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Original research

## Physical exercise and cognitive function across the life span: Results of a nationwide population-based study

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### ABSTRACT

**Objectives:** To examine cross-sectional and longitudinal associations between physical exercise and cognitive function across different age groups in a nationwide population-based sample of adults aged 18–79 years in Germany.

**Design:** Cross-sectional/prospective.

**Methods:** Cognitive function was assessed in the mental health module of the German Health Interview and Examination Survey for Adults (DEGS1-MH, 2009–2012, n = 3535), using a comprehensive neuropsychological test battery. Cognitive domain scores for executive function and memory were derived from confirmatory factor analysis. Regular physical exercise in the last three months was assessed by self-report and defined as no exercise, <2 and ≥2 h (hours) of exercise per week. A subgroup of DEGS1-MH participants who previously participated in the German National Health Interview and Examination Survey 1998 (GNHIES98, 1997–1999, n = 1624) enabled longitudinal analyses with a mean follow-up of 12.4 years.

**Results:** Compared to no exercise, more weekly physical exercise was associated with better executive function in cross-sectional (<2 h:  $\beta=0.12$ ; ≥2 h:  $\beta=0.17$ ; all  $p<0.001$ ) and longitudinal analyses (<2 h:  $\beta=0.14$ ,  $p<0.001$ ; ≥2 h:  $\beta=0.15$ ,  $p=0.001$ ) using linear regression models adjusted for age, sex, education, smoking, alcohol consumption, fruit and vegetable consumption and obesity. Slightly weaker associations were found for memory in cross-sectional (<2 h:  $\beta=0.08$ ,  $p=0.009$ ; ≥2 h:  $\beta=0.08$ ,  $p=0.026$ ) and longitudinal analysis (<2 h:  $\beta=0.09$ ,  $p=0.036$ ; ≥2 h:  $\beta=0.08$ ,  $p=0.114$ ). There was no evidence of interaction between physical exercise and age.

**Conclusions:** Higher levels of physical exercise were associated with better executive function and memory in cross-sectional and longitudinal analyses with no evidence for differential effects by age.

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### 1. Introduction

Cognitive impairment is a rising concern among aging populations across the world.<sup>1,2</sup> Global public health policy is increasingly focusing attention on prevention strategies to minimize the risks of developing cognitive impairment, especially given the lack of currently available curative therapy for dementia.<sup>1,3</sup> Increasing physical activity levels have been central to public health strategies for the prevention of cardiovascular disease for decades. Growingly, physical activity is regarded as an important prevention target for dementia and cognitive decline.

Studies examining the relationships between physical activity and cognition have focused mainly on older adults and the development of impaired cognitive function. Results from prospective studies, including meta-analyses, indicate positive effects of physical activity on cognitive function,<sup>4</sup> dementia risk and cognitive decline.<sup>5</sup> However, there is less evidence available for young or middle-aged adults, despite this being a potentially important target period for maintaining brain health. A recent systematic review for this age-group (18–50 years) reported positive associations between physical activity and cognitive function in studies with mostly small, non-population based, cross-sectional samples.<sup>6</sup> Longitudinal studies in this age group have reported mixed results on associations of physical activity with cognitive function.<sup>7–9</sup> Therefore, studies with large longitudinal population-based samples are

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needed to examine the differential effects of physical activity on cognitive function across the lifespan.

In a large, nationwide population-based sample of cognitively healthy adults aged 18 to 79 years in Germany we examine relationships between physical exercise and cognitive function across the life span. The aim of this study is: (1) to examine cross-sectional and longitudinal associations between physical exercise and cognitive function in two main cognitive domains (executive function and memory) and, (2) to examine whether these associations differ across the age span.

## 2. Methods

The design of the nationwide population-based German Health Interview and Examination Survey for Adults (DEGS1, November 2008–November 2011) and its mental health module (DEGS1-MH, September 2009–March 2012) have been described in detail elsewhere.<sup>10,11</sup> In brief, DEGS1 combines a longitudinal sample of individuals who have previously participated in the nationwide population-based German National Health Interview and Examination Survey 1998 (GNHIES98, October 1997–March 1999)<sup>12,13</sup> and a new cross-sectional sample also derived by a two-stage random sampling procedure of communities and local population registers.<sup>11</sup> The aim of these surveys is to obtain comprehensive information about the health of the community-living population aged 18–79 years in Germany and monitor both physical and mental health.

DEGS1 was approved by the federal and state commissioners for data protection and by the ethics committee of Charité-Universitätsmedizin Berlin (No. EA2/047/08). DEGS1-MH was additionally approved by the ethics committee of the Technische Universität Dresden (No. EK174062009). GNHIES98 was approved by the federal office for data protection. Written informed consent was provided by all participants prior to the interviews.

Data was collected by self-administered written questionnaires, standardised physician-administered computer-assisted personal interviews (CAPI), and a range of physical, laboratory and other measurements in DEGS1 and GNHIES98. Standardised computer-assisted Composite International Diagnostic Interview (CIDI), a detailed neuropsychological test battery, and self-administered questionnaires were used in DEGS1-MH.

There were 7124 participants in the GNHIES98 and the survey had an overall response rate of 61%.<sup>13</sup> DEGS1 response rates were 64% for previous GNHIES98 participants and 42% for the newly sampled participants.<sup>11</sup> Of 7987 DEGS1 participants aged 18–79 years, 4483 individuals also participated in DEGS1-MH.<sup>10</sup> The median time lag between DEGS1 and DEGS1-MH was 6 weeks (interquartile range: 5–25 weeks).

For the present cross-sectional analyses, the following exclusion criteria were consecutively applied to the DEGS1-MH sample ( $n = 4483$ ): neuropsychological test battery not completed ( $n = 94$ ); neuropsychological test battery completed by telephone ( $n = 483$ ); first language not German ( $n = 237$ ); deafness ( $n = 1$ ); profound learning difficulties ( $n = 1$ ); or due to missing data in cognitive domain scores ( $n = 24$ ), physical exercise ( $n = 46$ ) or any covariable ( $n = 62$ ). Therefore, a total of 3535 DEGS1-MH participants were included in these cross-sectional analyses.

For the longitudinal analyses, 1666 of 3643 DEGS1-MH participants with valid data in cognitive domain scores had previously participated in GNHIES98 and were eligible for longitudinal analyses. Of these, 42 participants were excluded because of missing data in GNHIES98 variables (i.e. physical exercise ( $n = 19$ ) or any covariables ( $n = 23$ )). Thus, 1624 participants were included in the longitudinal analysis. Mean follow-up time was 12.4 years (range, 10.5–14.4 years).

Cognitive function was assessed in DEGS1-MH by a comprehensive neuropsychological test battery<sup>10</sup> comprising the digit span backward test (DSBT) from the Wechsler Intelligence Scale for Adults,<sup>14</sup> the trail making tests (TMT-A, TMT-B),<sup>15</sup> the letter digit substitution test (LDST),<sup>16</sup> a verbal fluency test (VFT) from The Consortium to Establish a Registry for Alzheimer's Disease (CERAD),<sup>17,18</sup> and immediate (Trial 1–3) and delayed (Trial 4) recall of a 10-word list from CERAD (see Supplementary material Table A.1 for details on measurement).<sup>17,18</sup> All test scores were z-standardized. To permit comparable interpretation of all tests, the direction of TMT-A and TMT-B z-scores were reversed. Thus, larger z-scores indicate better performance for all tests.

Cognitive domain scores for executive function and memory were derived from confirmatory factor analysis in the form of latent factor scores, if at least three tests for executive function (DSBT, TMT-A, TMT-B, LDST, VFT) and memory (immediate and delayed recall) were available.<sup>19</sup> A two-factor solution with inter-correlated factors provided an excellent fit to the data, significantly outperforming a one-factor solution which yielded insufficient fit to the data. Loadings of the neuropsychological test scores on executive function ranged between 0.480 (DSBT) and 0.835 (LDST); and loadings on memory ranged between 0.705 (Trial 1 immediate recall) and 0.861 (Trial 4 delayed recall). Variance and mean of derived factor scores were fixed to one and zero, respectively, similar to a z-score. Higher values of cognitive domain scores represent better cognitive function.

In both surveys, regular physical exercise in hours (h) per week in the last three months was assessed by self-administered written questionnaire with the following question: "How often do you engage in physical exercise?"<sup>20</sup> The five response categories referred to one week: "not at all", "less than 1h", "regularly 1–2h", "regularly 2–4h", and "regularly more than 4h". To receive sufficient cell sizes for analyses, scores were categorized as 0h/week (no exercise), <2h/week or  $\geq 2$ h/week. The cut-off of  $\geq 2$ h per week was chosen because this cut-off-point comes closest to the 150 min moderate-intensity physical activity per week recommendation.<sup>21</sup>

Other measures were assessed comparably in DEGS1 and GNHIES98. Information on age and sex was obtained from local population registers. Level of education (low, medium, high) was measured according to the Comparative Analysis of Social Mobility in Industrial Nations (CASMIN) classification,<sup>22</sup> based on self-reported information on school, academic and professional qualifications.

Behavioral risk factors were assessed by self-administered questionnaires and included: current smoking (yes/no), alcohol consumption 0g/d;  $\leq 10/20$ g/d women/men;  $>10/20$ g/d women/men;<sup>23</sup> and the intake of fruit and vegetables in the last four weeks (<3 or  $\geq 3$  portions per day) according to a Food Frequency Questionnaire.<sup>24</sup> Obesity (yes/no) was defined as a body mass index of  $\geq 30$  kg/m<sup>2</sup> based on standardized measurements of body weight and height.

Cross-sectional associations between physical exercise categories and cognitive domain scores (executive function and memory) were examined by unadjusted and adjusted linear regression analyses. Several a priori defined sociodemographic (age, sex, level of education) and lifestyle factors (smoking, alcohol consumption, fruit and vegetable consumption, obesity) which are known to be associated with physical activity<sup>25</sup> and cognitive function<sup>26</sup> were taken into account as potential confounding factors and were included in adjusted models. Regression models were adjusted in three steps: (1) for age (mean centered and squared) and sex, (2) additionally for level of education and (3) additionally for behavioral risk factors (smoking, alcohol consumption, fruit and vegetable consumption, obesity).

To test longitudinal associations between physical exercise at baseline and cognitive function at follow-up, a similar approach to

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