current study set out to explore both brain and behavioral changes associated with long-term high-effort endurance exercise. We anticipated that our supervet group when compared to a non-sedentary socially active control group would show benefits both to cognition and brain structure as a result of their long-term exercise regime. We

1 hypothesized that long-term high-effort endurance exercise would protect against
2 the age-related decline in executive function, attention, and memory, including
3 prospective memory. We predicted the attenuation of age-related decline in
4 attentional capabilities (Prakash et al., 2011; Winker et al., 2010), and that this
5 would be particularly pronounced in the more difficult Stroop-switch task
6 (Predovan et al., 2012). We predicted that exercise would confer slower decline in
7 tasks requiring greater resource, specifically exposing exercise-related benefits to
8 the resource-needy non-focal PM conditions (McDaniel, Shelton, Breneiser, Moynan,
9 & Balota, 2011). We anticipated exercise-related benefits on measures of episodic
10 memory, incidental memory and working memory, in line with previous literature
11 (Erickson et al., 2009). We also hypothesized that long-term high-effort endurance
12 exercise would protect against the age-related decline in brain structure. We
13 predicted that supervets would show greater brain volume than controls (Bherer et
14 al., 2013; Colcombe et al., 2003, 2006; Hayes et al., 2013; C Niemann, Godde,
15 Staudinger, & Voelcker-Rehage, 2014; Ruscheweyh et al., 2011), especially in the
16 hippocampus (Erickson et al., 2009, 2011; Lövdén et al., 2012; Claudia Niemann,
17 Godde, & Voelcker-Rehage, 2014; Raz et al., 2010; Uylings & de Brabander, 2002).
18 We also predicted that supervets would have better white matter integrity than
19 controls, since poorer integrity is observed in older adults and is recognized as an
20 index of neural efficiency (eg. Burzynska et al., 2010). In normal aging declines in
21 brain structure can be detected in as little as 12 months (Erickson et al., 2011; Fjell
22 et al., 2009), so the study incorporated a 12-month longitudinal retest of both

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- 1 performance and brain structure to test for observable differences slope of change
- 2 between the non-sedentary and supervet groups.
- 3

2. Materials and Methods

Ethics Statement

Ethical approval was obtained from the University of Sussex Life Sciences & Psychology Cluster based Research Ethics Committee and the Brighton and Sussex Medical School Research Governance & Ethics Committee. Written consent was obtained from all participants.

2.1 Participants

Participants were non-smokers (never smoked or not smoked in the past 5 years), aged 60-85, on stable or no medication during the past 12 months, with English proficiency equivalent to that of a native speaker, and with no evidence of memory problems (MMSE > 27; Folstein, Folstein, & McHugh, 1975).

Exclusion criteria: history of stroke, myocardial infarction, recently diagnosed diabetes, high blood pressure (systolic above 200 and diastolic above 100), psychiatric or neurological disorders (self-reported), or clinical depression (Geriatric Depression Scale (GDS); Sheikh & Yesavage, 1986).

For our supervet group we required high-effort endurance exercise via running, swimming, and/or cycling (self-paced sports) for 20 or more years. We chose only self-paced sports because athletes of interceptive-dominant sports have been shown to have faster reaction times (Voss, Kramer, Basak, Prakash, & Roberts, 2010) which may affect cognitive performance. The Physical Activity Scale for the Elderly (PASE; Washburn, Smith, Jette, & Janney, 1993) was used to assess physical activity levels in both groups. Supervets were assured to be supervets through recruitment screening (participating

presently in routine high-effort endurance exercise and for at least the past 20 years) but also in the analysis of the PASE which showed a differentiation between our groups on this scale.

We recruited 27 supervets (6 female) and 23 control volunteers (9 female). At 1-year follow-up 23 supervets (6 female) and 19 controls (7 female) returned. From the sample recruited for behavioural testing, 15 supervets (4 female) and 14 controls (5 female) attended at baseline a session for acquisition of structural brain images, and 15 supervets (4 female) and 12 controls (4 females) returned at 1-year follow-up.

2.2 Demographic measures

The following measures were collected:

IQ: Full-scale pre-morbid IQ (National Adult Reading Test; Nelson, 1982).

Physical Activity: Physical Activity Scale for the Elderly (PASE; Washburn, Smith, Jette, & Janney, 1993), for measuring physical activity/exercise.

Diet: EPIC-Norfolk Food Frequency Questionnaire (FFQ; Bingham et al., 2001), from which we derived an adherence to Mediterranean diet score (Trichopoulou, Costacou, Bamia, & Trichopoulos, 2003).

Social Network: Lubben Social Network Scale (LSNS-6; Lubben et al., 2006).

Frequency of Cognitive Activities: Florida Cognitive Activities Scale (FCAS; Schinka et al., 2005).

Physiological Indices

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Lung function measures taken using a spirometer (Microplus, Micro Medical Limited, Kent, UK) included: Forced Expiratory Volume 1st Second (FEV1), Forced Vital Capacity (FVC), Forced Expiratory Ratio (FER), and Peak Expiratory Flow (PEF).

Bioelectrical impedance assay (Bodystat Quadscan 4000 or Bodystat 1500; Douglas, Isle of Man, UK) provided percent body fat. Hand-grip strength was acquired using a hand dynamometer (Grip-D, Takei Scientific Instruments, Japan).

2.3 Cognitive Tasks

Simple Reaction Time (SRT)

The Digit Symbol Substitution Task (DSST, Wechsler, 1981)

Trail Making Test A and B (Reitan, 1958)

Controlled Oral Word Association Test (COWAT, Spreen & Strauss, 1991)

20-Word Item Episodic Memory Task (Rusted & Warburton, 1989)

Backward Digit Span (Wechsler, 1981)

Prospective and Retrospective Memory Questionnaire (PRMQ; Crawford et al, 2003)

Prospective Memory Card Sort Task (Rusted, Sawyer, Jones, Trawley, & Marchant, 2009)

Focal and Non-Focal Prospective Memory Task (McDaniel et al., 2011)

Map Test of Everyday Attention (Robertson, Ward, Ridgeway, & Nimmo-Smith, 1996)

Rapid Visual Information Processing (RVIP; Wesnes & Warburton, 1983)

Stroop-Switch Task (Hutchison et al., 2010)

Speed of Processing & Executive Function

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1 Simple Reaction Time (SRT) was used for assessing simple reaction time and
2 calculating intra-individual RT variability (Bunce et al., 2007). Here participants
3 made a button press as soon as they could while maintaining accuracy when they
4 saw a fixation cross turn into an “X” which was presented at a randomly determined
5 interval between 300 and 1000ms. This task consisted of 8 practice trials and 48
6 test trials. The computer recorded the reaction time to each button press.

7 The Digit Symbol Substitution Task (DSST, Wechsler, 1981) - Symbol Copy
8 provided a speed of processing component, and subtracting mean time per item in
9 Symbol Copy from the Digit Symbol Substitution yielded a measure of higher mental
10 function (Glosser et al., 1977; Storandt, 1976 as cited in Joy, Fein, & Kaplan, 2003).
11 We also included the incidental memory portion measuring immediate recall of
12 symbol pairings.

13 Trail Making Test A and B (Reitan, 1958) - Part A provided a speed element,
14 while the difference score provided an estimate of executive function.

15 Controlled Oral Word Association Test (COWAT, Spreen & Strauss, 1991) was
16 used to measure verbal fluency.

17

18 *Memory*

19 Episodic Memory:

20 Episodic memory was measured using a 20-item word list on the computer
21 screen at the rate of one word every two seconds, followed by an immediate written
22 recall.

23 Working Memory:

1 The Backward Digit Span (Wechsler, 1981) was used to assess working
2 memory during the follow-up only.

3 Prospective memory (PM):

4 *Subjective Memory Rating*

5 Prospective and Retrospective Memory Questionnaire (PRMQ; Crawford et
6 al, 2003).

7 *Event-based PM Tasks*

8 1. Card Sort Task (Rusted et al., 2009)

9 Participants sorted playing cards into hearts and spades, while ignoring
10 diamonds and clubs. The non-focal PM intention was to press the spacebar for
11 number 7 cards regardless of suit. In each trial the back of the playing card was
12 shown for 1000ms and then the face card was shown for 750ms, automatically
13 advancing between front and back and the next trial. The baseline condition
14 (without PM intention) had 52 trials (one deck), while the PM condition had 104
15 trials (two decks).

16 2. Focal and Non-Focal Prospective Memory Task (McDaniel et al., 2011)

17 The ongoing task was a category decision task. The three counterbalanced
18 PM conditions were: 1) a no PM control condition; 2) a focal PM condition – the PM
19 cue was a specific word, i.e. Tortoise; 3) a non-focal PM condition – the PM cue was
20 part of a word, i.e. “tor” as found in words like **history**. PM targets for the focal and
21 non-focal conditions were presented 3 times during their appropriate condition and
22 not presented again in the other conditions. Participants practiced the ongoing
23 category decision task first, which included six trials giving speed and accuracy

1 feedback to encourage optimization of both. Then three conditions consisting of 106
2 word-pair trials (not including prospective memory trials) were used.

3
4 *Attention*

5 The Map Test of Everyday Attention (Map TEA; Robertson, Ward, Ridgeway,
6 & Nimmo-Smith, 1996) provided a visual search measure. Participants circled as
7 many petrol stations as they could find on a complex version of the standard map,
8 which contained other symbols as well, for two minutes, switching colors at the one
9 minute interval.

10 Rapid Visual Information Processing (RVIP; Wesnes & Warburton, 1983)
11 provided a sustained attention measure. The computer recorded responses and
12 reaction times. In our version we presented one stimulus per second. We had five
13 80-second intervals, with eight target sequences presented in each interval. The
14 total time for the task was 6:20.

15 The Stroop-Switch Task (Hutchison et al., 2010) combines the traditional
16 Stroop Task with a task-switching paradigm, intermixing trials requiring color
17 naming and word naming, switching the task every two trials. Trials advanced when
18 participants made a vocal response and there were 24 practice trials and 88 trials.
19 The computer recorded reaction times, while the experimenter recorded errors.

20

21 **2.4 Procedure**

22 Data collection

23 Participants' cognitive assessment was completed in the School of Psychology
24 and MRI sessions at the Clinical Imaging and Sciences Centre, at Sussex University.

1 Time intervals between MRI and cognitive sessions at baseline and follow-up were as
2 closely linked as possible, allowing for the individual availability of the volunteers.

3 Participants were consented by a researcher on each occasion. The cognitive
4 testing sessions lasted approximately 3 hours, including breaks as and when volunteers
5 wanted. MRI scans took less than 30 minutes. Participants were compensated for their
6 transport costs and parking.

7 MRI protocol

8 All images were acquired on a Siemens 1.5 Tesla Avanto MRI scanner (Siemens,
9 Erlangen, Germany). High-resolution anatomical images were acquired using a three-
10 dimensional T1-weighted magnetization prepared rapid acquisition gradient echo
11 (MPRAGE) sequence [TR = 1160 ms; TE = 4.44 ms; inversion recovery time (TI) = 600
12 ms; field of view (FOV), 230 x 230 mm²; matrix size, 256 x 256; flip angle θ = 15
13 degrees; voxel dimensions, 0.9 x 0.9 x 0.9 mm³; acquisition time, 5 min].

14 Diffusion-weighted images were acquired using an echo planar imaging sequence
15 [TR = 12.4 s; TE = 111 ms; echo spacing, 0.83 ms; FOV, 240 x 240 mm²; matrix size, 96
16 x 96; voxel dimensions, 2.5 x 2.5 x 2.5 mm³; acquisition time, 7 min]. Diffusion gradients
17 were applied along 30 noncollinear directions ($b_{\max} = 1000 \text{ s/mm}^2$). A nondiffusion-
18 weighted ($b \sim 0$) volume was also acquired.

19

20 **2.5 Analyses**

21 For all statistical tests an alpha of .05 was adopted.

22 *2.5.1 Demographics & Experimental Tasks*

For demographic comparisons, we used independent t-tests to compare groups (supervets vs. controls) at each time point. For lifestyle factors and cognitive measures at the baseline time point we used independent t-tests between groups to compare means. ANOVAs were used if a task had a repeated measures factor. Follow-up analyses used mixed factor ANOVAs with time point as a repeated measures factor. Any post-hoc tests used a Sidak correction and therefore Sidak-adjusted p-values are reported.

2.5.2 Image post-processing

We used whole volume analysis (Erickson et al., 2009, 2011; Resnick et al., 2003), automated segmentation (Resnick et al., 2003), Voxel-Based Morphometry (VBM) (Tseng, Uh, et al., 2013), longitudinal VBM (Colcombe et al., 2003, 2006), and Tract-Based Spatial Statistics (TBSS) (Tseng, Gundapuneedi, et al., 2013).

Raz et al. (2013, 2010) used manual tracing to segment their volumes, but automated segmentation has been shown to be highly correlated in volume and shape with manual tracing especially using Freesurfer (Morey, Petty, & Xu, 2009) with the additional benefits of no operator bias and taking less operator time. For these reasons we used Freesurfer to autosegment our volumes. For volume and cortical thickness analyses we looked specifically at areas most previously seen to be affected by aging and/or were previously shown to be different for those that exercised. Using Freesurfer, we were able to do both these analyses within the same software package. For volumes we chose hippocampus (Erickson et al., 2009, 2011; Lövdén et al., 2012; Raz et al., 2010; Uylings & de Brabander, 2002), cerebellar cortex (Raz et al., 2013, 2010; Tseng, Uh, et al., 2013), cerebellar white matter (Raz et al., 2013, 2010; Tseng, Uh, et al., 2013), and caudate (Raz et al., 2013, 2010). For cortical thickness we looked at entorhinal cortex (Raz et al.,

2010), frontal lobes (Colcombe et al., 2003, 2006; Raz et al., 2013; Resnick et al., 2003; Uylings & de Brabander, 2002), and parietal lobes (Colcombe et al., 2003; Resnick et al., 2003; Tseng, Uh, et al., 2013).

With our DTI measures, we also used the more recently developed histogram analysis, which is sensitive to subtle diffuse differences in the brain in the specific diffusivity measures of mean diffusivity (MD), axial diffusivity (λ_1) and radial diffusivity (RD) (Tofts, Davies, & Dehmshki, 2003), whereas TBSS detects localized differences (S. M. Smith et al., 2006).

DTI

Histogram analysis:

Histogram analysis is sensitive to subtle diffuse disease (Tofts et al., 2003) and aging (Charlton et al., 2006). For example, comparing patients with multiple sclerosis (MS) to controls without MS, Cercignani, Bozzali, Iannucci, Comi, & Filippi (2001) observed diffuse tissue damage in the white matter of patients with MS, in the form of increased overall MD values. Looking at aging, Charlton et al. (2006) observed cross-sectionally middle-aged and older adults and found progressive reduction in FA and increase in MD with age, which correlated with declines in cognitive measures. DTI data were pre-processed using the FMRIB's Software Library (FSL) suite version 5.04 (S. M. Smith et al., 2004; Woolrich et al., 2009). DTI volumes were realigned using the eddy current correction module tool. The diffusion tensor was calculated for each image voxel to give MD, FA, RD, λ_1 . To restrict analyses we generated WM and GM ROIs using the

1 New Segment tool in SPM (Statistical Parametric Mapping, Functional Imaging
2 Laboratory, University College London).

3 The frequency distribution of each MR parameter was plotted and the resulting
4 histogram was normalized to 20 units and smoothed using a gaussian kernel. Smoothing
5 kernels were: 0.009 and 0.02 for grey matter and white matter FA, respectively; 20×10^{-6}
6 mm^2/s and $10 \times 10^{-6} \text{mm}^2/\text{s}$ for grey matter and white matter respectively for MD, $\lambda 1$, and
7 RD. We then calculated peak height (PH), peak position (PP), and mean for each
8 histogram per ROI per DTI parameter.

9 MR parameter indices (PH, PP, Mean) were compared at each time point using
10 ANCOVAs between groups (supervet vs. control), $p < .05$, with age and sex (Hsu et al.,
11 2008; Kanaan et al., 2012) as covariates.

12 Tract-based Spatial Statistics (TBSS):

13 Tract-based spatial statistics (TBSS) (S. M. Smith et al., 2006), part of FSL, was
14 performed on DTI data following the procedure outlined in (Dowell et al., 2013) to
15 generate TBSS maps of FA, MD, $\lambda 1$, and RD. TBSS allows for detection of differences
16 in DTI indices in local white matter tracts.

17 TBSS inference testing was employed to identify differences between supervet
18 and control groups. As the null distribution was not known, a permutation-based
19 inference method was employed (Nichols & Holmes, 2002). A two-sample
20 nonparametric test was carried out with 10000 permutations using a threshold-free cluster
21 enhancement (TFCE) method. In contrast with other such techniques, this method has the
22 advantage that no arbitrary initial cluster-forming threshold needs to be selected. The

1 computed cluster is tested against a critical cluster size: if the resulting cluster is larger
2 than the critical size, the cluster is significant.

3 *Anatomical*

4 Whole brain volume analysis:

5 Whole volume analysis allowed us detect global differences. MPRAGE volumes
6 were segmented into white matter (WM), grey matter (GM), and cerebral spinal fluid
7 (CSF) ROIs. This was added together to get the intracranial volume (ICV). Whole brain
8 (WB) volume was calculated by adding WM and GM. Then each ROI – WM, GM, WB –
9 was divided by the ICV to calculate the percentage of the whole volume each ROI took.
10 All data was then compared using two-tailed t-tests between groups, $p < .05$ at baseline.
11 When including the follow-up time point, mixed ANCOVAs were used with time point
12 as a repeated measures factor, groups as an independent measures factor, and age and sex
13 (Good et al., 2001) as covariates.

14 Voxel-based morphometry (VBM):

15 VBM allowed an unbiased voxel-by-voxel analysis of the whole brain without the
16 need to specify a priori ROIs. For baseline VBM, we used Christian Gaser's VBM8
17 toolbox (<http://dbm.neuro.uni-jena.de/vbm/>) for the SPM8 package (Wellcome
18 Department of Cognitive Neurology, London, UK (J Ashburner & Friston, 2000)) in
19 Matlab R2007a (MathWorks, Natick, MA, USA). We skull stripped and warped T1-
20 weighted anatomical images into MNI space and segmented GM, WM and CSF within a
21 unified segmentation model (John Ashburner & Friston, 2005). Modulated normalized
22 segmentations of GM and WM were then smoothed using an $8 \times 8 \times 8$ -mm³ kernel. Two-

1 sample t-tests were defined to detect significant group volume differences. The family-
2 wise error correction was carried out at $p < 0.05$.

3 Including follow-up, we used VBM longitudinal analysis in VBM8. Follow-up
4 participants' volumes were non-linearly registered to their own baseline volumes and
5 spatial normalization is estimated for baseline volumes only and applied to all time
6 points. Mixed ANOVAs were defined to detect group volume differences, time point
7 volume differences, and interactions between the two. The family-wise error correction
8 was carried out at $p < 0.05$.

9 Freesurfer volume and cortical thickness:

10 Freesurfer allowed using specific surface-based and volumetric ROI analysis
11 using a priori determined ROIs. Both time points were automatically processed using the
12 longitudinal stream in Freesurfer 5.3.0 (Reuter, Schmansky, Rosas, & Fischl, 2012).

13 For volume and cortical thickness analyses we looked specifically at areas most
14 reported to be affected by aging and/or were previously shown to be different for those
15 that exercised. For volumes we chose hippocampus (Erickson et al., 2009, 2011; Lövdén
16 et al., 2012; Raz et al., 2010; Uylings & de Brabander, 2002), cerebellar cortex (Raz et
17 al., 2013, 2010; Tseng, Uh, et al., 2013), cerebellar white matter (Raz et al., 2013, 2010;
18 Tseng, Uh, et al., 2013), and caudate (Raz et al., 2013, 2010). For cortical thickness we
19 looked at entorhinal cortex (Raz et al., 2010), frontal lobes (Colcombe et al., 2003, 2006;
20 Raz et al., 2013; Resnick et al., 2003; Uylings & de Brabander, 2002), and parietal lobes
21 (Colcombe et al., 2003; Resnick et al., 2003; Tseng, Uh, et al., 2013).

22 Volumes for each hemisphere across subjects and between time points were
23 extracted and divided by ICV; age and sex were used as covariates and groups were

compared using ANCOVAs at the baseline time point, $p < .05$. For the follow-up time point mixed ANCOVAs were used with time point as a repeated measures factor, group as an independent measures factor, and age and sex as covariates.

Baseline cortical thickness and cortical thickness symmetrized percent change (SPC), which divides the rate of change by average thickness over the two points, giving more statistical power than percent change relative to time point 1 thickness (since average thickness is less noisy than thickness at time point 1), were extracted. At baseline, age and sex were used as covariates, and groups were compared using ANCOVAs, $p < .05$. With the follow-up cortical thickness SPC, mixed ANCOVAs were used with time point as a repeated measures factor, group as an independent measures factor, and age and sex as covariates.¹

Correlations with cognitive data

For the purposes of these analyses, correlations were computed using between group differences found in cognitive data and group differences in MRI data. These were for cognitive data: Reaction Time cost in a PM task, and Switch RT in a modified Stroop task.² For MRI measures we entered follow-up White Matter Axial Diffusivity, percentage white matter change, and percentage whole brain change, right hippocampal volume percent change, left and right cerebellar volume percent change, and right frontal lobe cortical thickness symmetrized percent change. Correlations were all corrected for multiple comparisons using a bonferonni correction.

3. Results

3.1 Demographics

3.1.1 Demographics

Results for Demographics are shown in Table I.

There were no significant differences between groups at either the initial and follow-up time points in sex, age, education, IQ, or depression levels.

3.1.2 Physical Activity

Results for Physical Activity are in Table II: Physical Activity.

As expected and desired, on the PASE the supervets took part in more physical activities than the controls at baseline and this difference was maintained in both baseline and follow-up analyses. Specifically, at the baseline time point supervets took part in significantly more strenuous sports, $t(34.58) = 4.59, p < .001$, and muscle strength and endurance activities, $t(30.41) = 2.78, p = .009$. Including the follow-up time point in the analysis, there was a group by leisure activity interaction, $F(3.09, 117.33) = 6.20, p = .001$. Again supervets ($M = 1.08$ hours per day) participated in more strenuous sports than controls ($M = .20$), $F(1, 38) = 27.93, p < .001$. Also supervets ($M = .12$) participated in more muscle strength and endurance activities than controls ($M = .03$), $F(1, 38) = 8.88, p = .005$. The groups did not differ in time spent on other leisure activities. For both groups, there was an increase in moderate activity at follow-up ($M = .28$ hours per day) vs. baseline ($M = .12$), $F(1, 38) = 4.31, p = .045$, while other activities did not change.³

3.1.3 Diet

Results for Diet are in Table II: Diet.

1 There were no differences between groups in adherence to Mediterranean diet at
2 the initial or follow-up time point.

3 3.1.4 Lung Function

4 *Results for Lung Function are in Table II: Lung Function.*

5 At initial and including follow-up there were no significant differences between
6 groups in lung function measures: FEV1, FVC, FER, and PEF. Lung function measures
7 are not affected by exercise training (Dempsey, 1986), and comparability of groups
8 indicates that both have similar potential for cardiovascular performance and that both
9 groups were capable of achieving the same level of fitness.

10 At follow-up, FVC had declined in both groups, $F(1, 30) = 5.62, p = .024$, and
11 PEF increased, $F(1, 33) = 4.97, p = .033$.

12 3.1.5 Physiological

13 *Results for Physiological Measures are in Table II: Physiological.*

14 Because of physiological differences between males and females, these measures
15 were analyzed by gender.

16 In physiological measures, expected differences between our groups were
17 confirmed at the initial time point and at follow-up. Supervets had significantly less
18 percent body fat in both sexes. Male supervets trended towards stronger hand-grip than
19 male controls at the initial time point and this difference was significant at follow-up.
20 Females did not differ in hand-grip strength at either time point. At follow-up,
21 percentage fat increased in both groups for both sexes: males, $F(1, 24) = 23.25, p < .001$;
22 females, $F(1, 11) = 5.46, p = .039$.

23 3.1.6 Social and Cognitive Activities

1 *Results for Social and Cognitive Activities are in Table II: Social and Cognitive*
 2 *Activities.*

3 There were no significant differences between the groups in LSNS score or FCAS
 4 score either at the initial time point or at follow-up, $Qs < 1$.

6 **3.2 Experimental Tasks**

7 *3.2.1 Speed of Processing*

8 *Results are shown in Table III: Speed of Processing.*

9 At the initial time point there were no significant differences between groups
 10 for the mean reaction time for correct trials in the Simple Reaction Time task. When
 11 including the follow-up time point in analyses, there was still no main effect of
 12 group, $F(1, 38) = 3.59, p = .066$.

13 For both Intra-Individual Variability (IIV) and Intra-Individual Coefficient of
 14 Variability (ICV) there were no significant differences between groups at both the
 15 initial time point and including the follow-up time point. IIV was significantly higher
 16 at follow-up than at the initial time point, $F(1, 38) = 4.21, p = .047$.

17 There were no significant differences between groups for the Trail Making
 18 Test part A (Trails A) or Symbol Copy task at both the initial time point and
 19 including follow-up, $Qs < 1$.

21 *3.2.2 Executive Function*

22 *Results are shown in Table III: Executive Function.*

1 For DSST higher mental function, there were no differences between groups
 2 at the initial time point (power = .29) and when including follow-up, $F < 1$; power:
 3 between factors = .16, within factors = .51, within-between interaction = .11. For
 4 Trails B, accounting for motor speed, there were no differences between groups at
 5 the initial time point (power = .58) or when including follow-up, $Q < 1$.

6 In the COWAT, there were no significant differences between supervets and
 7 controls in verbal fluency at the initial time point (power = .24) nor when including
 8 the follow-up time point, $F < 1$; power: between factors = .09, within factors = .98,
 9 within-between interaction = .99.

10

11 3.2.3 Memory

12 *Results are shown in Table III: Memory.*

13 Incidental and Episodic Memory:

14 There were no main effects between groups for incidental memory
 15 performance (from the DSST) nor for episodic memory performance at the initial
 16 time point nor when including the follow-up time point, $F(1, 34) = 1.46$, $p = .236$ and
 17 $F < 1$ respectively.

18 Working Memory:

19 At follow-up, there was no main effect between groups for the Backwards
 20 Digit Span.

21 Prospective Memory:

22 *Subjective Rating of Memory*

23 *Results for this measure are shown in Table III: Memory.*

1 For the Prospective and Retrospective Memory Questionnaire, there were no
2 differences between groups for ratings by supervets and controls of their own
3 prospective and retrospective memory. When including the follow-up time point,
4 there were also no differences.

5 *Card Sort PM Task:*

6 *Results for this task are shown in Table IV.*

7 There were no differences between groups at either time point on PM accuracy,
8 but at the initial time point, performance on the ongoing (card-sorting) task was
9 differentially affected by the requirement to carry a PM intention, with supervets making
10 more errors than controls, $t(30.94) = 2.17$, $p = .038$: supervets, $M = 3.66\%$, controls, $M =$
11 1.09% , $M_{diff} = 2.66$, 95% CI [0.33, 4.86], $p = .031$. Reaction time to complete the ongoing
12 task was not different between groups in either condition at either time point.

13 *McDaniel PM Task:*

14 *Results for this task are shown in Table V.*

15 There were no differences between groups in either condition at either time point
16 on PM accuracy. There were no differences between groups in any condition at either
17 time points in accuracy of the ongoing task (category decision) but there were differences
18 in reaction times. A condition by group linear interaction trend, $F(1, 38) = 3.61$, $p = .065$,
19 was explored with Sidak-corrected pairwise comparisons. As in the card sort PM,
20 supervets, were more impacted when required to carry a PM intention, with longer RTs
21 when maintaining either focal ($p = .011$) or non-focal ($p < .001$) PM intentions. For
22 control volunteers, ongoing task RTs were longer only when maintaining a non-focal PM
23 intention ($ps < .001$).

1

2

3 *3.2.4 Attention*

4 Map TEA:

5 *Results are shown in Table III: Attention.*

6 There were no significant differences between groups at initial time point or
7 when including follow-up.

8

9 Stroop Switch Task:

10 *Results for this task are shown in Table VII.*

11 The standard Stroop effects were replicated but did not differentiate our
12 groups.

13 *Errors*

14 There was a group by time point interaction, $F(1, 36) = 4.37, p = .044, \eta^2p =$
15 $.108$, qualified by a group by time point by cue interaction, $F(1, 36) = 8.04, p = .007,$
16 $\eta^2p = .183$: sidak-corrected pairwise comparisons confirmed that only in supervets
17 at the follow-up time point did color naming produce more errors than word
18 naming ($p = .008, d_z = 0.63, \text{power} = .79$).

19 *Reaction Time*

20 There was a cue by switch interaction, $F(1, 46) = 4.99, p = .030, \eta^2p = .098,$
21 qualified by a group by cue by switch interaction, $F(1, 46) = 5.92, p = .019, \eta^2p =$
22 $.114$: sidak-corrected pairwise comparisons confirmed that reaction time difference
23 were limited to word-naming trials, where 1) supervets were faster than controls in
24 switch trials only ($p = .046, d = 0.61, \text{power} = .67$) and 2) switch trials were slower

1 than non-switch trials for controls only, $F(1, 21) = 30.89, p < .001, n^2p = .595$.

2 However this didn't appear to have any obvious theoretical significance.

3 Including follow-up, there was a cue by switch interaction, $F(1, 36) = 9.60, p =$

4 $.004, n^2p = .210$, qualified by a group by cue by switch interaction, $F(1, 36) = 4.65, p$

5 $= .038, n^2p = .114$, qualified by group by cue by switch by time point interaction, $F(1,$

6 $36) = 8.03, p = .007, n^2p = .182$, attributable to the initial time point already

7 described; the interaction at the initial time point was not replicated at follow-up.

8 RVIP:

9 *Results for this task are shown in Table VI.*

10 *Number of Correct Responses*

11 There were no group differences; for both groups, performance deteriorated over

12 time at initial, $F(4, 184) = 8.11, p < .001$, and including follow-up time point, $F(4, 140) =$

13 $12.37, p < .001$. At follow-up, a time-bin by group interaction, $F(4, 140) = 2.78, p = .029$,

14 was explored using Sidak-corrected pairwise comparisons: Supervets correctly identified

15 significantly more targets in the first time-bin than any of the other time-bins, ($ps = .001$

16 or less). Controls correctly identified significantly more sequences in the second and

17 fourth time-bin than in the fifth time-bin, $p = .031$ and $p = .009$ respectively.

18 *Reaction Time*

19 At the initial time point and including follow-up there was a significant group by

20 time-bin interaction, $F(4, 180) = 2.55, p = .041, F(4, 136) = 2.87, p = .025$ respectively.

21 Sidak-corrected pairwise comparisons showed that at both time points, for supervets only,

22 reaction times in the first time-bin were significantly faster than the second bin ($p = .004$,

$p < .001$, respectively), which did not differ from subsequent bins; for controls the first 3 time-bins were faster than the fifth time-bin ($p = .019$, $p = .042$, $p = .030$ respectively).

3.3 MRI data

3.3.1 Initial Time Point

At the initial time point there were no significant differences between groups for any of the structural indices: DTI histogram, $ps > .05$; TBSS; Whole Brain Volume in GM, WM, and WB, $Fs < 1$; and VBM.

3.3.2 Follow-up Time Point

DTI

Supervets ($M = 1004.00 \times 10^{-6} \text{ mm}^2/\text{s}$, $SD = 33.12$) had significantly higher white matter axial diffusivity (λ_1) than controls ($M = 971.67 \times 10^{-6} \text{ mm}^2/\text{s}$, $SD = 28.87$), $F(1, 23) = 5.96$, $p = .023$. There were no other differences between groups for any of the other indices in all parameters. No differences were found between groups using TBSS, indicating that these differences were not localized to any specific white matter tracts.

Trending Anatomical Differences

At follow-up trends towards group differences emerged on a number of measures; exploratory analyses applying a more liberal threshold ($p < 0.05$ without correction for multiple comparison) are reported.

Whole Volume Analysis:

For white matter percentage, there was a group by time point interaction trend, $F(1, 22) = 4.14$, $p = .054$: relative to supervets ($M = 0.03\%$, $SD = 0.14$) controls

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1 decreased in percentage volume ($M = -0.09\%$, $SD = 0.11$). This interaction trend was
2 reflected in the whole brain analysis, where there was a marginal group by time point
3 interaction trend, $F(1, 22) = 3.98$, $p = .058$: relative to supervets ($M = -0.02\%$, $SD = 0.10$)
4 controls decreased in whole brain volume ($M = 0.17\%$, $SD = 0.21$).

5 Freesurfer Volume:

6 Including follow-up, for right hippocampal percentage there was a significant
7 effect of time point, $F(1, 22) = 5.29$, $p = .031$: both groups decreased in volume from
8 initial ($M = 0.28\%$ ICV, $SD = 0.03$) to follow-up time point ($M = 0.27\%$ ICV, $SD = 0.03$).

9 For left and right cerebellar cortex percentage volume there were group by time
10 point interactions, $F(1, 22) = 5.49$, $p = .032$, $F(1, 22) = 4.31$, $p = .050$, respectively:
11 relative to supervets (left: $M = -0.04\%$, $SD = 0.006$; right: $M = -0.04\%$ ICV, $SD = 0.07$)
12 controls increased in percentage volume (left: $M = 0.09\%$, $SD = 0.17$; right: $M = 0.09\%$,
13 $SD = 0.21$).

14 Freesurfer Cortical Thickness:

15 There was a significant difference between groups for symmetrized percent
16 change in frontal lobe in the left hemisphere, $F(1, 22) = 6.75$, $p = .016$: relative to
17 supervets ($M = -0.15\%$, $SD = 1.29$), controls increased in thickness ($M = 1.43\%$, $SD =$
18 1.36); no significant difference was observed in right hemisphere, $F(1, 22) = 3.63$, $p =$
19 $.070$.

20 VBM Analysis:

21 There were no significant differences.

22 Correlations with Cognitive Data

23 We found no correlations between any cognitive and MRI measure entered.

1 **4. Discussion**

2 In this study, we explored cognitive and brain structural differences between
 3 superveteran athletes (older adults engaging in long-term high-effort endurance exercise)
 4 and non-sedentary volunteers of similar age and lifestyle; we also completed a 12 month
 5 follow-up on these same measures. Our study avoided confounds present in many
 6 previous studies by using groups that were statistically similar in age, sex, education, IQ,
 7 depression levels, cognitive activities, social network, adherence to Mediterranean diet,
 8 and potential for fitness.

9 Both groups had the same potential for fitness, as demonstrated by lung function
 10 measures, but our supervet group was indeed more physically fit than our control group,
 11 as demonstrated by lower percentage body fat in all supervets and stronger hand-grip in
 12 males. The decrease in FVC, although statistically significant, was within the error of the
 13 instrument ($\pm 3\%$ from Micro Medical website) and the amount of decrease was not a
 14 physiologically significant amount as well. As for PEF, there was a small increase ($\sim 15\%$
 15 in supervets, less in controls), but with a very wide range of values at both time points
 16 (T0: 106 - 756 L/min, T1: 247 – 703 L/min). There is no real reason why there would be
 17 a change in PEF and in physiological terms, it is unlikely that this would occur.

18 Cognitively, we found surprisingly few differences between our two groups in our
 19 tasks addressing key domains.⁴

20

21 *Speed of Processing*

22 We found no differences between supervets and non-sedentary controls in simple
 23 reaction time and speed of processing tasks (Trails A and DSST).

24

1 *Executive Function*

2 We found no differences between supervets and non-sedentary controls in executive
3 function tasks (DSST higher mental function, Trails B, COWAT).

4
5 *Memory*

6 We found no differences between supervets and non-sedentary controls in
7 working memory (Backwards Digit Span), incidental memory (from DSST), and episodic
8 memory.

9 In prospective memory tasks, carrying in mind a non-focal PM intention requires
10 increased attentional resource compared to focal PM intention (Einstein, McDaniel,
11 Manzi, Cochran, & Baker, 2000). Thus, we anticipated that supervets would show
12 smaller costs in carrying a PM intention, based on the evidence that exercise increases
13 attentional resources used for monitoring (Barnes et al., 2003; Voss et al., 2010;
14 Angevaren et al., 2008, Smith et al. 2010; Erikson et al., 2011; Winker et al., 2010; Voss
15 et al., 2010a). In contrast, in both tasks, supervets showed greater cost in carrying a PM
16 intention. In the Card Sort Task, this was indexed by poorer ongoing task accuracy, and
17 in the McDaniel PM Task, by longer reaction times under the focal PM condition.

18 Einstein & McDaniel's (2000) multiprocess theory suggests that the less complex focal
19 PM condition should rely more on spontaneous retrieval than monitoring, and therefore
20 should show no cost in reaction time. Results from our controls are consistent with this.

21 The significant cost in reaction time in the focal PM condition for supervets suggests this
22 group may engage in active monitoring when there is any PM component, regardless of
23 focality. The fact that this did not improve PM performance is consistent with findings of
24 Einstein et al. (2005) and those of Marsh, Hicks, & Cook (2005).

In both PM tasks completed here a parsimonious explanation of our results is that the supervets were applying higher effort in the form of active monitoring, regardless of whether or not the added effort actually resulted in a performance benefit. Anecdotally, it was clear that the supervets were a highly motivated group who were a) much more keen to attend the 4 hour testing sessions and b) individually committed to the view that their exercise regimen improved their cognitive health and wellbeing. Previous studies have reported that motivational differences in participants elicit better performance on lab-based cognitive tasks (Deaton & Parasuraman, 1993; Tomporowski & Tinsley, 1996). It is therefore doubly surprising that, with such motivation, the supervets did not demonstrate superior performance across the task battery compared to the control group.

Attention

We found no differences between supervets and non-sedentary controls in visual search (Map TEA).

On tasks that engaged significant attentional control, small and subtle differences emerged. These seem best interpreted as differences in strategy between supervets and controls. On the RVIP task, supervets started with faster reaction times and greater accuracy, but rapidly adjusted to a slower pace to sustain accuracy. Controls maintained a more paced performance from the start, with a shallower fatigue curve. These results correspond well with reports from the sports psychology literature. Elite marathoners are reported to employ an “effort sense”, a strategy to adjust their effort and achieve relatively stable running pace (Morgan & Pollock, 1977). The RVIP results may reflect this greater metacognitive awareness and attentional control. This is line with previous research as well observing that older expert orienteers, older cyclists, and older athletes

1 having better attentional skills to modulate their attention and reaction time than non-
 2 athletes (Pesce, Cereatti, Casella, Baldari, & Capranica, 2007; Pesce, Cereatti, Forte,
 3 Crova, & Casella, 2011) and children participating in exercise interventions having
 4 increased meta-cognition as compared to their peers (Tomprowski, McCullick,
 5 Pendleton, & Pesce, 2015).

6 Our results on this comprehensive battery of cognitive tasks complement
 7 outcomes from other recent studies of senior athletes (Tseng, Uh, et al., 2013; Winker et
 8 al., 2010). Both reported benefits only on fluency tasks, though substantive test batteries
 9 were administered in each of these studies. All results could be simply interpreted as
 10 advantages emerging only under conditions where strategic effort can influence outcome
 11 measures.

12 This study provides valuable data on an under-researched group. Long-term high-
 13 effort endurance athletes who are continuing their regimes beyond the sixth decade of life
 14 are a specialist and elite group. Their numbers are limited, and our group sizes, while
 15 larger than those reported previously (Tseng, Gundapuneedi, et al. (2013) and Tseng, Uh,
 16 et al. (2013) reflect this.

17 A strength of the present study was the inclusion of longitudinal structural
 18 imaging data in the same group of volunteers who contributed cognitive data. This MRI
 19 data similarly recorded very few differences between groups. Notably, however,
 20 supervets showed higher white matter axial diffusivity than controls at the follow-up time
 21 point. Differences in this MR parameter have been interpreted in terms of myelin content
 22 (Klawiter et al., 2011), with higher levels reflecting greater neural integrity (Madden et
 23 al., 2009; Zhang et al., 2007). Age-related decreases in axial diffusivity have been

1 reported in many regions (Bennett et al., 2010; Burzynska et al., 2010); higher diffusivity
 2 in supervets would suggest they are showing less age-related decline. Potentially higher
 3 axial diffusivity in supervets, while not producing functional differences now, may
 4 advantage supervets in the longer term.

5 In terms of hippocampal volume, we did not observe higher volumes in supervets
 6 compared to controls at baseline nor were there differences in hippocampal volume
 7 changes over the 12-month follow-up. This contrasts with the results from studies by
 8 Erickson et al. (2009, 2011) measuring effects of exercise on sedentary older adults.
 9 Similarly, we did not observe differences in baseline or longitudinal VBM analyses, in
 10 contrast to Colcombe et al. (2003, 2006) and Tseng, Uh, et al. (2013), nor localized
 11 differences when using TBSS, in contrast to Tseng, Gundapuneedi, et al. (2013). We did
 12 not observe any significant differences or differences in rate of change in volume or
 13 cortical thickness ROIs.

14 As already stated, a key difference between our study and previous ones was our
 15 selection of controls. Unlike Tseng et al. (2013a&b) and Winker et al. (2010), we
 16 explicitly used non-sedentary controls. In addition, and unlike the earlier studies, our
 17 controls were overall similar to supervets in social network, cognitive activity, and
 18 depression levels; they were physically mobile and engaging in similar amounts of
 19 moderate physical activity as our supervets. Differences between comparator groups
 20 would certainly represent potential confounds in the earlier studies (Kim et al., 2011; Lee
 21 et al., 2014; Richards et al., 2003; Scherder et al., 2013; Sturman et al., 2005; Thomas &
 22 O'Brien, 2008) Overall, our regular moderately-exercising controls do not seem to be at a
 23 disadvantage when compared to superveteran athletes.

1 A second difference from previous studies is the exercise time frame. It is
2 plausible that the cognitive and brain structural benefits of exercise reflect acute effects of
3 relatively short-term interventions in previously sedentary groups, and that benefits are
4 not sustained in extreme long-term exercisers.

5 The use of a longitudinal design improved the power of our results and the
6 consistency of the null results across the two time points lends further credence to our
7 assertion that these populations don't differ much at this point in time. Where differences
8 were observed at follow-up, mainly in our MRI measures, these were found either using
9 ANOVAs including both time points or using change values, indicating a rate of change
10 difference between the two groups. Exercise may be retarding age-related change but
11 only after a certain threshold is reached. Therefore a longer-term follow-up may have
12 found larger differences beginning to emerge, as older adults exercising at lower levels
13 would reach that threshold more quickly. Alternatively a more holistic view can be taken
14 that the trajectory of age-related change reflects the cumulative impact of all lifestyle
15 factors that affect cognitive function. In this view, the key to good cognitive health in
16 older aging would then be to participate more frequently in cognitive activities, have
17 larger social networks, adhere more to Mediterranean-style diets, and to exercise a bit but
18 not necessarily to the level of an athlete. Indeed, by the logic of additive factors,
19 moderate adherence to a number of moderators would produce greater overall benefits
20 than singular adherence to one.

21 Our sample also had high mean IQs and high mean education; these two may be
22 protective factors, promoting higher cognitive reserve in both groups (Alexander et al.,
23 1997; Stern, Alexander, Prohovnik, Mayew, & Stern, 1992; Tucker & Stern, 2011). This

1 may also account for why we did not see much change in either group over the one-year
2 follow-up. Longer term observation may have differentiated our sample, and this was
3 somewhat indicated in the scanning indices where we observed at follow-up a supervet
4 advantage in white matter axial diffusivity and some trends towards emerging volumetric
5 differences also.

6 We measured physical activity using a questionnaire, but it has become more
7 common for recent interventions and epidemiological studies to use accelerometers for a
8 more objective assessment (Guiraud et al., 2012; Motl, McAuley, & Dlugonski, 2012;
9 Opdenacker, Boen, Coorevits, & Delecluse, 2008). The accelerometers allow one to
10 monitor the number of steps one takes as well as the intensity level of their activity. The
11 only drawback to accelerometers is that they can be quite expensive.

12

13 **Conclusion**

14 The results across the wide battery of cognitive tests and brain structure indices show
15 that supervets participating in long-term high-effort endurance exercise display only
16 small cognitive and brain structural differences relative to non-sedentary volunteers of
17 similar age, social, cognitive, and neuropsychiatric profile. Cognitively, these small
18 differences manifest in tasks requiring application of effort and strategy, and potentially
19 index differences in effort, metacognitive awareness, or motivation in the supervets. That
20 there are diminishing returns for exercise on cognition, and that these effects do not
21 compare with the benefits seen in a sedentary population, is not surprising. That effects
22 may emerge as brain structural benefits over the longer term allows for the possibility
23 that cognitive benefits too will increase with age. To confirm this, however, it would be

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- 1 necessary to follow this elite cohort beyond the 6th decade and for longer than the 12-
- 2 month period tested here.

1 **Conflict of Interest**

2 The authors declare no conflicts of interest.

3

4

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28

1 **Footnotes**

2 ¹ Between baseline and 12-month follow-up MRI sessions the MRI scanner gradients
 3 were upgraded yielding an increase in gradient amplitude (from 33mT/m to 44 mT/m)
 4 and slew rates. For our DTI measures we ensured diffusion gradient amplitudes were
 5 identical for both time points, but differences remained in the imaging gradients. As a
 6 result, the DTI data between sessions were not directly compared. Daily independent QA
 7 data using the EPI sequence also showed there were no SNR step changes as a result of
 8 the upgrade. Any potential differences in T1-weighted MPRAGE scans as a result of the
 9 hardware upgrade were accounted for in analyses: participants' volumes at each time
 10 point were normalized to templates (Freesurfer longitudinal); normalized to baseline time
 11 point volumes (VBM longitudinal), or intracranial volumes at each time point were used
 12 to normalize the data as is standard practice.

13 ² PM task was a Focal PM task, switch reaction time was from the Word-Neutral
 14 condition, which was the easiest switch trial.

15 ³ Note there were violations of normality and some homogeneity of variance violations in
 16 follow-up ANOVAs for the follow-up time point, so these must be interpreted with
 17 caution.

18 ⁴ Multiple regression analyses using the cohort as a single continuous group and physical
 19 activity / physiological measures as predictors did not alter these outcomes. Medium to
 20 low power for detection also has to be considered when interpreting some of the non-
 21 significant findings.

LONG-TERM HIGH-EFFORT ENDURANCE EXERCISE IN OLDER ADULTS

1 Table I

2 Means, Standard Deviations, and Significances between Supervet and Control Group for Demographics

Measure	Supervets Mean (SD)	Controls Mean (SD)	Significance at T0	Supervets Mean (SD)	Controls Mean (SD)	Significance at T1
<u>Demographics:</u>						
Sex^a	6 female	9 female	$p = .158$	6 female	7 female	$p = .577$
Age (years)	67.88 (5.45)	68.35 (5.81)	$p = .771$ $d = 0.09$	69.29 (5.07)	69.21 (5.83)	$p = .965$ $d = 0.02$
Education (years)^b	15.26 (3.59)	16.18 (3.38)	$p = .363^{\ddagger}$ $d = 0.27$	16.00 (3.59)	16.16 (3.45)	$p = .888$ $d = 0.05$
IQ^c	117.66 (3.92)	119.93 (4.51)	$p = .077^{\ddagger}$ $d = 0.55$	118.37 (5.72)	120.70 (4.34)	$p = .170^{\ddagger}$ $d = 0.47$
Depression^d	0.52 (0.89)	1.18 (1.71)	$p = .139^{\ddagger}$ $d = 0.52$	0.71 (1.10)	1.11 (1.82)	$p = .428^{\ddagger}$ $d = 0.27$

3 Note: a. Chi-squared test used. b. Years of full-time education. c. Full Scale Pre-morbid Intelligence Quotient derived from

4 National Adult Reading Test. d. From Geriatric Depression Scale score. $\ddagger$ - From 1000-sample bootstrap results.

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LONG-TERM HIGH-EFFORT ENDURANCE EXERCISE IN OLDER ADULTS

1 **Table II**
2 *Means, Standard Deviations, and Significances between Supervet and Control Groups Physiological,*
3 *Diet, Social, and Cognitive Activities Characteristics*

Measure	Supervet s Mean (SD)	Controls Mean (SD)	Significanc e at T0	Supervets Mean (SD)	Controls Mean (SD)	Significance with T0 and T1
<u>Physical Activity:</u>						
PASE^a	221.70 (71.24)	169.39 (66.03)	$p = .011^*$ $d = 0.77$	230.60 (60.39)	160.87 (55.12)	$p = .001^{\Omega*}$
Walking (Avg Hours / Day)	1.09 (0.76)	0.92 (0.96)		0.99 (0.70)	0.77 (0.43)	
Light Sports (Avg Hours / Day)	0.45 (0.59)	0.46 (0.92)		0.60 (0.70)	0.38 (0.67)	
Moderate Sports (Avg Hours / Day)	0.20 (0.29)	0.10 (0.18)		0.37 (0.58)	0.19 (0.33)	
Strenuous Sports (Avg Hours / Day)	1.14 (1.00)	0.18 (0.38)		1.02 (0.69)	0.19 (0.31)	
Muscle Strength / Endurance Exercise (Avg Hours / Day)	0.15 (0.24)	0.03 (0.06)		0.11 (0.14)	0.02 (0.06)	
<u>Diet:</u>						
Mediterranean Diet Score	4.81 (1.62)	4.64 (1.81)	$p = .690^{\ddagger}$ $d = 0.10$	4.84 (1.89)	4.78 (1.86)	$p = .494^{\Omega}$
<u>Lung Function:</u>						
Forced Expiratory Volume 1st Second (L)	2.87 (0.72)	2.78 (0.78)	$p = .686$ $d = 0.12$	2.97 (0.66)	2.86 (0.72)	$p = .999$ $n^2p < .001$
Forced Vital Capacity (L)	3.78 (0.87)	3.38 (0.93)	$p = .153$ $d = 0.46$	3.77 (0.84)	3.36 (0.81)	$p = .235$ $n^2p = .047$
Forced Expiratory Ratio (%)	78.01 (8.93)	83.20 (8.88)	$p = .079^{\ddagger}$ $d = 0.60$	77.25 (8.92)	84.75 (9.20)	$p = .085^{\Omega}$
Peak Expiratory Flow (L/min)	411.89 (143.83)	421.95 (155.24)	$p = .875$ $d = 0.07$	481.37 (119.32)	458.25 (132.21)	$p = .963$ $n^2p < .001$
<u>Physiological:</u>						
Body Fat Males (%)	22.05 (4.07)	26.77 (4.07)	$p = .003^*$ $d = 1.20$	25.03 (4.38)	28.14 (4.09)	$p = .031^*$ $n^2p = .180$
Body Fat Females (%)	32.50 (4.19)	39.38 (6.59)	$p = .042^*$ $d = 1.28$	35.45 (2.94)	40.84 (3.44)	$p = .030^*$ $n^2p = .361$
Hand-grip Strength Male (kg)	40.65 (7.00)	36.12 (5.68)	$p = .079$ $d = 0.71$	43.69 (5.66)	37.34 (5.27)	$p = .006^*$ $n^2p = .339$
Hand-grip Strength Female (kg)	27.17 (4.71)	25.22 (3.28)	$p = .361$ $d = 0.54$	26.17 (4.70)	26.08 (3.44)	$p = .768$ $n^2p = .009$
<u>Social and Cognitive Activities:</u>						
Social Network^b	20.07 (4.74)	20.09 (6.24)	$p = .992$ $d < 0.01$	20.95 (4.30)	19.00 (7.19)	$p = .728^{\Omega}$
Cognitive Activities^c	46.48 (10.49)	50.89 (6.81)	$p = .114^{\ddagger}$ $d = 0.50$	48.86 (8.24)	50.48 (7.60)	$p = .434^{\Omega}$

4 Note: a. Physical Activity Scale for the Elderly score. b. From Lubben Social Network Scale. c. From Florida Cognitive
5 Activity Scale. $\ddagger$ - From 1000-sample bootstrap results. Ω - From mixed ANOVA on trimmed means *- Statistically significant

LONG-TERM HIGH-EFFORT ENDURANCE EXERCISE IN OLDER ADULTS

1 **Table III**
2 *Means, Standard Deviations, and Significances between Supervet and Control Groups on Speed of*
3 *Processing and Cognitive Tasks*

Measure	Time Point 0			Time Point 1		Significance with T0 and T1
	Supervets Mean (SD)	Controls Mean (SD)	Significance at T0	Supervets Mean (SD)	Controls Mean (SD)	
<u>Speed of Processing:</u>						
Simple Reaction Time (ms)	301.71	326.29	$p = .093$	300.78	333.95	$p = .066$
	(48.65)	(52.62)	$d = 0.50$	(48.80)	(92.05)	$n^2p = .086$
IIV (SD, ms) ^a	78.64	81.75	$p = .695$	94.09	86.59	$p = .734$
	(26.10)	(29.03)	$d = 0.12$	(39.30)	(41.92)	$n^2p = .003$
ICV (SD/mean * 100) ^b	25.63 (7.21)	24.55 (6.98)	$p = .599$	30.39	25.23	$p = .090$
			$d = 0.16$	(10.92)	(9.06)	$n^2p = .074$
Symbol Copy (secs/item) ^c	0.91 (0.19)	0.91 (0.17)	$p = .964$	0.89 (0.14)	0.85 (0.14)	$p = .909$
			$d = 0.01$			$n^2p < .001$
Trails A (secs) ^d	30.95 (6.88)	31.90	$p = .971$	31.74	32.17	$p = .963^{\Omega}$
		(11.33)	$d = 0.11$	(6.67)	(13.04)	
<u>Executive Function:</u>						
DSST Higher Mental Function (secs/item) ^e	1.12 (0.28)	1.00 (0.31)	$p = .167$	1.09 (0.32)	1.03 (0.27)	$p = .385$
			$d = 0.42$			$n^2p = .020$
Trails B - A (secs) ^f	39.90	26.32	$p = .093$	35.63	23.14	$p = .500^{\Omega}$
	(27.03)	(12.55)	$d = 0.64$	(14.34)	(12.35)	
Verbal Fluency (total correct) ^g	45.89 (9.82)	50.23	$p = .657$	48.86	50.63	$p = .580$
		(14.27)	$d = 0.37$	(9.74)	(15.31)	$n^2p = .008$
<u>Memory:</u>						
Incidental Memory (percent recalled) ^g	41.20	48.15	$p = .382^{\ddagger}$	49.71	48.37	$p = .720$
	(21.85)	(27.74)	$d = 0.29$	(25.76)	(23.55)	$n^2p = .004$
Episodic Memory (percent recalled)	28.42	30.71	$p = .635^{\ddagger}$	28.33	26.15	$p = .859$
	(13.44)	(11.91)	$d = 0.01$	(11.13)	(14.02)	$n^2p = .001$
Backward Digit Spans (number of digits recalled)				5.76 (1.04)	5.95 (1.55)	$p = .673^{\ddagger}$
Subjective Prospective Memory ^h	19.01 (3.21)	19.00 (3.53)	$p = .991^{\ddagger}$	18.76	19.95	$p = .667^{\Omega}$
			$d < 0.01$	(2.86)	(3.11)	
Subjective Retrospective Memory ^h	18.06 (3.95)	17.18 (3.17)	$p = .393^{\ddagger}$	18.14	18.59	$p = .603^{\Omega}$
			$d = 0.25$	(3.07)	(3.56)	
<u>Attention:</u>						
Visual Search (total no. correct) ⁱ	57.89	56.09 (9.32)	$p = .587^{\ddagger}$	56.90	54.05	$p = .936^{\Omega}$
	(12.93)		$d = 0.16$	(12.28)	(10.84)	

4 Note: a. Intra-individual Variability. b. Intra-individual Coefficient of Variability. c. From Digit Symbol Substitution Task
5 for 30 seconds. d. Trail Making Test part A time taken. e. Digit Symbol Substitution Task, time per item accounting for
6 copying speed. f. Trail Making Test time taken for part B with part A subtracted. g. From Digit Symbol Substitution Task. h.
7 From the Prospective and Retrospective Memory Questionnaire. I. From Map Test of Everyday Attention. $\ddagger$ - From 1000-
8 sample bootstrap result. Ω - From mixed ANOVA on trimmed means. * - Statistically significant.

LONG-TERM HIGH-EFFORT ENDURANCE EXERCISE IN OLDER ADULTS

1 **Table IV**

2 *Means, Standard Deviations, and Significances Between Supervet and Control Groups on the Card Sort*

3 *PM Task*

Condition	Time Point 0			Time Point 1		
	Supervets Mean (SD)	Controls Mean (SD)	Significance at T0	Supervets Mean (SD)	Controls Mean (SD)	Significance with T0 and T1
PM Accuracy (%)	77.98 (28.75)	84.38 (18.53)	$p = .410^{\ddagger}$ $d = 0.27$	92.19 (12.81)	90.41 (11.29)	$p = .993$ $n^2p = .001$
Card Sort Accuracy without PM (%)	97.36 (2.27)	97.44 (2.38)	$p = .924^{\ddagger}$ $d = 0.04$	97.16 (2.89)	98.18 (1.68)	$p = .568^{\Omega}$
Card Sort Accuracy with PM (%)	93.87 (4.34)	96.22 (2.33)	$p = .038^*$ $d = 0.69$	95.51 (3.12)	95.75 (4.19)	$p = .156^{\Omega}$
Card Sort Reaction Time without PM (ms)	557.55 (77.23)	548.99 (61.13)	$p = .722$ $d = 0.12$	566.23 (77.46)	566.01 (62.64)	$p = .547^{\Omega}$
Card Sort Reaction Time with PM (ms)	697.37 (78.85)	676.20 (77.62)	$p = .335$ $d = 0.28$	713.42 (69.25)	702.67 (102.32)	$p = .847^{\Omega}$

4 Note: $\ddagger$ - From 1000-sample bootstrap result. Ω – From mixed ANOVA on trimmed means. * - Statistically significant.

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LONG-TERM HIGH-EFFORT ENDURANCE EXERCISE IN OLDER ADULTS

1 **Table V**
2 *Means and Standard Deviations on the McDaniel PM Task for PM Accuracies, Ongoing Category*
3 *Decision Task Accuracies, and Ongoing Category Decision Task Reaction Times*

Task Condition	<u>Time Point 0</u>		<u>Time Point 1</u>	
	Supervet Mean (SD)	Control Mean (SD)	Supervet Mean (SD)	Control Mean (SD)
PM Accuracy				
Focal PM (%)	89.39 (26.00)	88.89 (25.57)	91.67 (19.25)	97.62 (8.91)
Non-Focal PM (%)	62.12 (38.89)	70.37 (41.05)	56.25 (35.94)	76.19 (33.15)
Ongoing Category Decision Task Accuracy				
No PM (%)	95.54 (2.31)	95.96 (2.42)	96.29 (2.54)	95.62 (2.73)
Focal PM (%)	95.83 (2.07)	95.75 (1.95)	95.92 (1.78)	93.64 (8.15)
Non-Focal PM (%)	95.62 (1.92)	95.12 (2.33)	95.17 (2.55)	95.48 (2.23)
Ongoing Category Decision Task Reaction Time				
No PM (ms)	1396.81 (291.31)	1404.57 (316.10)	1239.52 (159.75)	1359.82 (323.64)
Focal PM (ms)	1519.76 (316.99)	1472.48 (319.86)	1395.84 (179.76)	1513.19 (422.99)
Non-Focal PM (ms)	1887.80 (431.72)	1732.57 (405.14)	1726.73 (269.58)	1728.35 (424.93)

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LONG-TERM HIGH-EFFORT ENDURANCE EXERCISE IN OLDER ADULTS

1 Table VI

2 Means and Standard Deviations for RVIP Task, Number of Correct Responses and Reaction Times (ms)

Bin	<u>Time Point 0</u>				<u>Time Point 1</u>			
	<u>Supervets</u>		<u>Controls</u>		<u>Supervets</u>		<u>Controls</u>	
	Correct (SD)	RT (SD)	Correct (SD)	RT (SD)	Correct (SD)	RT (SD)	Correct (SD)	RT (SD)
1	6.73 (1.37)	492.42 (63.46)	6.59 (1.79)	519.36 (80.17)	7.19 (0.75)	491.61 (61.21)	6.31 (1.89)	511.30 (72.91)
2	5.50 (2.18)	530.88 (64.54)	6.36 (2.13)	508.41 (75.77)	5.81 (1.40)	530.41 (66.31)	6.31 (2.21)	529.26 (56.10)
3	5.23 (1.86)	523.36 (77.11)	5.59 (1.92)	511.91 (72.07)	6.00 (1.58)	522.30 (75.73)	6.19 (2.34)	518.85 (64.30)
4	5.73 (1.37)	524.55 (52.13)	5.82 (1.76)	530.25 (75.12)	5.95 (1.36)	533.53 (76.36)	6.19 (2.26)	529.65 (75.14)
5	5.31 (2.09)	523.00 (52.81)	5.55 (2.26)	537.39 (87.84)	5.48 (1.57)	529.61 (72.74)	5.06 (2.29)	569.38 (90.75)

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LONG-TERM HIGH-EFFORT ENDURANCE EXERCISE IN OLDER ADULTS

1 **Table VII**

2 *Means and Standard Deviations for Stroop-Switch Task Reaction Times (ms) and Percent Errors*

Condition	Time Point 0				Time Point 1			
	Supervets		Controls		Supervets		Controls	
	Mean %		Mean %		Mean %		Mean %	
	Mean RT (SD)	Error (SD)	Mean RT (SD)	Error (SD)	Mean RT (SD)	Error (SD)	Mean RT (SD)	Error (SD)
Color:								
Incongruent:								
Switch	1020.13 (303.15)	14.38 (16.06)	1018.68 (268.01)	18.63 (18.87)	925.13 (181.06)	12.56 (17.08)	986.26 (169.35)	11.17 (11.34)
Non-Switch	1035.75 (306.19)	14.96 (15.81)	1037.82 (219.88)	16.47 (15.07)	952.75 (186.47)	19.93 (18.61)	997.00 (202.16)	10.14 (8.02)
Neutral:								
Switch	912.16 (255.06)	6.65 (10.49)	926.89 (191.37)	9.52 (9.42)	811.12 (153.16)	8.26 (17.80)	876.61 (129.08)	1.93 (4.45)
Non-Switch	870.95 (210.24)	4.83 (10.18)	940.57 (219.85)	4.77 (9.02)	852.27 (168.91)	8.00 (13.75)	881.00 (193.76)	2.36 (4.58)
Word:								
Incongruent:								
Switch	795.40 (182.97)	3.55 (7.16)	878.62 (211.71)	2.34 (5.46)	755.82 (191.29)	3.75 (6.33)	829.84 (209.95)	5.03 (5.60)
Non-Switch	778.62 (240.93)	1.08 (4.00)	780.26 (153.86)	1.52 (4.18)	725.83 (162.13)	1.36 (4.45)	740.47 (124.01)	2.40 (4.90)
Neutral:								
Switch	739.40 (170.82)	8.29 (13.13)	872.67 (191.09)	6.16 (7.65)	752.27 (180.34)	5.93 (9.53)	804.11 (197.82)	7.15 (7.18)
Non-Switch	755.37 (160.76)	5.81 (10.67)	768.33 (157.91)	4.79 (6.98)	717.98 (160.54)	3.06 (7.39)	776.00 (156.15)	1.73 (3.98)

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