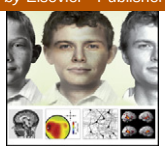
Developmental Cognitive Neuroscience 1 (2011) 530–539

Developmental Cognitive Neuroscience

journal homepage: http://www.elsevier.com/locate/dcn



How the aging brain translates motivational incentive into action: The role of individual differences in striato-cortical white matter pathways

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ARTICLE INFO

Article history:
Received 28 March 2011
Received in revised form 15 June 2011
Accepted 17 June 2011

Keywords:
Aging
Action control
Reward processing
Antisaccade
Striatum
Probabilistic tractography

ABSTRACT

The anticipation of reward enhances actions that lead to those rewards, but individuals differ in how effectively motivational incentives modulate their actions. Such individual differences are particularly prominent in aging. In order to account for such inter-individual variability among older adults, we approach the neurobiological mechanisms of motivated behavior from an individual differences perspective focusing on white matter pathways in the aging brain. Using analyses of probabilistic tractography seeded in the striatum, we report that the estimated strength of cortico-striatal and intra-striatal white matter pathways among older adults correlated with how effectively motivational incentives modulated their actions. Specifically, individual differences in the extent to which elderly participants utilized reward cues to prepare and perform more efficient antisaccades predicted structural connectivity of the striatum with cortical areas involved in reward anticipation and oculomotor control. These striatal connectivity profiles endow us with a network account for individual differences in motivated behavior among older adults. More generally, the data suggest that capturing individual differences may be crucial to better understand developmental trajectories in motivated behavior.

1. Introduction

Developmental models of motivated behavior can be constrained and better articulated with knowledge of structural and functional brain systems. However, interpreting brain–behavior correlations across age groups is difficult because of large inter-individual differences in performance (Crone and Ridderinkhof, 2011). This holds especially for the study of the elderly (Hedden and Gabrieli, 2004). Brain-imaging studies (Berkman et al., 1993; Cabeza et al., 2002; Rosen et al., 2002) have stimulated a growing interest in the neurobiological basis for individual differences among high-performing older adults. For example, "successful aging" refers to adaptive resources that sustain mental capacities in some older adults more than in others (Gallagher et al., 2006). A characterization of individual differences in adaptive behavior among older adults may allow a more sensitive approach to detect adaptive neuroanatomical circuitry that might be disguised by simply comparing old participants with young.

One area of research that might benefit from an individual-differences approach is motivation, or the incentives that energize goal-directed behavior. Humans adapt the degree of effort they expend according to the magnitude of reward they anticipate (Pessiglione et al., 2007). Such a process has been proposed as an operant concept of motivation (Robbins and Everitt, 1996;

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doi:10.1016/j.dcn.2011.06.005

Schultz, 2006; Berridge, 2004) and seems to remain intact in old age (Harsay et al., 2010). Here we investigated the white matter circuitry in older adults that allows motivational incentives to facilitate goal-directed behavior. Specifically, we tested whether individual differences in the white matter pathways of the striatum (measured through diffusion-weighted MRI) predicted individual differences in reward-guided action. We focused on action control within the oculomotor system, using an antisaccade task in which participants inhibited an eye movement toward a peripheral stimulus and instead generated an eye movement in the opposite direction. This requires the appropriate selection of a volitional command over the predominantly automatic command (Hallett, 1978; Munoz and Everling, 2004). Even successful aging entails impairments in planning and initiating many day-to-day activities (Hedden and Gabrieli, 2005). Experimentally, these impairments can be captured using the antisaccade task. We previously showed that although antisaccade performance declines with age, antisaccade action modulation by reward seems to be spared (Harsay et al., 2010). This provides a useful context for examining the neuroanatomical basis for linking motivation-based action preparation with neuroanatomical circuits underlying reward and oculomotor functioning, and individual differences therein.

The anatomically well-characterized oculomotor network controls the volitional movement of the eyes, and includes subcortical (caudate, substantia nigra pars reticulata, pulvinar nucleus of the thalamus, superior colliculus) and cortical (frontal-, supplementary- and parietal eye fields, and parts of the lateral prefrontal cortex) regions (Law et al., 1997; Lynch and Tian, 2006; Petit et al., 1996; Pierrot-Deseilligny et al., 2003). For simplicity, we use the term "oculomotor control structures," although in addition to their shared eye-movement control functions, the described regions contribute to other functions such as attention, decision-making, memory, and planning of motor movements (Lynch and Tian, 2006). Cortical oculomotor control structures can modulate saccade behavior by targeting saccade generators in the superior colliculus directly, as well as indirectly through the caudate. Anatomically, the caudate is connected with several cortical eye fields in the frontal and parietal cortices, in part via the thalamus, and with the superior colliculi via the substantia nigra pars reticulata (Alexander and Crutcher, 1990; Alexander et al., 1990; Grahn et al., 2008; Haber, 2003; Hikosaka et al., 2000, 2006).

Reward anticipation also recruits a widespread network including the striatum (nucleus accumbens, putamen and caudate). According to neuroimaging and fiber tracing, reward-related information may access the striatum either by a subcortical route via the amygdala and/or hippocampus or by a cortical route via the orbitofrontal and/or anterior cingulate (Friedman et al., 2002; Lehericy et al., 2004; Pessiglione et al., 2007). The caudate is directly connected to cortical oculomotor-control structures, and therefore is a likely candidate for modulating saccades according to motivation/reward anticipation.

The nucleus accumbens, although a key component in reward-processing networks, is not considered part of the oculomotor network and has no connections in a strong position to directly initiate or control eye movements (Zahm, 2000). The putamen, similarly, has been found to encode reward value and directions for actions (Haruno and Kawato, 2006; Hori et al., 2009) but is also not considered as part of the oculomotor circuit, despite its direct connections to the frontal eyefields, which are less dense than the connections between caudate and frontal eyefields (Cui et al., 2003). In reward-guided oculomotor control, the putamen is hypothesized to guide actions toward their expected outcomes mainly by forwarding reward value and directions for actions via intra-striatal connections to the caudate that can directly mediate cortical oculomotor control.

Thus, interestingly, the striato-limbic reward network and the oculomotor network show strongest overlap in the caudate. Recent neuro-imaging findings in young adults show that functional connectivity of the caudate predicts individual differences in the extent to which motivational incentive modulates goal-directed oculomotor behavior (Harsay et al., in press). Based on observations that stable individual differences in behavioral characteristics such as personality traits and reward-based learning are related to striato-cortical white matter connectivity (Cohen et al., 2008, 2009), we hypothesized here that by combining structural white matter imaging of striato-cortical connectivity with individual differences in reward-modulated oculomotor performance, we can better understand the neural circuitry underlying the interface between motivation and action among older adults.

Specifically, if the striatum is the interface between the reward and the oculomotor system then the white matter pathways linking the striatum to both reward- and oculomotor structures might be stronger in individuals who are more effective in using reward anticipation to improve oculomotor performance. Specifically, we hypothesized that in such individuals the caudate shows stronger white matter pathways to cortical oculomotor structures, whereas the putamen and the nucleus accumbens show stronger intrastriatal white matter pathways and stronger pathways to limbic reward evaluation structures. We quantified the white matter pathways of the caudate, accumbens and putamen in older adults using probabilistic tractography based on diffusion tensor imaging (DTI), and we examined whether individual differences in the strength of the striatal white matter pathways predicts individual differences in the efficacy of motivational incentives on oculomotor responses in the antisaccade task.

2. Methods

2.1. Participants

16 Healthy right-handed volunteers (age 64–76, $M = 68 \pm 4$, 11 female), with normal or corrected-to-normal vision participated in the experiment. They were recruited from a database of healthy elderly participants (www.SeniorLab.nl) who had previously expressed their interest in participation in cognitive aging research. All participants were screened with a standard vision test for normal or corrected-to-normal vision for short and for

long distances. None of the participants reported having any psychiatric or neurological conditions or brain injuries in the past. All experimental procedures were approved by a local ethics committee, and conducted in accordance with the Helsinki Declaration, international laws, and institutional guidelines. For a detailed description please see Supplemental Material S1.1/S1.2.

2.2. The antisaccade task, eyetracking set-up and analysis

All participants completed an antisaccade task as used in our previous studies. Each of 128 trials (see Fig. 1) started with a central fixation dot surrounded by two square outlines (each subtending 3.8° visual angle) on the left and right side of the fixation dot (distance 12.4°). After this fixation display a central visual instruction cue was presented (for 600 ms) followed by a variable delay of 4.5–6 s, terminated by a peripheral antisaccade target (a white asterisk subtending 2°). The antisaccade target was presented for 500 ms in the center of the left or the right square outline (in pseudorandom order). The target indicated that participants should make an immediate eye movement to the opposite side of the screen. Their response was immediately followed by presentation of a feedback image (presented for 500 ms). The length of the delay period between the visual instruction cue and the antisaccade target varied across trials between 4.5 and 6 s. A black screen with jittered duration (16, 500, 1000, 1500 ms) was displayed between trials.

To investigate the effect of reward anticipation and oculomotor preparation on antisaccade performance, we presented instruction cues before the appearance of the peripheral antisaccade target. In a 2×2 factorial design the instruction cues independently manipulated the level of reward expectation (two levels: reward and no reward expected) and the level of response preparation (two levels: direction-specific oculomotor preparation or direction-nonspecific oculomotor preparation of the antisaccade response), by means of color and shape: In reward trials the instruction cue was a gold circle; in neutral trials the instruction cue was a silver circle. The colors of the reward and the neutral cue colors were calibrated to equal luminance using Colorfacts 7 and the color calibration system EyeOneMonitor (www.datacolor.eu). Oculomotor preparation was manipulated by the content of the instruction cue: in direction-specific preparation trials, an arrow was displayed in the center of the circle, indicating where the antisaccade target would appear; in the direction-nonspecific preparation trials, a bar replaced the arrow.

On rewarded trials, the post-response reward feedback was symbolically represented as an image of a golden Euro coin. On neutral trials, a silver blank disk of the same size, shape and luminance was displayed. After an incorrect or too slow response a silver ring with a black circle in the middle was presented. Colors of rewarded, non-rewarded and error feedback were calibrated to equal luminance using Colorfacts 7 and EyeOneMonitor. Participants were informed that they would receive a monetary reward on golden reward trials in which they were fast and correctly but not on the silver neutral trials. In line with other imaging work with monetary reward (Ramnani and Miall, 2003) the exact monetary value was not displayed in the feedback to avoid mental calculation. Details of the eyetracking and stimulus delivery set-up and the antisaccade analysis are presented in Supplemental Material S1.3/S1.4 or in Harsay et al. (2010).

2.3. DTI acquisition and preprocessing

Diffusion-weighted images (DTIs) and T1 structural (gray matter) images were acquired on a Philips (Philips, The Netherlands) 3 T MRI system using a standard head coil for radio frequency transmission and signal reception. High-resolution anatomical images were acquired using a 3-D T1-weighted scan in steady state sequence also to assess cortical atrophy (TE/TR = 4.6/9.69 ms; 182 sagittal slices; slice thickness 1.2 mm, interslice gap 0.3 mm; FOV = 250 mm) and FLAIR images to assess white matter hyperintensities and ischemic lesions. The diffusion-weighted images (DTIs) (TR 7720 ms, TE 94 ms, flip angle 90°, FOV 22× 224 mm, matrix size 128×128, 40 slices, $b = 600$, 94 ms) were measured in 32 non-collinear directions. The end of each series of directions was preceded by acquisition of a non-diffusion-weighted volume for purposes of registration for motion correction. Each DTI acquisition phase lasted for 5.2 min. Because diffusion data have relatively low signal-to-noise ratio, we collected two data sets in succession enabling us to increase the signal-to-noise ratio by averaging the data sets. Preprocessing and analysis of fractional anisotropy of DTIs was conducted using FSL tools (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). For detailed description please see Supplemental Material S1.5/S1.6.

2.4. Probabilistic tractography

Segmentations of caudate, putamen and nucleus accumbens were used for probabilistic tractography using connectivity-based seed classification to quantify striato-cortical fiber tract strengths. Probabilistic tractography quantifies the connectivity between the relevant brain areas but gives no information on directionality. This analysis has been detailed in our previous studies; for a detailed description Supplemental Material S1.7 or Cohen et al. (2008).

2.5. Individual differences analysis

To locate white matter networks of the basal ganglia that are linked to motivated behavior, we computed correlations between basal ganglia seeded probabilistic tractography on the one hand, and performance benefits from reward anticipation obtained from the oculomotor data on the other. This approach has been used successfully in previous studies using similar analysis of links between individual differences in behavior and measures of probabilistic tractography (Cohen et al., 2008; Forstmann et al., 2010). Across participants we correlated tractography results at each voxel with the antisaccadic benefit from reward anticipation $[(RT_{\text{no reward anticipation}} - RT_{\text{reward anticipation}})/(RT_{\text{no reward anticipation}})]$. To test for the

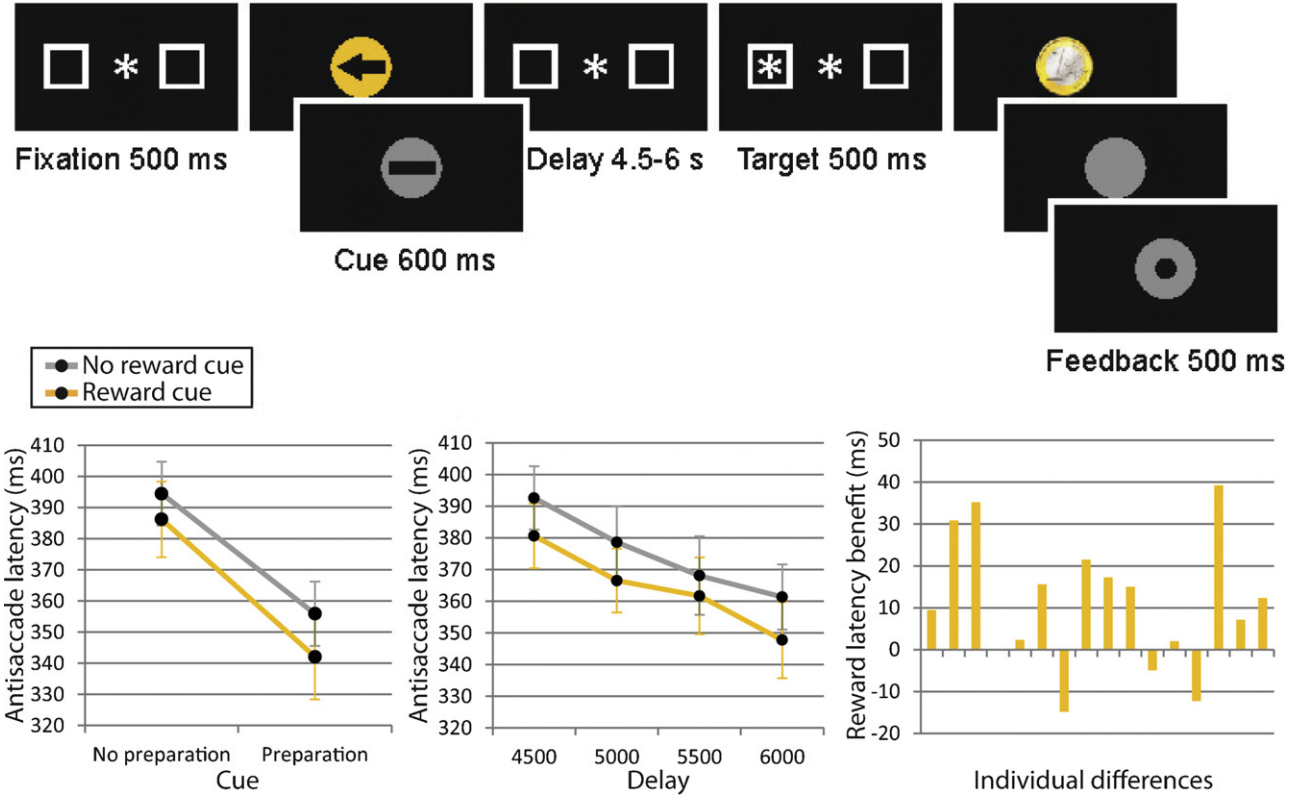

Fig. 1. (Top) Instruction cues before the appearance of the peripheral antisaccade target independently manipulated the level of reward expectation (two levels: reward and no reward expected) and the level of response preparation (two levels: direction-specific oculomotor preparation or direction-nonspecific oculomotor preparation of the antisaccade response): in reward trials the instruction cue was a gold circle; in no-reward anticipation trials the instruction cue was a silver circle. Oculomotor preparation was manipulated by direction-specific preparation trials: an arrow was displayed in the center of the circle, indicating where the antisaccade target would appear; in the direction-nonspecific preparation trials, a bar replaced the arrow. After a variable delay the antisaccade target was presented in the center of the left or the right square outline. The target indicated that participants should make an immediate eye movement to the opposite side of the screen. Their eye response was immediately followed by presentation of a feedback image. On rewarded trials, the feedback was an image of a golden Euro coin. On correct responses after no-reward anticipation cues, a silver blank disk was displayed. An incorrect or too slow response was followed by a silver ring with a black circle in the middle. (Bottom) Figures (A) and (B) show means and standard deviations in antisaccade latency. Mean antisaccade latency was significantly reduced when participants expected a reward for a well-performed antisaccade. This antisaccade latency benefit from reward anticipation occurred (A) irrespective of the level of direction-specific oculomotor preparation, (B) irrespective of the cue-target delay length and (C) varied considerably across participants.

specificity of the basal ganglia networks for behavior that is modulated by motivation (versus non-motivational factors) we further computed correlations between basal ganglia seeded tractography and antisaccadic benefit from spatial preparation [$(RT_{\text{direction-nonspecific prep}} - RT_{\text{direction-specific prep}})/(RT_{\text{direction-nonspecific prep}})$]. The resulting brain image displayed a value for each voxel representing the connectivity value between that voxel and the voxels in the basal ganglia seed region that varied with the level of performance benefit. To identify significant regions, we used a cluster corrected threshold of $p < .01$ with at least 20 contiguous voxels (Cohen et al., 2008). For a more detailed description please see Supplemental Material S1.8.

3. Results

3.1. Behavioral performance

3.1.1. Reward expectation facilitated the onset of antisaccades

In line with previous results (Harsay et al., 2010), mean antisaccade latency and antisaccade accuracy were significantly reduced when elderly participants expected a reward for a well-performed antisaccade (Fig. 1). The significant effect of reward expectation on antisaccade latency ($F(1,15) = 7.84$, $p < .013$), amounted to a 11 ms (±16) decrease in latency and occurred irrespective of the level of specific oculomotor preparation ($F(1,15) = 1.386$, $p < .257$), cue-target delay length ($F(3,13) = 0.443$, $p < .724$), run ($F(1,15) = 0.335$, $p < .572$), and cue direction ($F(1,15) = 1.48$, $p < .242$). Individual differences in reward-related benefit could not be explained by overall performance on the task, age or gender: reward-related latency benefit did not correlate with global mean latencies ($r = -0.19$; $p < .48$) nor with age ($r = 0.261$; $p < .329$). Age also did not correlate with mean antisaccade latencies ($r = -0.137$; $p = .613$). ANOVA revealed no effect of gender ($F(1,15) = 0.57$; $p < .46$) on mean antisaccade and a moderate effect on reward related latency benefit ($F(1,15) = 3.696$, $p < .075$): males seemed to benefit slightly more from reward. Reward-related latency benefits and reward-related accuracy benefits correlated to a near-significant extent ($r = 0.464$; $p < .070$). Reward-related accuracy benefits ($F(1,15) = 7.10$, $p < .018$) amounted to a 2.7% (±4.0) increase in accuracy and also occurred irrespective of the level of spatial response preparation ($F(1,15) = 2.77$, $p < .117$), cue-target delay length ($F(3,13) = 0.45$, $p < .718$), run ($F(1,15) = 0.001$, $p < .980$), and cue direction ($F(1,15) = 0.134$, $p < .719$).

3.1.2. Direction preparation facilitated the onset of antisaccades

Direction-specific oculomotor preparation cues facilitated the onset latency of antisaccades ($F(1,15) = 18.77$, $p < .001$) irrespective of reward expectation ($F(1,15) = 1.386$, $p < .257$), cue-target delay length ($F(3,13) = 1.69$, $p < .183$), run ($F(1,15) = 2.92$, $p < .108$) and cue direction ($F(1,13) = 0.015$, $p < .903$). Likewise, direction-specific preparation cues improved antisaccade accuracy ($F(1,15) = 12.05$, $p < .003$) irrespective of reward expectation ($F(1,15) = 2.77$, $p < .117$), cue-target delay length ($F(3,13) = 0.14$, $p < 0.937$), run ($F(1,15) = 2.92$, $p < .108$) and cue direction ($F(1,13) = 0.217$, $p < .648$). As cue-target delay length, run, and cue direction did not interact with incentive motivation benefits nor with the direction-specific oculomotor preparation benefits, we pooled across the levels of these factors in the remainder of the analyses (see Table 1 for an overview on mean latencies and accuracy values for reward expectation, direction-specific response preparation and delay length). The current in-scanner behavioral results replicated the behavioral results acquired from the same group of elderly outside the scanner (Harsay et al., 2010). Please see for more detailed behavioral results Supplemental Material S2.1.

Table 1
Brain regions showing ipsilateral white matter pathways depending on white matter pathways in the (A) nucleus accumbens, (B) caudate and (C) putamen, which were stronger in participants who saccaded faster when anticipating reward than others. Local maxima of correlation coefficients (r) of all significant clusters (cluster corrected threshold of $p < .01$ with at least 20 contiguous voxels) are displayed. All coordinates are given in MNI space. *Note*: R = right, L = left.

(A) Seed nucleus accumbens	*X*, *Y*, *Z*	Max *r*
R frontal pole	14, 60, 8	0.73
R anterior medial prefrontal cortex (aMPFC)	14, 48, 4	0.56
(B) Seed caudate	***X*, *Y*, *Z***	**Max *r***
L frontal eye fields	−30, −4, 42	0.73
L primary motor cortex	−26, −36, 42	0.85
L intra-parietal sulcus	−36, −52, 24	0.68
L pre-supplementary motor area	−14, −4, 46	0.53
L putamen	−20, 4, −10	0.73
L accumbens	−12, 10, −10	0.73
L thalamus	−12, −20, 12	0.75
R thalamus	10, −20, 12	0.89
R inferior frontal gyrus	36, 18, 26	0.83
R middle frontal gyrus	44, 18, 24	0.71
L superior longitudinal fascilicus	−32, −52, 22	0.68
R anterior thalamic radiation	30, 30, 22	0.77
(C) Seed putamen	***X*, *Y*, *Z***	**Max *r***
L amygdala	−24, −4, −18	0.77
R amygdala	28, −16, −8	0.72
R thalamus	14, −16, 14	0.72
L thalamus	−12, −10, 6	0.77
L hippocampus	−26, −26, −12	0.64
R inferior frontal gyrus	46, 24, 20	0.86
L inferior frontal gyrus	−58, 16, 10	0.80
R anterior medial prefrontal cortex	10, 66, 12	0.69
R middle frontal gyrus	26, 38, 24	0.66
L middle frontal gyrus	−20, 38, 24	0.76
L frontal eye fields	−32, −22, 52	0.82
Dorsal cingulate	−14, 22, 24	0.81

3.2. DTI results

3.2.1. Probabilistic tractography of the striatum

The overall patterns of striatal subregion-seeded fiber connectivity were consistent with invasive histological tracing in non-human primates (Cui et al., 2003; Haber et al., 2006; Haber and Knutson, 2010; Lehericy et al., 2004; Lynch and Tian, 2006). For example, the caudate showed connectivity with the thalamus, nucleus accumbens, frontal eye fields and intraparietal sulcus; the nucleus accumbens showed connectivity with the medial and

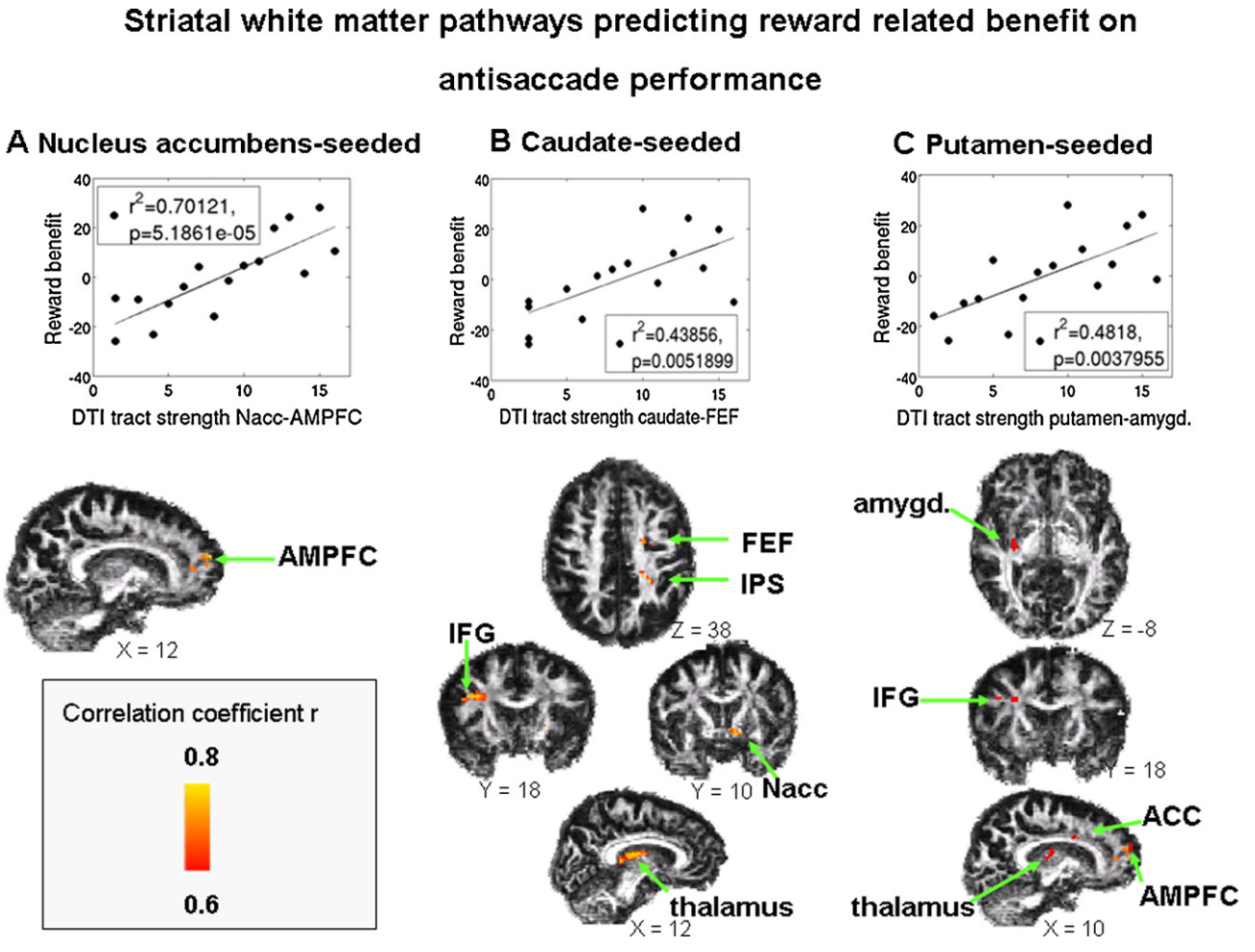

Fig. 2. White matter pathways of the striatum as associated with the effect of motivational incentives on the latency of antisaccades. The extent to which participants made faster antisaccades when they expected reward showed stronger white matter pathways between striatal subregions (nucleus accumbens, caudate, putamen) and a distinct network of oculomotor-, limbic- and action-monitoring-structures. (A–C) Scatterplots, displaying the spread of data points, the best-fit line and effect-size of reward latency benefit versus white matter tract strength and all clusters that survived statistical thresholding seeded from the nucleus accumbens, caudate, and putamen, respectively.

Table 2
Brain regions showing ipsilateral white matter tracts depending on fiber tracts in the caudate, that were stronger in participants who reacted faster with advance knowledge on the upcoming antisaccade than others. Local maxima of correlation coefficients (r) of all significant clusters (cluster corrected threshold of $p < .01$ with at least 20 contiguous voxels) are displayed. All coordinates are given in MNI space. *Note*: R = right, L = left.

Seed caudate	*X*, *Y*, *Z*	*r*
R frontal eye fields	42, −6, 34	0.86
L inferior occipital fasciculus	−26, 24, 22	0.81
L anterior thalamic radiation	−26, 28, 18	0.78

orbitofrontal cortices, the insula and the brainstem; and the putamen showed connectivity with the amygdala, hippocampus, thalamus, right inferior frontal gyrus, caudate, frontal eye fields and intraparietal sulcus.

3.2.2. Results of individual difference analysis

3.2.2.1. Striatal white matter pathways predicted reward-related performance benefits. In general, participants who speeded their responses when expecting reward showed stronger striatal–striatal connectivity as well as stronger cortico-striatal connectivity.

From the nucleus accumbens seed, the reward benefit predicted connectivity strength with the ipsilateral anterior medial prefrontal cortex and frontal pole (Fig. 2A and Table 1A).

From the caudate seed, behavioral reward benefit predicted ipsilateral fiber tracts to the nucleus accumbens and the putamen. Furthermore, from the caudate seed, behavioral reward benefit predicted ipsilateral fiber tracts to cortical oculomotor structures including the frontal eye fields (FEF) and intra parietal sulcus (IPS) and also to the thalamus, the anterior cingulate (ACC) and to the inferior frontal gyrus (IFG) (Fig. 2B and Table 1B).

Finally, from the putamen seed, reward benefit predicted connectivity strength with the thalamus, amygdala, hippocampus, anterior medial prefrontal cortex, ACC, FEF and IFG (Fig. 2C and Table 1C). Note that Fig. 2 displays most but not all of the regions described in the results and Table 1.

3.2.2.2. Striatal connectivity and direction-specific oculomotor preparation cues. Individual differences in performance benefit from direction-specific oculomotor response preparation relied on the strength of white matter pathways between the caudate and the FEF, and with clusters in the anterior thalamic radiation and the fronto-occipital fasciculus. Significant correlations within striato-striatal white matter pathways were not observed (see Table 2, Supplementary Fig. 2.2). Taken together, corticostriatal pathways between caudate and frontal eyefields were apparent in this condition, but not the more motivationally/limbic processes as observed in the motivational benefit condition. Please see for more results of the individual difference analysis Supplemental material S2.3/S2.4.

4. Discussion

The primary aim of this study was to link individual differences in the white matter pathways of the striatum in older adults to motivation-modulated oculomotor behavior. To this end, we correlated probabilistic tractography strength from three striatal targets (nucleus accumbens, caudate and putamen) with individual differences in the reward anticipation-related improvement of antisaccade task performance. After replicating the improved antisaccade performance following reward anticipation (Harsay et al., 2010), we found that individual differences in this behavioral benefit could be predicted by individual differences in the white matter pathways of (1) the caudate to ipsilateral oculomotor networks, (2) the nucleus accumbens to medial prefrontal cortex, (3) the putamen to thalamo-cingulate networks and (4) intrastriatal white matter pathways between caudate, nucleus accumbens and putamen.

From an anatomical connectivity perspective, the findings are sensible. Histological tract tracing in the non-human primates shows that the caudate (and to a lesser extent also the putamen) integrates with cortical oculomotor structures including the FEF and intraparietal sulcus (Baizer et al., 1993; Cavada and Goldman-Rakic, 1991; Cui et al., 2003; Lynch and Tian, 2006). The striatum has been conceptualized as an output channel for information about the hedonic/aversive valences of stimuli from the limbic system. This information may enter the striatum either by a subcortical route via the amygdala and/or hippocampus or by a cortical route via the orbitofrontal and/or anterior cingulate areas (Friedman et al., 2002; Lehericy et al., 2004). Animal work further shows that output from the accumbens does not reach cortical, brainstem or spinal cord generators of motor patterns (Groenewegen and Russchen, 1984; Zahm, 2000; Zahm and Heimer, 1993). Based on these neuroanatomical findings and the present results, we suggest that the putamen and the nucleus accumbens bias actions by forwarding reward value to the caudate, which in turn is able to directly modulate oculomotor processes. This proposition is supported by studies in non-human primates showing that the caudate incorporates reward anticipation into movement-related decision-making (Pasquereau et al., 2007) and into the control of oculomotor action (Lauwereyns et al., 2002). Our results suggest that individual differences in the strength of these pathways may account (at least in part) for individual differences in motivated behavior.

The current analyses of structural connectivity, however, do not allow inference about directionality of this effect. The caudate may project "upwards" to the cortical eyefields to mediate the formation of early action plans. The cortical oculomotor structures (intraparietal sulcus, frontal eye fields) in turn may project "downwards" into the indirect path, back to the caudate, which can gate the superior colliculus for direct cortical input.

4.1. The specificity of striato-cortical connectivity for motivated behavior

Behaviorally, antisaccade performance improvement from reward showed no interactions or correlations with performance improvement from non-motivational, spatial oculomotor preparation (direction-specific knowledge about the upcoming response, Fig. 1 bottom). This inde-

pendent motivational effect on behavior paralleled the distinct configuration of the "motivational" and "non-motivational" connectivity patterns. That is, the strength of white matter connectivity between the three main subdivisions of the striatum – caudate, nucleus accumbens, and putamen –, and cortical pathways seeded in all the three striatal subdivisions predicted reward benefit, whereas only cortical pathways seeded in the caudate predicted "non-motivational" connectivity patterns.

Analysis of local fractional anisotropy confirmed this distinction between white matter densities related to motivational and non-motivational performance improvement: non-motivational performance benefits correlated with higher white-matter integrity predominantly in oculomotor structures (supplementary motor cortex, fronto medial and occipital cortex). Reward-related performance improvements on the other hand correlated with fractional anisotropy in both striatal areas and oculomotor structures (nucleus accumbens, caudate, thalamus, frontal eyefields, inferior frontral gyrus and orbitofrontal cortex (Supplemental Material S2.4)).

This profile provides further evidence (Harsay et al., in press) for differential roles of the caudate (integrate reward information into oculomotor action control) versus the putamen and the nucleus accumbens (forward value-evaluations and generic action directions to caudate) in the motivational modulation of oculomotor control. The nucleus accumbens and putamen may play a role in generic reward related action monitoring, whereas the caudate plays a more specific role in using reward information to guide actions by functionally interfacing with cortical areas involved in saccade planning and execution.

4.2. Striato-cortical white matter pathways and oculomotor and reward networks

These findings are best viewed from a networks perspective. Oculomotor structures are connected through several loops, one of which projects from the frontal eye fields through the caudate and the substantia nigra reticulata to the saccade generators in the brainstem. Through "looping" interactions, the cortical and subcortical parts of the oculomotor network can communicate with each other and coordinate their activity (Harting and Updyke, 2006; Hikosaka et al., 2000). Whereas the caudate and putamen appear involved in oculomotor control (Alexander et al., 1990; Lehericy et al., 2004; Lynch and Tian, 2006; Taniwaki et al., 2003), lesion studies, imaging, and neurophysiological experiments suggest a role for the nucleus accumbens in monitoring motivationally relevant context information (Grahn et al., 2008; Schultz et al., 2003). Nucleus accumbens white matter pathways to the prefrontal cortex have previously been found to predict individual differences in the personality trait reward dependence (Cohen et al., 2009) and amygdala-related brain circuits have been found to mediate different aspects of reward-guided learning (Cohen et al., 2008). Also, in non-human primates striato-limbic interactions have been suggested to affect the processes by which reward-related stimuli come to affect action (Robbins et al., 1989). In the current data the white matter pathways to the accumbens and putamen may enable the caudate to reinforce looping oculomotor signals for action plans that lead to a reward: The evaluation of potential action-outcomes supported by the nucleus accumbens-frontopolar white matter pathways and the expectancies of reinforcers supported by the putamen–thalamo–amygdala fibertracts (Holland and Gallagher, 2004) may be communicated via the caudate to the thalamocortical oculomotor networks to modulate oculomotor plans (Cromwell and Schultz, 2003; Grahn et al., 2008).

4.3. Investigating motivated behavior in older adults with an individual difference approach

The observation that individual differences in motivated behavior among older adults are related to striato–cortico–limbic white matter pathways may help clarify seemingly contradictory evidence from recent neuroimaging studies. In particular, Samanez–Larkin and colleagues (Samanez-Larkin et al., 2007) suggested that reward anticipation is intact in elderly, but Schott et al. (2007) argued that reward anticipation in elderly is deficient compared to that of younger adults. If a large amount of individual variability is present, such discrepancies may occur. The current results suggest that differences in structural properties of the striatum might partly account for discrepancies in reward function among older adults. The individual differences approach reveals patterns that might be obscured by simply comparing older participants with the young, and suggests that the capacity to employ motivation to improve declining cognitive function is determined by individual differences beyond those related strictly to age. In the present study, the individual differences in reward-related benefit could not be explained by age (here between 64 and 76 years of age), gender, or overall performance (global mean antisaccade latencies) on the task. It is also important to note that the viability of our approach depended on the exclusion of sources of disability or illness in older adults (as determined by neuropsychological, medical and neuroradiologic tests for adverse cognitive and physiological conditions) that could influence performance in behavioral measures independent of critical cognitive functions.

It is tempting to speculate that individuals with higher tract strength values and thus a higher effectiveness of fiber bundles can transmit information more efficiently between brain regions as bundles with a higher degree of myelination are able to process information more rapidly (Beaulieu, 2009). Although more investigations are needed to confirm this interpretation, white matter tractography is becoming increasingly relevant for understanding neurocognitive function (Cohen et al., 2008, 2009; Johansen-Berg and Behrens, 2006; Johansen-Berg et al., 2007). Although neuroimaging studies of functional architecture will continue to rely on information from classical neuroanatomy to guide their interpretation (Johansen-Berg, 2009), the in–vivo quantification of human white matter fibers opens new possibilities for understanding the neurobiological underpinnings of the development of motivation.

These kinds of anatomical individual differences may be even more relevant for the developmental period of adolescence, in which the brain is not yet fully developed. For example, the reward system is still developing in the adolescent brain. It requires more intense stimulation (Bjork et al., 2004) and it is coupled with less developed regulatory areas (e.g., PFC) (Casey et al., 2008; Fareri et al., 2008). Although speculative, the current results suggest an important role for individual differences in network connectivity affecting the reward/regulation balance during adolescence. Understanding the neural network core underlying changes in reward/regulation processes may contribute to a more mechanistic understanding of the development of affective disorders in this age group (Forbes and Dahl, 2005).

Within this network-approach, individual differences in motivational behavior should correspond to more global network profiles of activity that are distributed and balanced throughout multiple brain regions and systems. Of course, white matter pathways are not the only sources of individual differences; there are many neurochemical (dopaminergic, GABA-ergic, peptidergic and amino-acid containing) and neuronal (e.g., inhibitory and excitatory mechanisms) biological properties that should be expected to vary across individuals (and across development within individuals) that may impact reward-guided behavior.

5. Conclusions

In conclusion, we report that older individuals differed in how effectively motivational incentives modulated their actions. We conclude that individual differences in motivated behavior are related to, if not (at least to some extent) driven by differences in structural anatomy. Specifically, individuals who increased their efficiency more when they expected reward had stronger fibers in white-matter circuits throughout multiple striato-cortical loops. This may allow the basal ganglia to achieve efficient extraction of reward information that may then be used for execution and planning of forthcoming actions. Our results suggest that there is considerable significance in understanding the role of striato-cortical white matter pathways in the impact of motivational cues on actions across development and specifically, the role of individual differences in the maturation of white matter pathways for the early development of disruptions in the regulation of motivation.

Acknowledgements

We thank Renee Visser and Hilko van Rooijen for their assistance in testing the subjects. Jasper Wijnen is gratefully acknowledged for his technical support.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.dcn.2011.06.005.

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