

## Mini Review

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# Exercise-induced changes in basal ganglia volume and their relation to cognitive performance

Becker L<sup>1</sup>, Kutz DF<sup>2</sup>, Voelcker-Rehage C<sup>1\*</sup><sup>1</sup>Institute of Human Movement Science and Health, Sports Psychology, Technische Universität Chemnitz, Thüringer Weg 11, 09126 Chemnitz, Germany<sup>2</sup>Institute of Human Movement Science and Health, Theory and Practice of Sports, Technische Universität Chemnitz, Thüringer Weg 11, 09126 Chemnitz, Germany

## Article Info

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### \*Correspondence:

Dr. Claudia Voelcker-Rehage

Institute of Human Movement Science and Health,  
Sports Psychology, Technische Universität Chemnitz,  
Thüringer Weg 11, 09126 Chemnitz, GermanyE-mail: [claudia.voelcker-rehage@hsw.tu-chemnitz.de](mailto:claudia.voelcker-rehage@hsw.tu-chemnitz.de)

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## Introduction

Physical activity, especially cardiovascular fitness training, has been shown to enhance cognitive performance and to counteract age-related cognitive decline<sup>1-5</sup>. Furthermore, regular physical activity has been demonstrated to diminish age-related volume-shrinkage in several brain regions particularly in the prefrontal cortex and hippocampus<sup>6-10</sup>. In the same vein, physical activity and high levels of cardiovascular fitness seem to enhance neurocognition during childhood<sup>11-13</sup>. In this context, the basal ganglia and its components, the caudate nucleus, the putamen and the globus pallidus, are of special interest as animal research indicates that exercise also seems to influence the molecular architecture and the metabolic capacity of the basal ganglia<sup>14,15</sup>. Besides their fundamental role in motor execution<sup>16</sup>, the basal ganglia are also involved in many cognitive functions like mental flexibility<sup>17</sup>, task-switching ability<sup>18</sup> and cognitive control<sup>19</sup>. Furthermore, age-related disorders like Parkinson's disease are related to a decline in the dopamine circuits of the basal ganglia<sup>20,21</sup>.

The striatum is the input nucleus of the basal ganglia and is composed of caudate nucleus and putamen. The pars interna of the globus pallidus is (together with the substantia nigra pars reticulata) the output region of the basal ganglia and conveys information from the striatum to the thalamus and back to the frontal areas<sup>22</sup>. The striatum, which is essential for cognitive flexibility and attentional control, shows an increase during childhood and adolescence<sup>23,24</sup> and a particularly rapid and early age-related change<sup>9,25</sup> in older adults. Furthermore, the described cognitive functions are essential for academic success of children and young adults. Thus, it is of particular interest to find appropriate interventions that could mitigate both the volume-shrinkage and the (presumably) related cognitive decline in older adults and/or that could support academic success in children. In this review, we will summarize research that investigated whether physical activity has the potential to be such an intervention. First, we will show that neuroplasticity in the basal ganglia is possible in principle. Second, we will report studies where the relationship between physical fitness level and volume of the basal ganglia and its relation to cognitive performance were investigated. Besides cross-sectional studies, we will report studies that investigated exercise-induced changes in the volume of the basal ganglia and related changes in cognitive performance after long-term fitness interventions.

## Neuroplasticity of basal ganglia volumes

The basal ganglia are, prospectively, positively influenced by physical activity because animal research indicated that cardiovascular exercise does not only seem to influence angiogenesis, synaptogenesis and the release of growth hormones in motor cortex<sup>26</sup>, cerebellum<sup>27</sup> and hippocampus<sup>28,29</sup>, but also in the basal ganglia<sup>15</sup>. Furthermore, the striatum is the second region – besides the hippocampus – where neurogenesis in humans has been proven<sup>30,31</sup>. Plasticity of basal ganglia has been proven in motor learning studies. It has been shown that motor learning can lead to changes in basal ganglia volumes after minimal training. For example, Hamzei and colleagues<sup>32</sup> found that young adults (mean age 23.8 years) showed an increase in the volume of the right ventral striatum after three days of a 30-minute training of writing their signature with the non-dominant hand. Taubert and colleagues<sup>33</sup> found structural changes in the right putamen of young adults ( $25.9 \pm 2.8$  years) after six weeks of a dynamic whole-body balancing training (1 training session per week; 45 minutes each). Thus, neuroplasticity in the basal ganglia is possible in general. However, from these learning studies it cannot be determined whether structural changes can also be induced by cardiovascular training and other forms of exercise (as opposed to motor skill learning), and whether changes in the gray matter lead to additional changes in cognitive performance. Furthermore, it cannot be concluded whether the reported effects can be generalized to other age groups.

## Relations between physical activity, volume of basal ganglia and cognitive performance

So far, only a few human studies have investigated the association between regular physical activity and the volume of basal ganglia and their relation to cognitive performance. These studies differ with regard to the sample (children versus adult subjects), study design (cross-sectional versus interventional studies), type of exercise (cardiovascular versus coordinative exercise) and outcome variables (basal ganglia volume and additionally cognitive performance). An overview about the reported studies is provided in Table 1. First, we will give an overview of cross-sectional studies that compared volumes of basal ganglia between groups with different levels of physical fitness (e.g., high-fit vs. low-fit) in relation to their cognitive performance. Second, interventional studies that investigated the impact of fitness interventions on cognitive performance and on the volume of basal ganglia will be reported.

### Cross-sectional studies

Chaddock and colleagues<sup>34</sup> found that higher cardiovascular fitness levels were associated with higher volumes of the left caudate nucleus, the bilateral putamen

and the bilateral globus pallidus in preadolescent children ( $N = 55$ ,  $10.0 \pm 0.6$  years; Region of Interest (ROI) analysis, of the striatum and globus pallidus, FMRIB's Software Library (FSL)). Additionally, the volumes of the putamen and the globus pallidus positively correlated with performance in a Flanker task. The Flanker task is a selective attention paradigm, that is often employed to examine cognitive control performance (especially the aspect of cognitive interference control)<sup>35</sup>. The classical task is for example to respond to an arrow's direction that is either congruent or incongruent to the direction of neighboring arrows. Chaddock and colleagues<sup>34</sup> concluded that the association between the volume of the dorsal striatum and the cognitive control performance supports the assumption that these nuclei are also involved in motor integration and response resolution. In a follow-up study, Chaddock and colleagues<sup>36</sup> found that approximately one year later, the high-fit children still showed superior performance in the Flanker task compared to the low-fit children. The authors attributed these better cognitive performances to the previously measured higher fitness levels and to the greater volumes of the putamen and globus pallidus measured one year earlier.

For healthy young adults ( $N = 33$ ,  $23.9 \pm 3.4$  years), Peters and colleagues<sup>37</sup> found that higher levels of cardiovascular fitness were related to larger volumes of the basal ganglia (whole brain analysis, voxel-based morphometry (VBM)). No differences in memory performance were found between the groups. The authors did not investigate other cognitive functions (like cognitive control performance) in that the basal ganglia might be more involved.

For healthy older adults ( $N = 179$ ,  $66.6 \pm 5.6$  years), Verstynen and colleagues<sup>38</sup> found (by means of the same analysis tool as Chaddock and colleagues<sup>34, 36</sup>) that higher cardiovascular fitness levels correlated positively with task-switching performance and thus with cognitive flexibility. Furthermore, the volumes of the caudate nucleus, the putamen and the globus pallidus were positively related to task-switching performance as well. No effects were found for the Flanker task. A mediation analysis revealed that the volume of the caudate nucleus partially explained the relationship between the cardiovascular fitness level and the task-switching performance, but no mediating effect between the volume of the putamen or the volume of the globus pallidus and the task-switching performance was found.

In most studies, only the association of cardiovascular fitness level (trained by exercises like walking, swimming, bicycling) on the volume of basal ganglia and on cognitive performance was examined. Motor fitness level, comprising coordinative abilities such as balance, eye-hand coordination, and arm-leg coordination, can be associated with cognitive performance as well<sup>5</sup>. Niemann and

Authors	Fitness type	Group (mean age in years $\pm$ SD)	N	Cognitive tests	Main findings
<b>Cross-sectional</b>					
Chaddock et al. (2010)	Cardiovascular fitness	Children (10.0 $\pm$ 0.6)	55 (25 high-fit, 30 low-fit)	FT	Relationship between basal ganglia volume and interference in the FT for the putamen (left: $r = -.33$ , $p = .01$ ; right: $r = -.247$ , $p = .06$ ) and the globus pallidus (left: $r = -.201$ , $p = .05$ ; right: $r = -.35$ , $p = .009$ ).
Chaddock et al. (2012)	Cardiovascular fitness	Children (10.1 $\pm$ 0.6)	32 (14 high-fit, 18 low-fit)	FT	Relationship between basal ganglia volume (measured 1 year earlier) and reaction time in the FT (measured in the follow-up session) for the putamen ( $r = -.37$ - $-.43$ , $p < .05$ ) and the globus pallidus ( $r = -.37$ - $-.49$ , $p < .05$ ).
Peters et al. (2009)	Cardiovascular fitness	Young adults (23.9 $\pm$ 3.4)	33 (21 high-fit, 12 low-fit)	MT	Volumes of the right globus pallidus and the bilateral putamen were larger for the high-fit than for the low-fit participants ( $p < .001$ ). No differences in memory performance were found between participants with different fitness levels.
Verstynen et al. (2012)	Cardiovascular fitness	Adults (66.6 $\pm$ 5.6)	179	TS, FT	Mediation pathway between fitness level and accuracy in the TS through volume of the caudate nucleus ( $ab = .0037$ , $p = .003$ , $R^2 = .1661$ ). No effects for the FT.
Niemann et al. (2014)	Cardiovascular and motor fitness	Adults (68.5 $\pm$ 3.6)	70	FT, VS	No relationship between cognitive performance, CF level and the volume of the basal ganglia. The volume of the whole basal ganglia volume partially moderated the relationship between MF and cognitive performance for participants with small basal ganglia volumes in the FT ( $p < .10$ ).
<b>Interventional</b>					
Erickson et al. (2011)	Cardiovascular fitness	Adults (67.6 $\pm$ 5.8)	120 (60 intervention, 60 control group)	MT	No change of the volume of the caudate nucleus in the intervention group. No relationship between caudate nucleus volume and MT performance.
Niemann et al. (2014)	Cardiovascular and motor fitness	Adults (cardiovascular fitness: 67.7 $\pm$ 2.8; motor fitness: 69.5 $\pm$ 4.7; control group: 69.6 $\pm$ 3.4)	36 (13 cardiovascular fitness intervention, 14 motor fitness intervention, 9 control group)	FT, VS	A marginally significant effect ( $p = .065$ ) of the intervention on the volume of the basal ganglia was found for CF training. The MF training increased the volumes of both the caudate nucleus ( $p = .05$ ) and the globus pallidus ( $p = .022$ ). Accuracy in the FT was positively associated with MF training ( $p = .019$ , $\eta^2 = .45$ ), but not with CF training.

Note: FT: Flanker task; TS: task switching task; MT: memory task; VS: visual search task; CF = cardiovascular fitness; MF = motor fitness.

**Table 1.** Human studies that investigated both the basal ganglia volumes and the cognitive performance.

colleagues<sup>39</sup> showed (ROI analysis of basal ganglia, manual morphometry) that the total volume of the basal ganglia and the volumes of the putamen and the globus pallidus partially explained the relationship between motor fitness level (but not cardiovascular fitness level) and cognitive control performance in a Flanker task in healthy older adults ( $N = 70$ , 68.5  $\pm$  3.6 years). In participants with low basal ganglia volume, the motor fitness level was positively related to cognitive control performance. However, this relationship was not found in participants with large

volumes of the basal ganglia. For a Visual Search task (as a measure of perceptual speed), the motor fitness level predicted cognitive performance, but no association with the volume of basal ganglia was found.

### Interventional studies

For healthy older adults ( $N = 60$ , 67.6  $\pm$  5.8 years), Erickson and colleagues<sup>40</sup> found no change in the volume of the caudate nucleus in an intervention group that participated in a 12-month cardiovascular training (ROI

analysis of the caudate nucleus, FSL). In addition, no correlation between the fitness level and the volume of the caudate nucleus was found. Interestingly, the authors found a decrease in the volume of the caudate nucleus in their stretching exercise control group across one year. This might indicate a general age-related decline in the caudate nucleus volume in the control group and preservation (i.e., a non-decline – probably due to the cardiovascular exercise) in the intervention group. Niemann and colleagues<sup>39</sup> investigated healthy older adults in both a one-year cardiovascular intervention (N = 13, 67.7 ± 2.8 years) and a one-year motor fitness level intervention (a coordination training, N = 14, 69.5 ± 4.7 years). They found that the coordination training increased the volumes of both the caudate nucleus and the globus pallidus (ROI analysis of basal ganglia, manual morphometry). The authors attributed this effect to the constant demand on adapting to new tasks in the coordination training, involving the same regions as in early stages of motor learning (e.g., the caudate nucleus<sup>41</sup> and the globus pallidus<sup>22</sup>). For the cardiovascular intervention, only a marginally significant effect (p = .065) of the intervention on the volume of the basal ganglia was found, indicating an volume increase during the first six months of the intervention and a decrease during the second half of the intervention. Cognitive control performance was positively associated with coordination training as well, but not with cardiovascular training. However, there was no direct association between the change in the volume of the basal ganglia after motor fitness intervention and the increase in cognitive performance.

## Discussion

Although the impact of physical activity on the volume of basal ganglia and its relation to cognitive performance has been sparsely examined in humans, there is some evidence for a direct relation between these factors in human research. Correlations were found for both cardiovascular and motor fitness level interventions. However, the reported effects are divergent.

For children, only one study (and a one year Follow-up study) investigated the relation between cardiovascular fitness and the volume of the basal ganglia and cognitive performance. The authors found an effect for the putamen and the globus pallidus<sup>34,35</sup>.

For older adults, the volume of the caudate nucleus explained the relationship between their cardiovascular fitness level and their cognitive performance in a cross-sectional data set<sup>38</sup>. Considering the high relevance of the caudate nucleus for cognitive flexibility, a high fitness level (correlating with the volume of the caudate nucleus) might prevent the age-related decline in mental flexibility performance. Physical activity has therefore the potential to increase the quality of life and the everyday functioning of older adults.

In contrast to the cross-sectional results, neither Erickson and colleagues<sup>40</sup> nor Niemann and colleagues<sup>39</sup> (in the second 6 months of their intervention) found by means of interventional designs that cardiovascular exercise (walking training) has any effect on the volume of basal ganglia (although data of Erickson and colleagues<sup>40</sup> might indicate reduced age-related decline due to regular cardiovascular activity).

While learning the appropriate walking technique might be highly processed with inclusion of the basal ganglia during the first half of the intervention of the study by Niemann and colleagues<sup>39</sup>, the adaptation of this now highly automated movement might be increasingly processed outside of the basal ganglia (e.g., in the cerebellum<sup>42</sup>) during the second half of the intervention.

Besides cardiovascular exercise, coordination training or motor fitness level training seem to be a promising means to increase basal ganglia volume. The total volume of the basal ganglia was related to coordinative aspects of fitness and partially explained the cognitive performance (for subjects with low basal ganglia volumes only)<sup>39</sup>. Furthermore, after a one-year motor fitness level intervention, the participants showed greater volumes of the caudate nucleus and the globus pallidus. Changes induced by coordination training might be related to changes in information processing<sup>43</sup> similar to early stages of motor learning. The exercise requirement might be the reason for the volume increase found in the caudate and the globus pallidus for subjects that attended the coordination training. Further research is needed to show if the same effect can be demonstrated for other populations (e.g., children, young adults, cognitive impaired participants) or for other forms of fitness training (e.g., strength training).

In the studies reported so far, if effects were found, the correlations between the volumes of the basal ganglia and the cognitive performances were always positive. This means that the impact of physical activity on cognitive performance corresponds to higher volumes of the basal ganglia in the reported cases. Different types of exercise and fitness seem to influence basal ganglia volume, but further research is needed to investigate whether the effects are induced by the same or by different (additive or sole) mechanisms. Furthermore, volume changes seem to occur on different time lines<sup>32,33,44</sup>.

In this line, results of studies that compared volumes of the basal ganglia between professional athletes and non-athletes are less clear. For the total striatum, larger volumes were found in skilled young basketball players (20.3 ± 1.1 years) than in a control group<sup>45</sup>. Contradictory, in the left putamen of young professional ballet dancers (24.3 ± 5.5 years)<sup>46</sup>, in the putamen and the globus pallidus of middle-aged highly skilled golfers (30.9 ± 6.2 years)<sup>47</sup> and in the left caudate nucleus of professional adolescent diving players



( $14.6 \pm 1.7$  years)<sup>48</sup>, smaller volumes than in control groups were found. Thus, the direction of change in the volume of the basal ganglia seems to differ between different sports, possibly attributable to different sport-specific requirements (e.g., recall of well learned, self-timed, highly automated movements versus instantaneous reaction to highly contextual, gameplay related contingencies). It is not yet clear if and how all induced changes in basal ganglia volume directly or indirectly result in changes in cognitive performance and whether certain mechanisms need to be induced to have translational effects from motor activity to cognitive performance.

The causes of the changes in the volumes of the basal ganglia are still unclear. Underlying biological mechanisms identified in animal research are characterized by synaptic changes including synaptogenesis, dendritic, astrocytic and glia cell hypertrophy<sup>49</sup>. These motor-demanding, exercise-based morphological brain changes might result in increasing or persistently larger volumes of the basal ganglia. However, methods used in human studies do not relate in a straightforward way to the underlying neuronal densities that can be assessed in animal research. In animal studies, results are based on invasive techniques like microscopy of brain slices. Tissue properties like cell density cell size or myelination might be possible underlying mechanisms of increased basal ganglia volume<sup>44</sup> but cannot be derived from the results of grey matter analysis in humans. Further research is necessary to clarify this.

Because of the small number of studies and the different investigated time lines, the reasons for the divergent effects especially between the cross-sectional and the interventional studies are not yet clear. Reasons might be different tools used for statistical analyses as well as for basal ganglia volume determination (semi-automated methods vs. manual morphometry)<sup>5,50</sup>, the small sample sizes in the interventional studies or differences in the absolute fitness levels between the participants. Thus, further research is needed to replicate the reported effects.

To conclude, physical activity, especially motor fitness level training, might be a promising tool that leads to structural changes in the basal ganglia. This might have the potential to diminish the cognitive decline in older adults and to support the academic success in children and young adults.

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