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Grit Is Associated with Structure of Nucleus Accumbens and Gains in Cognitive Training

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Abstract

■ There is a long-standing interest in the determinants of successful learning in children. "Grit" is an individual trait, reflecting the ability to pursue long-term goals despite temporary setbacks. Although grit is known to be predictive of future success in real-world learning situations, an understanding of the underlying neural basis and mechanisms is still lacking. Here we show that grit in a sample of 6-year-old children ($n = 55$) predicts the working memory improvement during 8 weeks of training on working memory tasks ($p = .009$). In a separate neuroimaging analysis performed on a partially overlapping sample ($n = 27$), we show that interindividual differences in grit were associated with differences in the volume of nucleus accumbens (peak voxel $p = .021$, $x = 12$, $y = 11$, $z = -11$). This was also confirmed in a leave-one-out analysis of gray matter density in the nucleus accumbens ($p = .018$). The results can be related to previous animal research showing the role of the nucleus accumbens to search out rewards regardless of delays or obstacles. The results provide a putative neural basis for grit and could contribute a cross-disciplinary connection of animal neuroscience to child psychology. ■

INTRODUCTION

The question of what makes children successful at learning has been discussed for decades. Motivation and cognitive abilities are two aspects that are frequently investigated as prerequisites of successful learning (Baddeley, 1992; Dweck, 1986). In addition, personality traits may be important. "Grit" is a personality trait that quantifies a person's ability to persist with an activity despite setbacks and to pursue long-term goals (Duckworth, Peterson, Matthews, & Kelly, 2007). This trait predicts drop-out rates in college, learning in the workplace, and success in spelling competitions (Eskreis-Winkler, Shulman, Beal, & Duckworth, 2014; Duckworth & Quinn, 2009; Duckworth et al., 2007).

Grit has been associated with successful learning, but it is based on subjective rating scales, and the neural mechanisms by which grit would influence learning are unclear. The effect of grit on success has been mediated by longer time spent in training or learning (Duckworth & Quinn, 2009; Duckworth et al., 2007), but it is unclear if it really predicts more successful learning when the amount of learning (or training) time is controlled.

The definition of grit has two aspects: motivation and self-control. This suggests two alternative hypotheses for the neural basis of grit. Motivation has mostly been studied in paradigms using external rewards, which depend on dopamine release in the ventral striatum, including the nucleus accumbens (NA; Tobler, Fiorillo, & Schultz, 2005; Wise, 2004; Schultz, Apicella, & Ljungberg, 1993). The extent to which the dopaminergic system underlies motivation independently of external rewards, such as internal motivation or grit, is unknown. Self-control, on the other hand, would be hypothesized to be related to activation and morphology of the pFC, which provides the neural basis for inhibition (Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2003), planning (Fuster, 2008), conscientiousness (Kapogiannis, Sutin, Davatzikos, Costa, & Resnick, 2013), cognitive control (Miller & Cohen, 2001), as well as impulsivity (Schilling et al., 2013). Although these latter concepts and grit have been related to each other, it has been consistently shown that grit explains an independent share of variance relative to, for example, self-control (Duckworth & Gross, 2014) and conscientiousness (Duckworth et al., 2007). In particular, although conscientiousness comprises aspect of perseverance, it also incorporates traits like responsibility, orderliness, and traditionalism (Roberts, Chernyshenko, Stark, & Goldberg, 2005); grit specifically focuses on perseverance and the ability to stick to the goal in the context of high challenge (Duckworth et al., 2007). As for self-control, Duckworth and Gross (2014) suggested that conscientiousness and self-control differ on their timescale: Although the former would be related to the ability to stay focused despite distraction within the time frame of a specific task, the latter would be related to the capacity of sticking to a goal whose achievement spans a longer time frame.

In this study, we aimed to (1) determine if grit affects training and transfer gain in a study of cognitive training in young children while training time and performance on each trial can be closely monitored and (2) determine

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the structural brain correlates of interindividual differences in grit with a well-validated method (Nemmi, Sabatini, Rascol, & Peran, 2015; Patenaude, Smith, Kennedy, & Jenkinson, 2011) in a subsample of the children included in the behavioral analysis.

We studied 106 typically developing, 6-year-old children who had volunteered to participate in an 8-week training program comprising working memory (WM) and reading, or WM and math, or math and reading, or reading-only adaptive training (Brehmer, Westerberg, & Backman, 2012; Holmes, Gathercole, & Dunning, 2009; Klingberg et al., 2005).

METHODS

Participants

This study included 106 children aged 6 years (78–87 months) recruited from 11 schools in the Stockholm County.

For the purpose of this study, three subsamples were studied:

1. One hundred fifteen children participated overall in the study. Data from 106 participants (mean age = 80.88 months, *SD* = 3.62; socioeconomic status [SES] = 4.44, *SD* = 1.05; 59 boys) who trained 32 days or more (32–43 days) were used to test the effect of WM training (n = 55, comprising the participants who have trained WM and reading, or WM and math) compared with reading-only training (used as an active control, n = 51).
2. Of the 106 participants, 55 children participated in WM training and also had a grit measure available (mean age = 80.96 months, *SD* = 3.70; SES = 4.58, *SD* = 0.90; 24 boys). Data from this subsample were used to test the association between grit and progress in the trained WM tasks (training gain) and untrained task (transfer gain), which were performed before and after completion of the training program. The same subsample was used to test associations between performance on WM tests and training enjoyment (i.e., evaluation questions) and between training gain and fluid intelligence.
3. All participants received a letter of invitation to partake in the neuroimaging part of the study. Of 106 participants, 36 participants (mean age = 81.96 months, *SD* = 3.56; SES = 4.43, *SD* = 0.89; 18 boys) volunteered to participate in the imaging protocol, which included a quality controlled T1 scan that was segmented. The MRI acquisition was performed before the beginning of the training. Twenty-seven participants had available T1. Data from this subsample was used to test the association between grit and striatal shape and associations between grit and prefrontal cortical thickness. This subsample was also used to determine the association between grit and gray matter density.

The study was approved by the research ethics committee at Karolinska University Hospital, Stockholm. Informed consent was provided by both parents by returning a signed form that was sent to them by mail together with information about the study and the contact information of the person responsible for the study. Information about SES is reported below.

Cognitive Training

Participants were assigned to one of four training groups, which included 30 min of training for each school day for 8 weeks. The training took place in the classes, where one teacher per class was in charge of monitoring the compliance of the children with the training. In the limit of possible and in accordance with academic needs, the training took place at approximately the same time of the day.

Participants were assigned to either train 50% WM and 50% mathematics, or 50% WM and 50% reading, or 50% mathematics and 50% reading, or 100% reading. Children were randomly assigned to the training groups after stratification for math and WM performance. Specifically, we ordered all participants based on baseline performance in mathematics and, if they had similar scores, based on performance on the WM tasks. The first four participants on the list were then randomized to each of the four conditions; then the next group of four participants was randomized, and so on. Supplementary Table 3 reports the distribution of gender and classroom, together with average age and grit breakdown by training groups, together with the relevant statistic for comparison. In the WM/mathematics group, WM/reading group, and mathematics/reading groups, the program automatically ensured that the child participated in training of the second domain by automatically switching training plan after 15 min of training and automatically logging out after 30 min of training. This ensured that all participants performed the same amount of training. The level of task difficulty was dynamically adapted according to a built-in algorithm that took the participant's performance into account to ensure that participants trained at the limit of their capacity. The WM training consisted of four different tasks that required the participant to immediately remember and repeat a sequence of dots or squares presented. In the mathematical training, the participants engaged in tasks such as deciding where on a number line a number would fall and how many individuals needed to be added to a group of individuals to make 10 individuals. Finally, during the reading training, the participants matched sounds to letters, were asked to spell words, matched words that rhymed, and completed crossword puzzles. More details about the training structure and tasks are reported in the Supplementary Information (SI; paragraph *Structure of the training* and *Training Tasks*).

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Transfer Gain: Pre- and Posttraining Assessment

To test transfer gain, WM capacity was tested before and after the 8-week training schedule using a visuospatial WM grid task presented on the iPad. During the WM task, participants were asked to repeat a sequence of cues presented within a 4×4 grid. The first sequence showed two dots, and each time the participant correctly repeated a sequence, the length was increased of one unit. The sequences were generated automatically, minimizing the possibility that the participant were presented with the same sequence twice. This task is based on the Automatic Working Memory Assessment (Alloway, 2007).

Training Gain

To quantify the training gains made by the 55 participants who participated in WM training, the training period was divided into four quarters (Days 1–7, Days 8–15, Days 16–23, and Days 24–32). A grand average and standard deviation of the level reached on each task (taking into account only the correct trials), for all participants on all days, were calculated. These statistics were used to transform the average level achieved by each participant in each quarter into z scores. The z scores of the available tasks in each quarter were then averaged to obtain a compound performance index for each quarter. The compound measures of the level reached by the participant during the first quarter and the fourth quarter were used to test for training gains.

Grit

Grit was measured using the 12-item grit scale presented in Duckworth et al. (2007), completed by the child's teacher. Three questions were modified with regard to timescale to be more suitable for 6-year-old children. The original scale together with the modified questions can be found in the SI (*Grit questionnaire*). The grit summary scores were normally distributed, and the scale had good internal consistency with Cronbach's alpha = .91 as measured by interitem correlations. In a separate sample of eleven 7-year-olds for whom grit was rated by two independent teachers, we identified an interrater reliability of .65. Higher scores indicate more grit.

Evaluation Questions

During the training, participants answered two questions each day on their iPads to evaluate their enjoyment of the training. The evaluation questions are reported in the SI (*Evaluation questions*).

Fluid Intelligence

Fluid intelligence was estimated using the matrices subtest of the Wechsler Intelligence Scale for Children, Fourth Edition. Participants are asked to complete a series of matrices of an abstract or concrete figure with an empty square. For each matrix, they need to choose the one correct answer from a set of alternatives. Standard scores were used.

Socioeconomic Status

SES was calculated according to the guidelines of Svenska Statistiska Centralbyrån (the Swedish central statistical bureau). For each child, the monthly income of the parent with the higher salary was asked, and the SES was coded as follows: less than 13,000 SEK (~1500 USD) was coded as 1, 13,000–22,5000 SEK (~1500–2600 USD) was coded as 2, 22,500–30,000 SEK (2600–3500 USD) was coded as 3, 30,000–40,000 SEK (3500–4600 USD) was coded as 4, and more than 40,000 SEK (4600 USD) was coded as 5.

Comparison of the Behavioral Sample and the Neuroimaging Subsample

We performed several analyses to ensure that the neuroimaging sample was representative of the behavioral one. These analyses are reported in the SI (*Comparison of the behavioral sample and the neuroimaging subsample*).

Behavioral Analyses

The training gains of the WM training group were tested using a paired t test of z scores reflecting performance on the WM tasks at the first and fourth quarters.

The effect of training on the transfer task was tested using the following mixed linear model:

$$\begin{aligned} WMgrid_{ij} = {} & \beta_0 + \beta_1 TrainingGroup_{(WM/Reading)} \\ & + \beta_2 Time_{(baseline/post)} + \beta_3 TrainingGroup \\ & \times Time + u_{0i} + u_{1i} Time + \varepsilon_{ij} \end{aligned}$$

The association of grit to training gains and transfer gains was tested using the following linear models:

$$4^{th}Qz = \beta_0 + \beta_1 Grit + \beta_2 1^{st}Qz + \varepsilon$$

$$WMgrid_{post} = \beta_0 + \beta_1 Grit + \beta_2 WMgrid_{baseline} + \varepsilon$$

Similar models were used to test the effect of enjoyment of the training and fluid intelligence as measured by the matrix reasoning task on trained and untrained tasks.

A mixed linear model was used to test the effect of the interaction between group (high and low grit) and time on the training gains as follows:

$$\begin{aligned} Z\ scores_{ij} = {} & \beta_0 + \beta_1 Group_{(High/Low\ \ Grit)} \\ & + \beta 2 Quarter_{\left(1stQz/2^{nd}Qz/3^{rd}Qz/4^{th}Qz\right)} \\ & + \beta_3 Group_{(High/Low\ \ Grit)} \times Time + u_{0i} \\ & + u_{1i} Time + \varepsilon_{ij} \end{aligned}$$

Differences in accuracy at the different loads of the WM grid task (i.e., transfer task) in each quarter of the 8-week

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training program were tested using a two-sample *t* test within each quarter and each level.

As a follow-up analyses, we tested the association between transfer gain and grit also within the subsample of participants that have trained math. The aim was to test if the effect of grit on training gain was specific for WM or if it could be a more general mechanism. Details on these analyses are reported in the SI (*Relationship between grit and training in the subsample training math*).

Throughout the paper, the effect sizes are reported either using Cohen's *d* or through standardized beta coefficient for linear model. For mixed linear models, the unstandardized parameter estimates together with standard errors are reported.

Neuroimaging Parameters

Magnetic resonance (MR) imaging data were acquired on a 3-T MR medical scanner (Discovery General Electric, Boston, MA) at the Karolinska Hospital in Solna, Sweden. The scanner was equipped with an eight-channel phased array receiving coil. We acquired the following sequences:

1. T1-weighted images were acquired with 1-mm^3 isotropic voxel size (echo time [TE] = 3.06 msec, repetition time [TR] = 7.9 msec, inversion time = 450 msec, field of view [FoV] = 24 cm, 176 axial slices, flip angle of 12°). T1 data were available for 27 participants.
2. Diffusion weighted imaging sequences were performed using a spin echo imaging tensor sequence (TE = 86 msec, TR = 7400 msec, FoV = 22 cm, 63 axial slices, 2.3 mm thickness, number of diffusion directions = 32). Diffusion weighted imaging data were available for 23 participants.
3. Functional MR sequences were performed with a gradient-echo pulse sequence using a voxel size of 3×3 mm (TE = 30 msec, TR = 2200 msec, FoV = 22 cm, 46 axial slices, 3 mm thickness, flip angle of 70°). A total of 130 volumes were acquired. fMRI data were available for 23 participants.

Neuroimaging Analysis

Subcortical Nuclei Segmentation

T1 3-D images were skull-stripped using the Brain Extraction Tool (Smith, 2002). The caudate nucleus, putamen, and NA were automatically segmented from T1 images using the FMRIB imaging registration and segmentation tool (FIRST; Patenaude et al., 2011; www.fmrib.ox.ac.uk/fsl/first/index.html). All of the free parameters were set at their default values based on prior optimization of these parameters (Patenaude et al., 2011; Patenaude, 2007). FIRST generated several coronal, axial, and sagittal slices with the superimposed segmented structure displayed, which enabled quality control of the segmentation. We segmented bilateral putamen, caudate nucleus, and NA.

Local Striatal Volume Analysis

The segmented subcortical nuclei were modeled as meshes, which are sets of vertices that describe the shape of the nuclei and retain the same spatial location between participants. The number of vertices differs from one structure to another but is consistent between participants for the same structure. In the shape analysis performed with FIRST, the meshes of the nuclei for the different participants are reconstructed in MNI space to align them. A mean shape of the sample is then calculated. For each vertex of each structure, the distance between that vertex and the same vertex in the mean shape was calculated to provide a measure of local volume (expansion/contraction relative to the mean shape of the structure in the sample). All meshes for each structure were reconstructed as 3-D volumes using interpolation to provide an image of each structure containing a signed value (distance from mean shape) in each voxel belonging to the structure's border. These images were used in nonparametric analyses of associations between shape and behavioral variables.

Correlation between Local Volume and Grit

We tested the association between grit and striatal shape using a linear model, including one vector for the grit summary measure. The significance of the correlation was tested with a nonparametric permutation test as implemented in the randomize tool, which is part of the FSL package (Hayasaka & Nichols, 2003). This tool compares the strength of the observed correlation with a null distribution obtained by a Monte Carlo permutation (5000 permutations) of the dependent variable (i.e., local volume). At the same time, the randomize procedure accounts for multiple comparisons using the threshold free cluster enhancement technique (Smith & Nichols, 2009). The statistical threshold was set to 0.05 corrected for multiple comparisons. The same approach was used to test the association between local volume and attitudes toward training and evaluation questions.

The localization was confirmed using the Oxford-GSK-Imanova Structural–Anatomical Striatal Atlas (Tziortzi et al., 2011).

We also tested the association between grit and striatal shape jointly for the three structures in the right hemisphere and for the ensemble of six structures (i.e., in both hemisphere) using PALM (Winkler, Ridgway, Webster, Smith, & Nichols, 2014), a statistical tool that enables permutation inferences over several structures (or modalities) at the same time, using a method similar to the one used by the FSL randomize tool. For this analysis, we had to use a stricter voxel-based correction for multiple comparisons rather than a more appropriate

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and more sensitive cluster-based correction. In fact, because of the nature of the cluster-based inference, the probability of false negatives becomes unfairly inflated for the smaller structures, when structures with different sizes are jointly tested. In particular, bigger structures allow space for larger clusters, which then dominate the distribution of the maximum. The clusters in the smaller structures tend to be toward the right tail of that distribution, getting smaller significance. In mathematical terms, the cluster-based method's lack of pivotality precludes its use for inference when structures of different sizes are used (Winkler et al., 2014).

In summary, association between grit and striatum was tested in six structures, at first separately and then jointly (i.e., performing multiple comparisons between regions).

Cross-validation of the Association between Local Volume in the NA and Grit

To confirm the association between grit and local volume, we performed a leave-one-out cross-validation. We performed the nonparametric analysis 27 times, each time using only 26 of the 27 participants in the subsample, making 5000 permutations using 26 participants. In each analysis, we identified a peak cluster (statistical threshold was set to $p < .1$ corrected for multiple comparisons to compensate for the slight anatomical differences that could exist between the average shapes of the 27 analysis), and then we extracted the shape value pertaining to the 27th participant from the NA cluster found in each analysis. The confirmatory analysis was then made by correlating the shape values extracted from this cross-validation with grit. Note that in the cross-validated analysis the key p value is not the one used to create the cluster (i.e., $p = .1$) but the p value of the correlation between the extracted values and grit. The statistical threshold for these latter analyses was set to the usual $p < .05$.

To cross-validate the spatial location of the cluster of association, we binarized and averaged the 27 clusters resulting from the cross-validation (each one calculated using a subsample of 26 participants). Then, we thresholded the resulting average cluster at a value of 0.99 (i.e., a voxel was present in all the 27 clusters), and we overlap it to the original cluster. The overlap index was calculated as

$$Overlap\ \ Index = Original\ \ Cluster \cap CV\ \ Cluster / Original\ \ Cluster \cup CV\ \ Cluster$$

Tissue Type Segmentation and Gray Matter Density Association with Grit and Training Gain

We segmented gray matter, white matter, and CSF from the T1-weighted images using FAST (Zhang, Brady, & Smith, 2001). To test the hypothesis that the positive association between shape values and grit was related to increased gray matter volume in this region, we used the cross-validation method outlined above to extract gray matter density values in the cluster we found in the right NA. We used the same clusters found in the cross-validation of the association between local volume and grit, using the inverse transform of the warp mapping the single subject T1 to MNI template to register these clusters in subject space. From this registered clusters, we extracted gray matter density and correlated these values with the grit summary score.

Cortical Thickness and Grit

Cortical reconstruction and calculation of cortical thickness were performed with the Freesurfer image analysis suite, which is documented and freely available for download online (surfer.nmr.mgh.harvard.edu). The details of these procedures are described in prior publications (Han et al., 2006; Segonne et al., 2004; Fischl & Dale, 2000; Dale, Fischl, & Sereno, 1999; Fischl, Sereno, & Dale, 1999; Fischl, Sereno, Tootell, & Dale, 1999; Dale & Sereno, 1993). Cortical thickness data were smoothed with a kernel of 10 mm FWHM, as commonly done in literature. Data from all participants were projected onto the fslaverage template by means of the standard freesurfer algorithm (Yeo et al., 2010; Fischl, Sereno, Tootell, et al., 1999). The same design matrix used for assessing associations between shape and grit in the striatum was used for assessing vertex-wise associations between grit and thickness by means of univariate statistic.

We created two ROIs for the frontal cortex: one including the entire frontal lobe excluding motor areas and the other only including the lateral surface of the frontal lobe. Association between grit and vertex-wise cortical thickness was tested using a liner model. Cluster-based correction for multiple comparisons was performed as a small volume correction (i.e., only inside the mask) for both the frontal cortex masks using Monte Carlo simulation. The statistical threshold was set to a liberal $p = .1$.

In summary, the association between grit and cortical thickness in the frontal lobe was tested in two ROIs.

The use of two different software for the vertex analysis of the subcortical nuclei (FIRST) and of cortical thickness (FreeSurfer) is related to the peculiarity of the two software and the type of analyses we wanted to run. FIRST has been specifically developed for the segmentation and the shape analyses of subcortical nuclei and provide a direct and validated method for vertex-wise comparison within the subcortical nuclei (Patenaude et al., 2011). FreeSurfer, on the other hand, provides a tessellation of the cortex (i.e., a vertex representation of the cortical ribbon) but does not provide the same representation for the subcortical nuclei (i.e., the subcortical nuclei in the FreeSurfer pipeline are labeled ROIs). This means that, although vertex-wise analyses of the cortex are implemented and validated within FreeSurfer,

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the same is not true for vertex-wise analyses of the subcortical nuclei.

Tractography

We corrected for eddy currents and head motion in all diffusion-weighted images using the FSL software (fsl.fmrib.ox.ac.uk/fsl/fslwiki/). The diffusion tensor parameters were then estimated for each voxel and image, and fractional anisotropy (FA) and radial diffusivity (RD) images were constructed. Nonlinear registration was carried out using the Tract-based Spatial Statistics (TBSS) script (Smith et al., 2006) to align all FA images to the mean FA skeleton.

With the aim to observe the anatomical connectivity of the cluster of correlation between local volume and grit in the right NA, we used this cluster as a seed point for probabilistic tractography. The cluster was first registered to the mean FA image, and then the back projection of the TBSS method was used to register the cluster into the DTI space of each individual. Probabilistic tractography was thus performed in the single-subject DTI space, initiating from all voxels within the clusters using the probtrackx tool of FDT v2.0 (Behrens, Berg, Jbabdi, Rushworth, & Woolrich, 2007; Behrens et al., 2003). For fiber tracking, we use the default parameters (5000 streamline samples, step length = 0.5 mm, curvature threshold = 0.2). At the individual level, the voxels with low connectivity probability were excluded using a threshold of 5% of the samples (Leh, Johansen-Berg, & Ptito, 2006). Subsequently, all of the traced white matter tracts were aligned using the TBSS method for non-FA images and then binarized and averaged across participants. For tractography, the sample comprised 23 participants for whom DTI data were available. As a more exploratory analysis following the results found in the NA using structural data (see Results), we extracted FA and RD from the traced tract and we perform a 0th order correlation between these two measures and grit.

BOLD Signal and Grit

Functional data were available for a subsample of 23 participants. These participants performed a WM task while in the MRI scanner. The task was similar to the WM grid task used for assessing WM, as the participants saw sequences of two (Load 2) or four (Load 4) dots appearing within a 4 by 4 grid. However, at variance with the behavioral task, the fMRI task was a forced two-choice task. Specifically, the participants saw a sequence of spatial position, then a question mark appeared, and the participant had to decide if the question mark was in one of the square included in the presented sequence by pressing a two-key pad. The control task was visually similar to the WM task (Control 2, Control 4), but the sequences presented were fixed (i.e., the mark appeared in the upper left and upper right corners of the grid for Load 2 control and in all the corners of the grid for Load 4 control). During the control task, question marks always appeared in the same position. Furthermore, the mark used for showing the sequences was a drawing of the planet earth during the experimental task, whereas it was a drawing of the sun during the control task. The participants were instructed to always press the NO button during the control task. Answers and RTs were registered.

Each participant underwent two runs with 32 trials in each run (8 Load 2 trials, 8 Load 4 trials, 8 Control 2 trials, 8 Control 4 trials). Load 2 and Control 2 trials lasted for 6000 msec, whereas Load 4 and Control 4 trials lasted for 8000 msec. Each trial was followed by an intertrial interval of 2 sec. Within each sequence, the planet that marked the spatial positions appeared, for each position, for 500 msec, followed by a 500-msec delay in which the grid was empty. Before the last position cued and the appearance of the question mark, there was a 1000-msec delay. The question mark remained on the screen for 3000 msec, which was the total time allowed for an answer. The experimental and the control tasks were presented separately in a block design: Each block comprised four sequences. The order of the tasks was the same for all participants: Load 2 control, Load 2 experimental, Load 4 control, Load 4 experimental; this sequence was repeated twice within each run.

One hundred and thirty functional volumes were submitted to a standard preprocessing pipeline performed in SPM8 (www.fil.ion.ucl.ac.uk/spm/software/spm8/), including slice timing correction, realignment, normalization to the MNI standard template, and smoothing with a FWHM kernel of 8 mm. The toolbox Artifact Detection Tools (ART) was used to identify volumes corrupted by excessive motion (defined as a frame-wise displacement > 2 mm or a root mean squared change in bold signal > 9). For first-level analysis, separated boxcar regressor modeled trials of the WM and the control task with a duration equal to the trials duration (6000 and 8000 msec respectively for Loads 2 and 8) plus the RT to take into account the whole time on task period. These regressors were convolved with the canonical hemodynamic response function, and together with regressors representing residual movement related artifacts, volumes marked as corrupted by the ART toolbox and the mean over scans represented the full model for each session. A first-level contrast of WM (Load 2 and Load 4) > Control (Load 2 and Load 4) was calculated for each participant. The mean beta weight for this contrast was extracted, for each participant, from the cluster of association we found between shape and grit in the ventral striatum. As a follow-up exploratory analysis to the results found in the NA using structural data (see Results), a 0th order correlation was then calculated between mean beta weight and grit.

Movement Confounds Analysis

To control for a possible confounding effect of movement during scanning, we used the functional imaging realignment procedure provided by the script fsl_motion_outliers

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(Jenkinson, Beckmann, Behrens, Woolrich, & Smith, 2012) to calculate the frame-wise displacement (FD). FD is a summary measure of between-volume movement that has been used to quantify movement during acquisition and to censure volume with high movement (Siegel et al., 2014; Power, Barnes, Snyder, Schlaggar, & Petersen, 2012). For our purpose, FD can be regarded as a proxy of participants' movements during the T1 acquisition. We calculated FD for the 17 participants whose functional imaging and local volume in the right accumbens cluster were available, and we examined the association between these two measures.

RESULTS

Effect of Training

Overall, children who had practiced WM tasks (n = 55, WM training) improved significantly on the trained tasks (last quarter of training period vs. first quarter of training period; $p < .001$, Cohen's d = 1.07 [95% CI 0.66, 1.47]) and showed a significantly greater improvement ($p < .001$, parameter estimate = 2.43 (0.39); Figure 1A) on the transfer task compared with children in the control group (n = 55 for the children who trained WM, n = 51 for the children who have not trained WM).

Effect of Grit on Training and Transfer Gains

At first, we calculated the association between WM at baseline and grit, finding a trend for the transfer task (r = .24, p = .072) and a significant association for the training tasks during the first quarter of the training period (r = .34, p = .009; n = 55, WM training).

We then analyzed if grit scores can explain interindividual differences in how much children improved during training, while controlling for baseline performance. The grit score was significantly associated with both training gains (p = .012, β = 0.21) and transfer gains (p = .009, β = 0.31) corrected for baseline performance (Figure 1B). In both models, baseline performance was also significantly related to gains ($p < .001$ for both models, β = 0.71 for training gains, and β = 0.44 for transfer gains). Importantly, the association between grit and gains remained significant when correcting for the

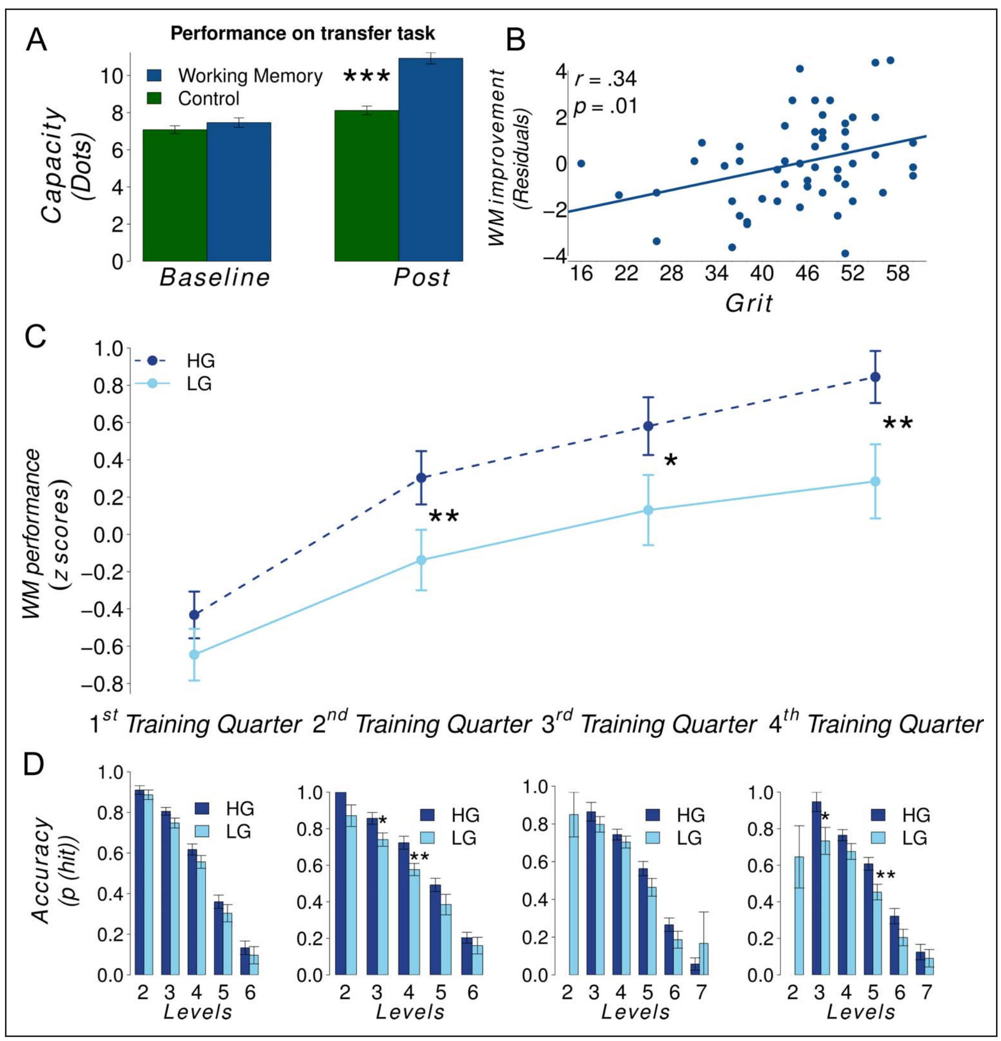

Figure 1. Behavioral analyses. (A) Performance on the transfer task for the WM training and control groups (means and *SE*). There was a significant interaction between time (baseline vs. posttraining) and group (WM training vs. control) $p < .001$. (B) Grit was significantly correlated with improvement on the WM transfer task within the WM training group (p = .01). WM improvement was calculated as the residuals in a linear model with transfer task performance after training as the dependent variable and transfer task performance at baseline as the independent variable to correct for any differences at baseline. (C) Mean z scores ($\pm SE$) for performance on the trained WM tasks for the high- and low-grit participants based on a median split. The groups did not differ at baseline, but a significant difference emerged with increasing training. (D) Mean ($\pm SE$) for one of the training task divided by quarters, levels, and groups (high vs. low grit). $^*p < .05$, $^{**}p < .01$, $^{***}p < .001$.

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Table 1. Cognitive Measures

Measure	*Mean (SD)*
Grit	44.4 (±9.6)
Fluid intelligence (matrix)	12.7 (±3.6)
Evaluation questions	3.1 (±0.7)

Mean (*SD*) of the cognitive measures used in this study.

total amount of time spent training (p = .013 for training gains and p = .005 for transfer gains; n = 55, WM training for all analyses).

To further explore the effect of grit on learning, participants in the WM training group were divided into a low-grit group and a high-grit group using a median split. When we evaluated performance over the four quarters of the 8-week training program, we found a significant effect of time (p < .001, parameter estimate = .38 (0.02)) and an interaction between grit and time (p = .038, parameter estimate = .07 (0.03); Figure 1C). If grit entered the model as a continuous variable rather than as a categorical variable, the crucial interaction between grit and time remained significant (p = .007, parameter estimate = .004 (0.001)). When performance was further examined based on the different WM loads, that is, difficulty level, there was a tendency for low- and high-grit participants to differ on lower loads at the beginning of the training program and higher loads at the end of training (Figure 1D; n = 55 WM training for all analyses). Grit was thus associated with gradual improvement in training over time, especially on more difficult items.

As for the math training, also in this group there was a positive significant effect of grit on transfer gain (p = .016, β = 0.27; n = 51, children who trained math).

Specificity of the Effect of Grit on Training and Transfer Gains

To evaluate the specificity of these findings, we also analyzed the scores from a set of questions intended to measure children enjoyment during training. During the training, the participants were asked specific questions each day regarding how fun and how difficult they found the tasks (i.e., evaluation questions). The answers to the evaluation questions during training were not associated with training or transfer gains (respectively p = .66 and p = .14, β = 0.03 and β = −0.17; n = 55, WM training).

Fluid intelligence was estimated as performance on a matrix reasoning task from the Wechsler Intelligence Scale for Children, version III. This measure was not associated with training gain (p = .29, β = 0.09) nor transfer gain (p = .085, β = 0.22) in the WM training group (n = 55, WM training).

Taken together, these results show that enjoyment of the training and fluid intelligence had no effect on training and transfer gain, suggesting a specific role for grit.

Evaluation questions and fluid intelligence were also entered as nuisance variables in models including grit as the variable of interest; these models and their results are reported in the SI (*Further analyses assessing the specificity of the association between grit and training gain*).

Table 1 reports the average (±*SD*) of the cognitive measures used in the behavioral analyses. Table 2 reports the correlations between the same measures. (Supplementary Tables 1 and 2 show similar table for the neuroimaging sample.) Supplementary Table 4 reports the sample size for each analysis, break down for training groups (http://www.klingberglab.se/wp-content/uploads/2014/12/Nemmi2016_SI.pdf).

Neural Correlates of Grit

Grit was significantly associated only with the shape of the ventral part of the striatum, corresponding to the NA (p < .05 corrected for multiple comparisons, peak voxel p = .021, $x = 12, y = 11, z = -11$, size = 38 mm^3; Figure 2A, B). This association was also confirmed using a leave-one-out cross-validation (r = .42, p = .027; Figure 2D). We also confirmed the spatial location of the cluster by means of cross-validation. We calculated the spatial overlap between the 27 clusters resulting from the cross-validation procedure (see Methods) and the cluster found in the vertex-wise analysis. The clusters overlapped by 76%.

To further confirm our result, we tested the association between shape and grit jointly for all the subcortical

Table 2. Correlation Matrix

	Grit	*Hyperactivity*	*Fluid Intelligence*	*Attitude toward Training*	*Evaluation of Training*	*Sample Size*
Grit	1	**−.43*****	**.28****	.23*	**.28****	55
Fluid intelligence	.28	−.31	1	.13	.23**	55
Evaluation	.28	−.31	.23	.35	1	55

The table reports the correlations between the cognitive measures used in the study. Correlation in bold survive family-wise error.

*p < .05.

**p < .01.

***p < .001.

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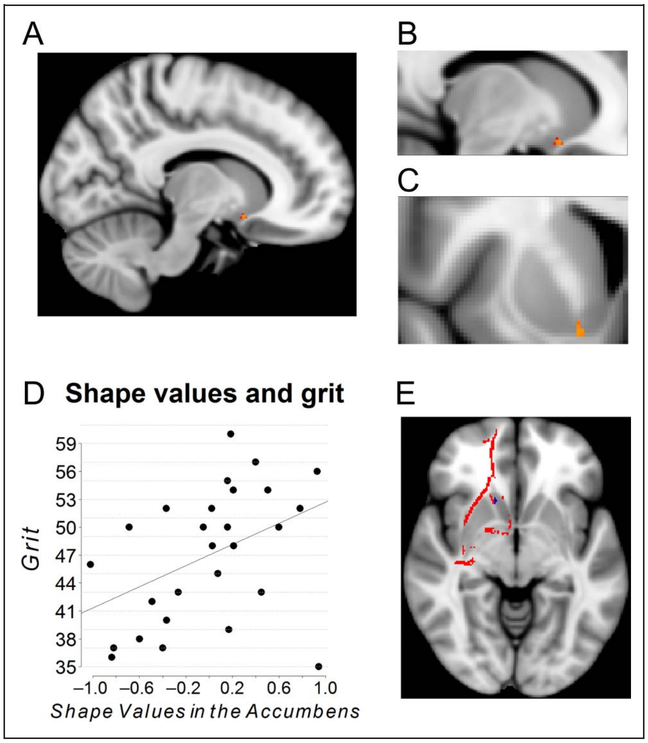

Figure 2. Neural associations to grit. (A) Cluster of correlation between NA shape values and grit scores superimposed to the standard MNI template. The same cluster is shown in (B) the sagittal section ($x = 12$) and (C) the coronal section ($y = 11$). (D) Scatterplot of the cross-validated correlation between shape values and grit scores ($r = .42$, $p = .027$). (E) Probabilistic tractography using the cluster of correlation between shape values and grit scores in the right NA. The reconstructed tract has been averaged and thresholded to show only those voxels in which the tract was present in the 95% of the participants. Seed point is shown in blue.

structures of the right hemisphere, where the original cluster was found, using a strict voxel-based correction rather than the more sensitive cluster-based correction. The peak voxel ($x = 12, y = 11, z = -11$) was significant ($p = .038$; when the analysis was performed on the bilateral striatum, the same voxel reached a significance of $p = .072$). For all these analyses, the direction of the association was positive (i.e., participants with greater local volume in the cluster of association showed higher grit).

The relationship between NA shape and grit is assumed to reflect localized differences in gray matter volume. To verify this, we used the cluster from the shape analysis as ROI applied to the T1-weighted images and performed a leave-one-out cross-validation of the correlation between gray matter density in the ROI and grit. This analysis confirmed that gray matter density was significantly associated with grit ($r = .44, p = .018$), consistent with the interpretation that the NA local shape associated with grit corresponds to a local increase in gray matter density. These analyses suggest that local NA volume is associated with grit in children. Furthermore, we tested the association between shape value in the NA cluster and improvement in the children who had trained WM and had available imaging data ($n = 13$) using 0th order correlation. Although not significant, the correlations were in the expected direction (training gain: $r = .46, p = .09$; transfer gain: $r = .29, p = .3$).

To qualitatively characterize the anatomy of the striatal region where grit was associated with shape, we used tract tracing based on diffusion weighted images to identify connectivity between NA and OFC. As expected, this showed strong connections between NA and OFC (Figure 2D), which is implicated in processing of external rewards in both human (Sescousse, Caldu, Segura, & Dreher, 2013) and animal studies (Rudebeck & Murray, 2011).

As a follow-up to the association between structure of the NA and grit, we extracted FA and RD from the tract traced using the cluster in the NA as seed, as well as BOLD signal during a WM task from the same cluster. FA and RD extracted from the traced tract were not associated with grit ($p > .2$). Similarly, BOLD signal during performance of a WM task was not associated with grit ($p > .36$).

Grit was not associated with cortical thickness in the frontal cortex (either broadly or restrictedly defined, see Methods), as assessed using vertex-wise analysis ($p > .1$).

Movement Confound Analysis

We found a near-zero association between FD and local volume values ($r = .09, p = .72$). In addition, we tested the association between FD and grit in the same sample and found that the correlation between the two measures was nonsignificant ($r = -.29, p = .22$). Although this is just a subsample of the participants included in the analysis to test the association between local volume and grit, these results suggest that movements during scanning are not associated with local volume values.

DISCUSSION

We found that our WM training was effective in improving WM of children on both the training tasks and a transfer measure. Although the control group also showed an improvement in the transfer measure, the WM training group improved significantly more than the control group. The improvement in the control group could have been related to a test–retest effect or to some nonspecific effect of the training regime they were submitted. This result underlines once again the importance of including an active control group in training studies. Our results show that grit is associated with improvements during and after WM training in 6-year-old children. These findings were specific in the sense that training and transfer gains were not related to measures of enjoyment of the training or fluid intelligence. Although baseline performance was identified as a significant predictor of training and transfer gains, the association between grit and WM

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improvement remains significant after correcting for baseline performance on WM tasks and reasoning ability in the investigated sample. The positive association between grit and transfer gain was present also for math in the math training group. These results suggest that the effect of grit is general and not limited to WM training. In turn, this would be expected if, as we propose, grit act as a motivational drive to overcome difficulties and pursue of highly valuable rewards even in front of high effort.

In a second study involving a subsample of the children included in the behavioral analysis, grit was found to be associated with the shape and size of NA, a structure related to motivation and reward seeking. To our knowledge, this is the first study to identify a personality trait that can predict improvements during cognitive training, providing at the same time a plausible neural substrate for the former. Although a direct association could not be proven between shape in the NA and improvement in the WM group, positive nonsignificant association were found between shape in the NA and both training and transfer gain.

Grit contains two components: First, grit is related to motivation and drive to pursue the same goal over an extended period of time (Duckworth & Quinn, 2009; Duckworth et al., 2007). Second, it is related to self-control, planning, and conscientiousness, which enable the individual to stick to certain goals in the presence of distractions, difficulties, and setbacks (Duckworth & Quinn, 2009; Duckworth et al., 2007). We hypothesized that the structural neural underpinnings of grit could include either the ventral striatum, which is related to motivation and reward seeking, or prefrontal areas, previously related to self-control and conscientiousness (Kapogiannis et al., 2013; DeYoung et al., 2010). We found that grit was associated to the size and shape of the NA but not with cortical thickness of the frontal cortex, although the lack of results for the latter could be related to low statistical power associated with a small sample size. The NA is not directly responsible for experiencing rewards or feelings of euphoria or "liking," as shown by animal studies where lesions of the NA disrupt drug seeking but does not abolish drug-taking behavior (Salamone & Correa, 2012; Everitt & Robbins, 2005; Ito, Robbins, & Everitt, 2004; Hutcheson, Parkinson, Robbins, & Everitt, 2001). Specifically, NA lesions result in a preference for low valued, immediately available rewards in face of more highly valued rewards available only after a delay or delivered only after a higher effort (Salamone & Correa, 2012; Denk et al., 2005; Salamone et al., 1991). In animal studies, the NA thus seems vital for the drive to search or work for future rewards. This characteristic is very similar to the definition of grit as a pursuit of long-term goals.

Previous neuroimaging results implicate the striatum in training-related WM plasticity. In particular, increased striatal activity has been associated with improvement in WM following training (Dahlin, Neely, Larsson, Backman, & Nyberg, 2008; Olesen, Westerberg, & Klingberg, 2004), although it is unclear if those regions overlap with the cluster identified in this study.

A tentative interpretation is that variability in grit (and possibly other personality traits related to motivation) is related to the variability of dopaminergic availability or sensitivity (e.g., receptor density) in the ventral striatum. This variability could influence the ability to stick to one task or to put effort into a task for long periods of time, which may also make gritty children benefit more from cognitive training. A recent study found that the rs1800497 polymorphism on the DRD2/ANKK1 gene was associated with improvement during WM training (Soderqvist, Matsson, Peyrard-Janvid, Kere, & Klingberg, 2014). A follow-up study found that an interaction between the same polymorphism and ventral striatal BOLD response was associated with WM capacity (Nymberg et al., 2014).

This study has several limitations. First, the grit questionnaire has been validated on adults and adolescents (Eskreis-Winkler et al., 2014; Duckworth & Quinn, 2009; Duckworth et al., 2007), but it has not been used in 6-year-old children. However, the internal consistency in the whole sample was alpha = .91, which shows a high reliability, also when compared with the results in adults using the same scale (Duckworth et al., 2007). Moreover, goal-directed behavior, the main focus of grit, can be hard to recognize for 6-year-old children. This is the main reason why we chose to have the teachers rate the children. We thought they would be better suited for scoring grit than children themselves (who could have had a hard time with introspection) or parents (who may not observe their children during structured challenges as the one schooling involves). Second, although two measures were included and found not to correlate with training gains (enjoyment of the training and fluid intelligence), there were practical limitations to the number of measures that could be completed in one study. Future studies could include estimates of intrinsic motivation as well as measure of inhibitory control, self-control, and conscientiousness. Conscientiousness, in particular, is a personality trait that has repeatedly been found to correlate with grit (Eskreis-Winkler et al., 2014; Duckworth & Quinn, 2009; Duckworth et al., 2007); however, it has been shown that grit and conscientiousness explain independent shares of variance in years of education and GPA score (Duckworth et al., 2007). The extent to which grit and conscientiousness share a common neural substrate is unknown. Finally, we do not draw any strong conclusions from the lack of association between grit and cortical thickness in the frontal lobe in this study. Interindividual differences in functional anatomy of the frontal lobe could be larger than in a smaller and well-defined structure as the NA, decreasing the probability of observing an association to grit.

In conclusion, this study shows that grit is associated with improvement after WM training, providing at the

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same time a plausible neural substrate for grit, defined as the capacity to pursue long-term goals and stick to them despite failure and setbacks.

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