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Age-related prefrontal impairments implicate deficient prediction of future reward in older adults

Ben Eppinger [a,*], Hauke R. Heekeren [b], Shu-Chen Li [a,c]

[a] Department of Psychology, Technische Universität Dresden, Dresden, Germany
[b] Department of Education and Psychology, Freie Universität Berlin, Berlin, Germany
[c] Center for Lifespan Psychology, Max Planck Institute for Human Development, Berlin, Germany

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ABSTRACT

Foresighted decision-making depends on the ability to learn the value of future outcomes and the sequential choices necessary to achieve them. Using a 3-stage Markov decision task and functional magnetic resonance imaging, we investigated age differences in the ability to extract state transition structures while learning to predict future reward. In younger adults learning was associated with enhanced activity in the prefrontal cortex (PFC). In older adults (OA) we found no evidence for PFC recruitment. However, high-performing OA showed enhanced striatal activity, suggesting that they may engage in a model-free (experience-based) learning strategy. Change point analyses revealed that in younger adults learning was characterized by distinct and abrupt shifts in PFC activity, which were predictive of behavioral change points. In OA PFC activity was less pronounced and not predictive of behavior. Our findings suggest that age-related impairments in learning future reward value can be attributed to a deficit in extracting sequential state transition structures. This deficit may lead to myopic decisions in OA if contextual information has to be temporally integrated.

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1. Introduction

In this study we used a three-stage Markov decision task and functional magnetic resonance imaging (fMRI) to investigate whether age-related decline in prefrontal cortex (PFC) function (Nyberg et al., 2010; Raz, 2005) may lead to impairments in older adults' (OA's) ability to learn sequential state transition structures that lead to future reward. The important feature of the Markov decision task (the Markov property) refers to the fact that a decision at certain state not only defines the reward that subjects obtain but also determines the next state that subjects transition to. Thus, to perform optimally in this task, participants have to learn the Markov property, that is the sequential transition structure of the task (see Fig. 1A)

Recent behavioral and electrophysiological findings suggest that OA are impaired in probabilistic reinforcement learning (RL), whereas these impairments are absent or less pronounced when reward is fully predictable (for a review see Eppinger et al., 2011). Evidence from functional imaging studies showed that age-related impairments in RL are associated with a reduced sensitivity of the ventral striatum to reward prediction errors in OA (Chowdhury et al., 2013; Eppinger et al., 2013a; Samanez-Larkin et al., 2014). There are currently (at least) 2 possible explanations for these effects. On the one hand it could be argued that changes in prediction error signaling in OA are due to compromised dopamine (DA) projections to frontostriatal circuits (Dreher et al., 2008). On the other hand, there is also evidence for the idea that age-related changes in prediction error signals result from deficits in the connectivity between frontal and striatal regions in OA (Bennett et al., 2011; Samanez-Larkin et al., 2012). Moreover, findings from multimodal imaging (positron emission tomography with fMRI) studies showed that striatal DA also affects frontal working memory and cognitive control functions (Braskie et al., 2008; Landau et al., 2009). For example, age-related DA decline in the striatum is associated with reduced metabolism and blood-oxygen-level dependent (BOLD) activity in the PFC, as well as deficits in flexible rule acquisition (Volkow et al., 1998, 2000). Moreover, evidence from animal research showed that age-related reductions in local prefrontal DA signaling lead to impairments in executive control by affecting the temporal precision of PFC neurons during the encoding of time-sensitive task information (Arnsten et al., 2012; Caetano et al., 2012).

Findings from a recent electrophysiological study on task set shifting in rats point into a similar direction. Results of this study showed that the acquisition of new discrimination rules was

* Corresponding author at: Technische Universität Dresden, Zellescher Weg 17, 01062, Dresden, Germany. Tel.: +49 351 463-39193; fax: +49 351 463 42194.
E-mail address: Benjamin.Eppinger@tu-dresden.de (B. Eppinger).

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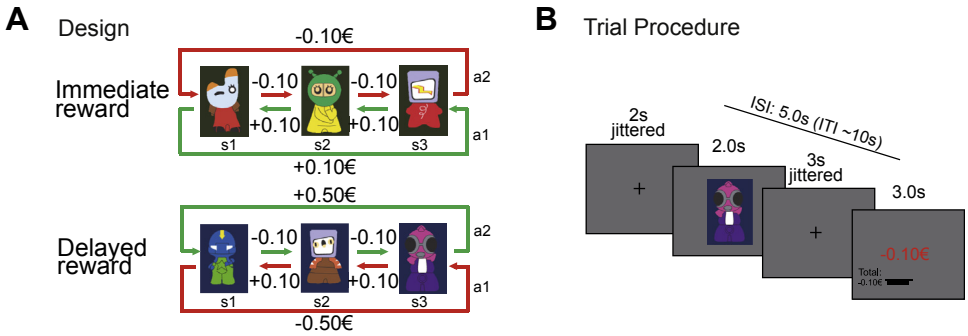

Fig. 1. (A) Schematic figure of the task. At each state (stimulus) participants were asked to make a choice between 2 actions. This choice not only affected the reward that participants received but also determined the transition to the next state (Markov property). In the immediate reward condition on action was rewarded (small gain) whereas the other action was punished (small loss). In the delayed reward condition 1 action was associated with small gains at the first 2 states and a large loss at the last state (suboptimal action, a1). The other action is associated with 2 small losses in the beginning and a large reward at the final state (optimal action, a2). (B) Schematic figure of the trial procedure. Abbreviations: ISI, inter-stimulus interval; ITI, inter-trial interval.

preceded by sharp transitions in PFC activity, presumably reflecting insights into the new rule (Durstewitz et al., 2010). Similar results were obtained in a study in humans that used a Markov decision task in combination with fMRI (Tanaka et al., 2004) In this study, participants had to learn the transition structure of a task to obtain a large future reward. Learning was associated with striatal activity, which reflected the discounting of future reward. Furthermore, learning was also associated with lateral PFC activity, suggesting that this area may be involved in mediating insights into the sequential transitions structure of the task (Tanaka et al., 2004). Taken together, these findings suggest that the PFC may have a specific role in mediating insights about sequential transition structures in a task.

Here, we investigated whether age-related impairments in learning to predict future reward can be attributed to deficits in extracting sequential state transition structures in OA. To this end, we used a modified 3-state Markov decision task (Tanaka et al., 2004) in an event-related fMRI design (see Fig. 1A). The task contained 2 experimental conditions: (1) one in which the participants' choices resulted in small immediate reward or loss and (2) one in which they had to extract the sequential structure of transitions across 3 choice states to obtain a large future reward.

Based on prior work (Mell et al., 2009; Volkow et al., 1998), we expected age-related impairments in learning to predict future reward. Furthermore, we predicted that learning of sequential state transition structures would be associated with enhanced lateral PFC activity (Boettiger and D'Esposito, 2005; Tanaka et al., 2004). Furthermore, given aging-related deficits in prefrontal DA modulation (Bäckman et al., 2006), as well as structural decline in the PFC (Raz, 2005), we hypothesized that OA's learning impairments would be associated with an under-recruitment of the lateral PFC. Based on the findings by Durstewitz et al. (2010), we expected that in younger adults (YA) learning-related shifts in choice behavior would be associated with rapid changes in prefrontal activity. In contrast, in OA we expected that deficits in PFC functioning would lead to slower and more gradual learning.

2. Materials and methods

2.1. Participants

Twenty-seven younger and 31 older right-handed adults participated in the study. One YA was excluded because of head motion (>2 mm in either direction). Three OA were excluded because their structural scans showed evidence for ischemic lesions. Two further OA had to be excluded because they were unable to stay in the MR scanner throughout the experiment. The effective sample thus consisted of 26 YA (mean age = 24.8, standard deviation [SD] = 2.6, 13 male, age range: 20–30 years) and 26 OA (mean age = 71.9, SD = 5.5, 13 male, age range: 61–80 years). Participants gave written informed consent. The study was approved by the Institutional Review Board of the Charité Universitätmedizin Berlin. During the screening session participants completed a demographical questionnaire, the behavioral inhibition score–behavioral approach score (BIS-BAS) scales (Carver and White, 1994), a working memory task and several psychometric tests: (1) Identical pictures test (Lindenberger and Baltes, 1997); (2) Raven's progressive matrices (Raven et al., 1998); (3) Spot-the-Word test (Baddeley et al., 1992). OA scored lower on the Identical Pictures Test and Raven's matrices than YA (p's < 0.001, η^2's > 0.51; Raven's: YA: mean: 25.9, SD: 6.8; OA: mean: 12.2, SD: 6.8; Identical Pictures: YA: mean: 31.0, SD: 4.9; OA: mean: 21.3, SD: 3.7). In contrast, OA reached higher scores compared with YA on the Spot-the-Word test ($p < 0.001$, $\eta^2 = 0.31$; YA: mean: 0.54, SD: 0.2; OA: mean: 0.75, SD: 0.2). Consistent with previous findings, these results suggest age-related declines in fluid intelligence and relative stability in crystallized intelligence (Li et al., 2004). We found no significant age differences in the BIS or BAS scores (p's > 0.28).

2.2. Materials and procedure

2.2.1. Stimuli

We created 24 colored figures ("GoGos") using a software available online on the www.gogosland.com Web site and processed them for presentation purposes in photoshop (see Fig. 1). Each block involved a new set of 3 figures. To make the learning conditions more distinguishable from each other the stimuli were displayed on different background colors (blue for delayed reward, green for immediate reward, see Fig. 1A). The feedback stimuli indicated small gains and losses of 10 cents and big gains and losses of 50 cents.

2.2.2. Task

In our Markov decision task, participants have to make a 2-choice decision upon presentation of each stimulus using 1 of 2 response buttons (left or right). After the action they receive a feedback about the amount of reward or loss associated with their choice. Markov property refers to the fact that a decision at a specific stimulus not only determines the reward that participants get but also determines the transition to the next stimulus (see Fig. 1A). That is, by

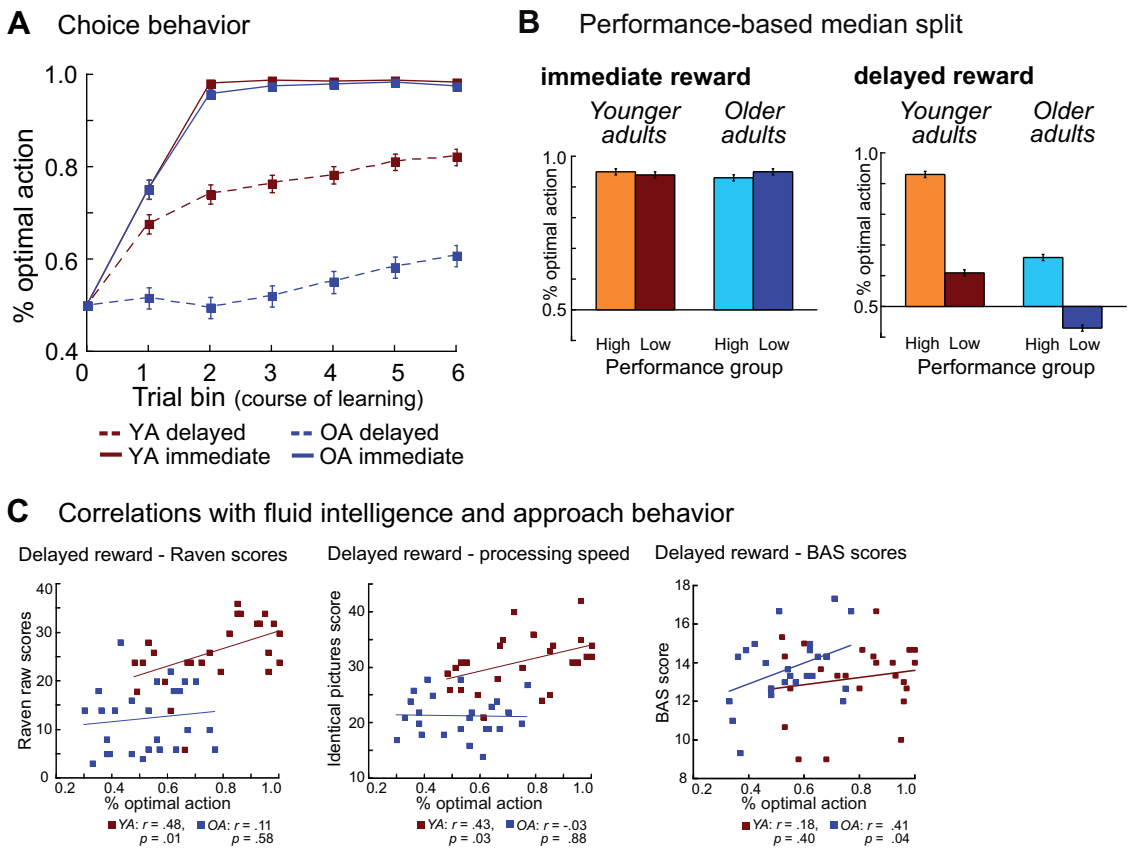

Fig. 2. (A) Choice performance in proportion optimal action (y-axis) averaged into 6 equally large trial bins (x-axis), displayed separately for the immediate reward condition (solid lines) and the delayed reward condition (dashed lines). Younger adults (YA) are shown in red, older adults (OA) are shown in blue. Error bars reflect the standard error of the mean (SE). (B) Median split for performance (proportion optimal action) in the delayed reward condition, displayed separately for the 2 age groups and the 2 learning conditions. High-performing groups are shown in lighter colors (orange and cyan), low performing groups are shown in darker colors (red and blue). Error bars reflect the SE. (C) Left panel: correlation between choice performance in the delayed reward condition (x-axis) and Raven scores (y-axis). Middle panel: correlation between performance in the delayed reward condition (x-axis) and processing speed (y-axis). Right panel: correlation between performance in the delayed reward condition (x-axis) and behavioral approach scores (BAS) (y-axis). YA are shown in red, OA are shown in blue. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

always choosing the optimal action participants would always see the same sequence of stimuli. Similar to the study by Tanaka et al. (2004), our task involved 2 learning conditions. In the immediate reward condition the optimal action was consistently rewarded at all 3 states of the task (+10 cents, see Fig. 1A), whereas the other action was consistently punished (−10 cents). In the delayed reward condition 1 (optimal) action was associated with small losses at the first 2 states and a big reward at the third state (+50 cents). The other (suboptimal) action was associated with small gains in the beginning, but a large loss in the end (−50 cents). Assuming optimal performance the pay-off is the same across learning conditions. The experiment also contained 2 control blocks: in the always reward condition participants always received a small reward (+10 cents), independently of their action, whereas in the no reward condition subjects always received a neutral outcome.

2.2.3. Trial procedure

Each trial started with the presentation of a fixation cross (mean interval of 2 seconds, jittered between 1–5 seconds). Then the stimulus was presented for 2 seconds. The stimulus was followed by a fixation cross (mean interval of 3 seconds, jittered between 2 to 6 seconds). Then the feedback stimulus was displayed for 3 seconds. The inter-stimulus intervals were jittered in 0.5-second steps according to a long-tailed exponential distribution ($\lambda = 3.0$), yielding a mean inter-stimulus interval of 5.0 seconds (Hagberg et al., 2001). The range of the inter-trial interval was 6–16 seconds with a mean of 10 seconds. If participants missed a 2-second response deadline the words “too slow” were presented and the trial was repeated. Time-out trials were discarded from analyses (no time-outs in YA, < 1% time-outs in OA).

2.2.4. Experimental design

The experiment consisted of a practice phase and an experimental phase. In the beginning of the practice phase we showed the participants all possible combinations of stimuli, actions, and outcomes to familiarize them with the conditions. We explicitly told the participants that in 1 condition they might have to accept minor losses to receive a big reward. Then they performed 2 practice blocks (1 per condition) using the same stimuli. The practice blocks were terminated once they reached a mean accuracy of 60% or performed a maximum number of 36 trials (immediate condition) or 72 trials (delayed condition).

In the MR scanner participants performed 8 experimental blocks (3 immediate reward blocks, 3 delayed reward blocks, and 2 control blocks (always small reward, or no reward). Each block involved 3 new stimuli and a total number of 36 trials (108 trials per condition). The control block involved 20 trials per condition. Block order was randomized across participants with the restriction that the 2 control blocks were always performed at the end of the experiment. This was necessary to avoid confusion about task instructions. Overall, participants performed 256 trials and it took them about 43 minutes to complete the task.

2.3. Procedure

The study consisted of 2 sessions. In the first session participants performed the psychometric tests and questionnaires and were screened for MR eligibility. In the second session they completed the 3-state Markov decision task and a second experimental task (data will be reported elsewhere) during MR scanning. Participants received the money they had earned throughout the task as compensation. Negative pay-offs were not subtracted from these earnings. Although YA earned slightly more money in the task than OA, this difference was small (on average YA earned €22.49, whereas OA earned €20.02).

2.4. Data acquisition

The stimuli were projected using MR compatible goggles (VisuaStim, Resonance Techology Inc). E-Prime 2.0 software (PST Inc, Pittsburgh, PA, USA) was used for stimulus presentation. Manual responses were registered using an MR-safe button box. A pillow and foam cushions were placed inside the head coil to minimize head movements.

2.4.1. fMRI data acquisition

MR image acquisition was performed on a 3 Tesla MRI scanner (Tim Trio; Siemens, Erlangen, Germany) at the Charité University Medicine Berlin, Campus Benjamin Franklin. High-resolution (1 mm3) T1-weighted structural images were acquired using an magnetization prepared rapid gradient echo (MP-RAGE) pulse sequence [176 axial slices; field of view, 244; repetition time (TR), 1550 ms; echo time, 2.34 ms; flip angle, 9°]. Anterior commissure-posterior commissure aligned functional images were acquired using a T2* weighted echo planar imaging (EPI) sequence [36 interleaved slices; voxel size: 3 × 3 × 4 mm; field of view, 216; TR, 2000 ms; echo time, 30 ms; flip angle, 80°].

2.5. Behavioral data analysis

Accuracy was analyzed using Matlab (MATLAB, MathWorks Inc, Natick, MA, USA) and SAS (SAS Institute Inc, Cary, NC, USA). Mean accuracy (proportion optimal action) was averaged for each participant and learning condition into 6 consecutive equally sized trial bins. To investigate individual differences in learning, we performed a median split and subdivided participants in each of the 2 age groups into high and low performing groups (for similar analyses with performance-based groupings see Chowdhury et al., 2013; Nagel et al., 2009). Although the use of median split analyses has been discouraged previously because of loss of power and information as well as the potential increase in type 1 errors (MacCallum et al., 2002), findings from recent simulation studies suggest these issues are only of concerns in situations in which multiple correlated predictor variables are used (Iacobucci et al., 2014), which is not the case in the present study. Furthermore, studies that criticized the use of median splits (see MacCallum et al., 2002) also acknowledged that 1 area where these procedures are potentially useful is in situations in which performance is a potential moderator of other relationships (e.g., brain-behavior relationships). Indeed, several previous aging studies (e.g., Chowdhury et al., 2013; Nagel et al., 2009) have shown that performance level moderates activity in frontostriatal or frontoparietal networks. To explore whether performance level may moderate task-related brain activity in the 2 age groups, we thus split the participants based on their performance and submitted the data to a 2 (age-group) × 2 (performance group) × 2 (condition) × 6 (trial bin) mixed effects analysis of variance (ANOVA).

2.5.1. Behavioral change point analysis

For the behavioral change point analysis, we calculated the cumulated sum of differences to the mean (CUSUM) as $(Si) = \sum_{j \le 1} (Sj - (S))$, where (S) is the mean of the behavioral time series (Durstewitz et al., 2010; Gallistel et al., 2004). The CUSUM curves were generated for each individual and block in the delayed reward condition. Change points were defined as the minima of the CUSUM curves and averaged across blocks for statistical analyses. Mean change points were analyzed using an ANOVA with age group and performance group as the between-subjects factor. By cumulating along the time series the CUSUM approach reduces variance and allows a reliable detection of changes in the mean of the time series (Durstewitz et al., 2010). CUSUM curves first decrease because the values are consistently below mean performance. After reaching the "change point" the cumulative sum of differences to the mean increases because the values are now above the mean.

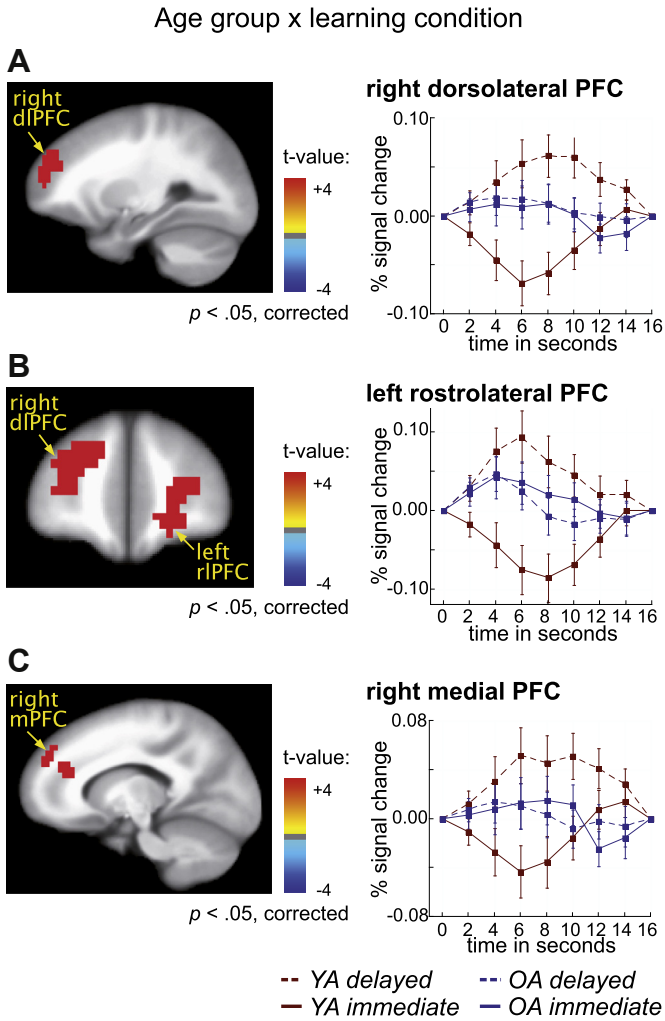

Fig. 3. Left panel: significant outcome-related activity (t-statistics) for the age group × learning condition interaction in the right dlPFC (Talairach co-ordinates: −20,−47, 25), left rlPFC (18, −54, 4), and right mPFC (−12, −36, 24). Activations are significant at $p < 0.05$, corrected. Right panel: time courses for activity in the left dlPFC, right rlPFC, and mPFC, displayed separately for the immediate reward condition (solid lines) and the delayed reward condition (dashed lines). Younger adults (YA) are shown in red, older adults (OA) are shown in blue. Error bars reflect the standard error of the mean (SE). Abbreviations: dlPFC, dorsolateral prefrontal cortex; mPFC, medial prefrontal cortex; rlPFC, rostrolateral prefrontal cortex. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

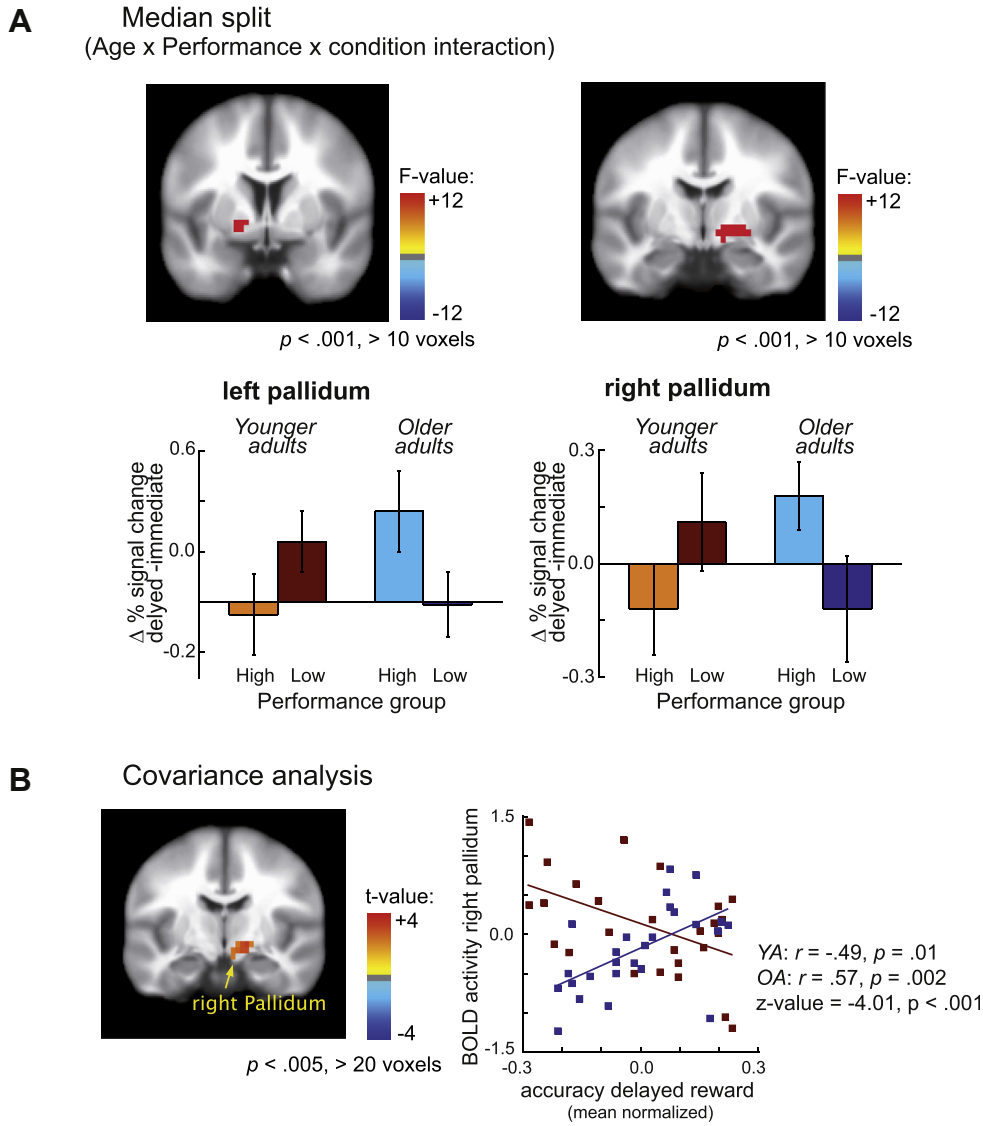

Fig. 4. A Upper panel: significant outcome-related activity (F-statistics) for the age group × performance group × learning condition interaction in the left and right pallidum (Talairach co-ordinates: −15, −1, −2 and 15, −1, −1, respectively). Activations are significant at $p < 0.001$, cluster size >10 voxels. Lower panel: mean BOLD signal difference between the delayed and the immediate reward condition in the left and right pallidum, displayed separately for younger (red) and older adults (blue) as well high (lighter colors) and low performance groups (darker colors). Error bars reflect the standard error of the mean (SE). (B) Left panel: significant outcome-related activity for the interaction between age group, learning condition, and performance (whole-brain analysis of covariance) in the right pallidum (Talairach co-ordinates: 13, −10, −4). Activations are significant at $p < 0.005$, cluster size >20 voxels. (B) Correlations between striatal BOLD activity (contrast between delayed and immediate reward condition) and mean centered performance in the delayed reward condition, displayed separately for younger (red) and older adults (blue). Abbreviations: OA, older adults; YA, younger adults. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

2.6. fMRI data preprocessing

Preprocessing and statistical fMRI data analyses were performed using Analysis of Functional NeuroImages (AFNI) software (Cox, 1996). We used the DARTEL toolbox as implemented in statistical parametric mapping (SPM) software for spatial normalization of the data (SPM8; Welcome Department of Imaging Neuroscience, London, UK). DARTEL allows to spatially normalize the fMRI data to a study-specific template, which is representative of the anatomies of both age groups. This was done to avoid a normalization bias toward the anatomy of YA (Samanez-Larkin and D'Esposito, 2008).

2.6.1. Preprocessing

The functional data were slice-time corrected to the second volume using Fourier interpolation and realigned using rigid-body 3D motion correction. Transient spikes in the EPI data were removed using the AFNI program 3dDespike. Percent signal change was calculated for each voxel with respect to the mean activation across the time series.

2.6.2. Spatial normalization

We first registered the functional images to the high-resolution T1 image (within individual) in AFNI using a local Pearson correlation cost function (Saad et al., 2009). Then functional and structural images were manually aligned with the SPM tissue probability maps. This was done to ensure that the images are approximately aligned with Montreal Neurological Institute and Hospital (MNI) coordinate space before segmentation and normalization. Then, we segmented the T1 images into their tissue components using the unified segmentation procedure (Ashburner and Friston, 2005). The resulting gray and white matter images were used to create the study-specific gray matter template (Ashburner, 2007; Harris et al., 2009). In addition to

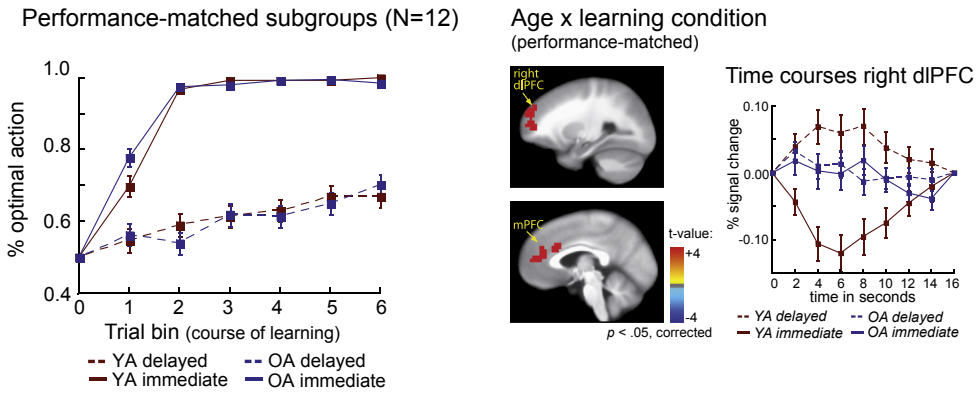

Fig. 5. Left panel: choice performance for performance-matched subgroups (N = 12 per group) in proportion optimal action (y-axis) averaged into 6 equally large trial bins (x-axis), displayed separately for the immediate reward condition (solid lines) and the delayed reward condition (dashed lines). Younger adults (YA) are shown in red, older adults (OA) are shown in blue. Error bars reflect the standard error of the mean (SE). Right panel: significant outcome-related activity (t-statistics) for performance-matched subgroups as well as time courses for BOLD activity in the right dlPFC. We found a significant age group × learning condition interaction in the right dlPFC (Talairach co-ordinates: −20, −47, 25), and right mPFC (−12, −36, 24). Activations are significant at $p < 0.05$, corrected. Abbreviations: dlPFC, dorsolateral prefrontal cortex; mPFC, medial prefrontal cortex. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

the template, the procedure results in so-called flow fields that parameterize the nonlinear deformations that are applied to match each individual image to the template. These flow fields were used to normalize the smoothed (Gaussian full width at half maximum 8 mm) EPI data to an MNI-registered version of the template. For further analyses in AFNI the functional data were aligned to Talairach space and are displayed on a Talairach space version of the International Consortium for Brain Mapping 452 T1 brain.

2.7. fMRI data analysis

For each participant's fMRI data, we performed a general linear model (GLM) analysis using 8 experimental regressors. Four of those regressors modeled the onset of stimuli in the different conditions (immediate reward, delayed reward, always reward, and no reward). Another set of 4 regressors modeled the onset of outcomes for the different conditions. The regressors were convolved with a canonical hemodynamic response function. Motion correction parameters were included in the GLM as regressors of no interest. Reaction time was included as a parametric regressor. Baseline drifts in the data were modeled using a fourth degree polynomial. In the single subject GLM analysis we performed outcome-locked contrasts between the 2 experimental conditions (delayed reward +1 vs. immediate reward −1). The beta-coefficients of these contrasts were subjected to a whole-brain mixed effects ANOVA (as implemented in the AFNI program 3dANOVA3 type 5) with fixed-effect factors of age group (YA vs. OA), performance group (high vs. low), and reward condition (delayed reward, immediate reward) and the random factor of subjects. We used the AFNI program AlphaSim to correct for multiple comparisons. We determined that a corrected (familywise) p-value of 0.05 is achieved with a minimum cluster size of 47 voxels, each significant at $p < 0.0005$.

2.7.1. fMRI change point analysis

For the analysis of neural change points, we used the AFNI program 3dSynthesize to extract the best fitting BOLD time series for a structural region of interest in the left dorsolateral PFC (dlPFC) (BA 9, as defined using Talairach atlas). We then subtracted baseline and motion coefficients from the time series using AFNI program 3dcalc. For each trial in the time series we averaged the BOLD signal from 4 to 8 seconds after stimulus onset. We then performed a baseline correction by subtracting the signal from the time-step (TR) immediately before stimulus-onset from the data. For each individual and learning block we then calculated the CUSUM as $(Si) = \sum_{j \le 1} (Sj - (S))$, where (S) is the mean of the neural (BOLD) time series. Change points were defined as the maxima of the CUSUM curves and then averaged across blocks for statistical analyses. Mean change points were analyzed using an ANOVA with the between-subjects factor age group and performance group.

3. Results

3.1. Choice behavior

The analysis revealed significant main effects of age group $F(1,48) = 74.09$, $p < 0.001$, $\eta^2 = 0.27$, and learning condition $F(1,48) = 513.91$, $p < 0.001$, $\eta^2 = 0.70$, as well as a significant age group × learning condition interaction, $F(1,48) = 70.21$, $p < 0.001$, $\eta^2 = 0.24$. Follow-up analyses showed age-related impairments in learning to predict future reward ($p < 0.001$, $\eta^2 = 0.51$); however, no significant age differences in learning from immediate reward were observed ($p = 0.46$) (see Fig. 2A). The analysis also revealed a significant main effect of the course of learning $F(5,240) = 68.62$, $p < 0.001$, $\eta^2 = 0.28$, $\varepsilon = 0.58$ and a significant interaction between learning condition and course of learning $F(5,240) = 22.51$, $p < 0.001$, $\eta^2 = 0.11$, $\varepsilon = 0.64$. As shown in Fig. 2A both age groups learned faster in the immediate than the delayed reward condition. Furthermore, the ANOVA showed a significant main effect of performance group $F(1,48) = 107.00$, $p < 0.001$, $\eta^2 = 0.35$, as well as an interaction between performance group and learning condition $F(1,48) = 119,68$, $p < 0.001$, $\eta^2 = 0.35$. Separate analyses for the 2 learning conditions revealed a significant effect of performance group in the delayed reward condition ($p < 0.001$, $\eta^2 = 0.62$), but not in the immediate learning condition ($p = 0.91$).

To examine correlations between learning and measures of fluid intelligence (Raven's matrices and processing speed) as well as behavioral inhibition and approach (BIS-BAS) scores (Carver and White, 1994), we performed correlational analyses. As displayed in Fig. 2B these analyses showed significant positive correlations between performance in the delayed reward condition and fluid intelligence in YA, (r's > 43, p's < 03) but not in OA (p's > 0.58). Furthermore, we obtained a significant positive correlation between learning in the delayed reward condition and behavioral approach (BAS) scores for OA (r = 0.41, $p = 04$) but not for YA ($p = 0.40$). We did not observe significant positive correlations between learning to predict future reward and working memory performance (YA: r = −0.04, $p = 0.83$; OA: r = −0.37, $p = 0.06$).

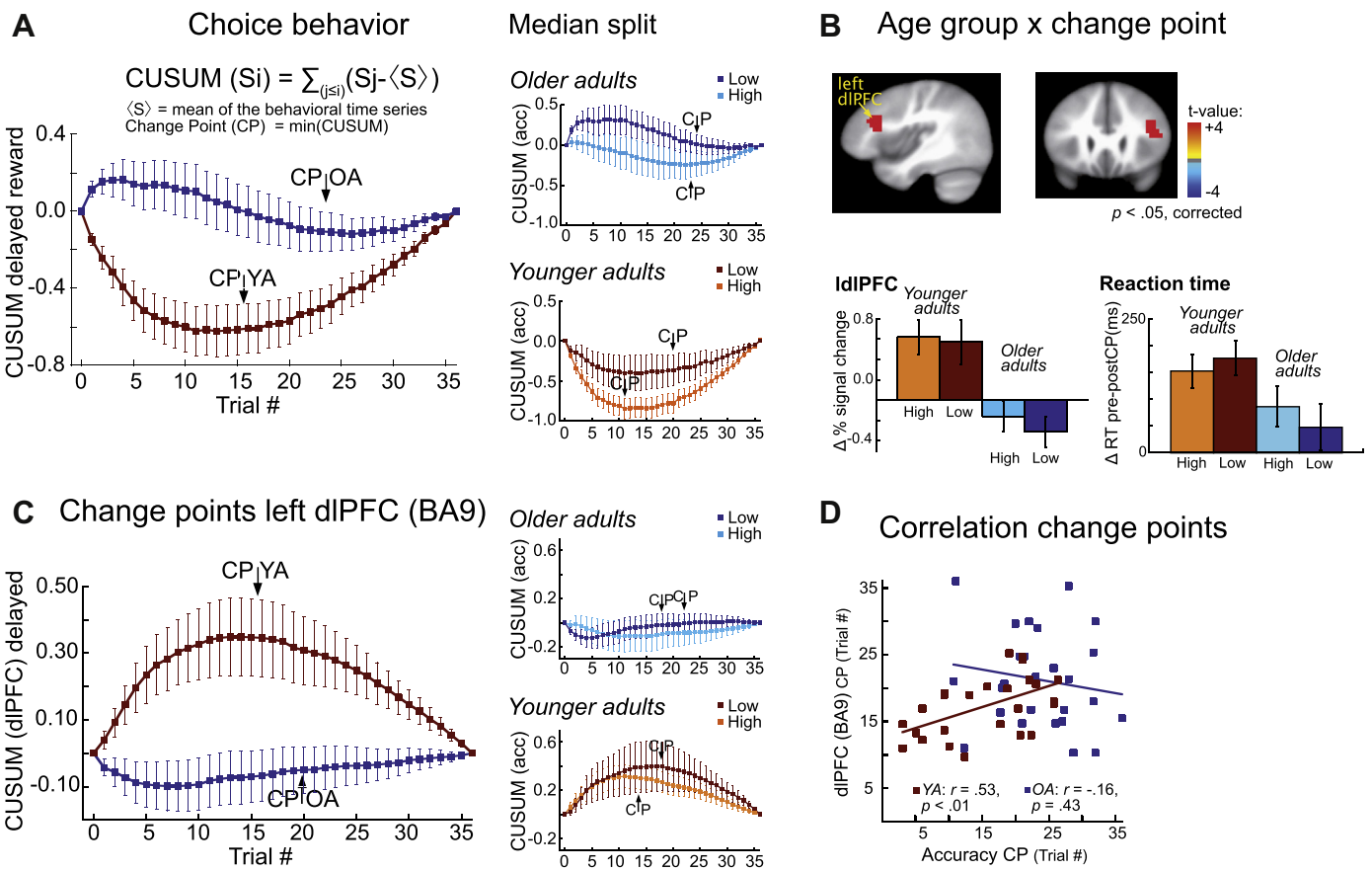

Fig. 6. (A) Left panel: CUSUM plots for choice behavior on the y-axis as a function of learning (x-axis) in the delayed reward condition. Younger adults (YA) are shown in red, older adults (OA) are shown in blue. Error bars reflect the standard error of the mean (SE). Right panel: CUSUM accuracy plots for high and low performing younger adults (lower panel) and high and low performing older adults (upper panel). (B) Upper panel: significant outcome-related activity (t-statistics) for the age group × change point interaction in the left dlPFC (Talairach co-ordinates: 41, −25, 22). Activations are significant at $p < 0.05$, corrected. Lower left panel: mean BOLD activity in the left dlPFC displayed as a function of age group and performance group. Lower right panel: reaction before and after change points, displayed as a function of age group and performance group. Error bars reflect the SE. (C) Left panel: CUSUM plots for BOLD activity in the left dlPFC (BA 9 as defined using Talairach atlas) on the y-axis as a function of learning (x-axis) in the delayed reward condition. YA are shown in red, OA are shown in blue. Error bars reflect the SE. Right panel: CUSUM dlPFC activity plots for high and low performing YA (lower panel) and high and low performing OA (upper panel). (D) Correlation between behavioral change points (x-axis) and dlPFC change points (y-axis). YA are shown in red, OA are shown in blue. Abbreviations: CUSUM, cumulated sum of differences to the mean; dlPFC, dorsolateral prefrontal cortex. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

3.2. fMRI data

The whole-brain fMRI analysis showed a significant interaction between age group and learning condition in the right dorsolateral, left rostrolateral and right medial PFC (t-scores > 4.0, p-values < 0.05; see Fig. 3). The time courses of the BOLD responses shown in Fig. 3 revealed a clear difference between age groups: YA showed a greater BOLD response in the delayed than the immediate reward condition in these PFC regions (main effect of condition t-scores > 4.0, p-values < 0.05, whereas OA showed no such effect.

In addition to the 2-way interaction, we also found significant interactions between age group, performance group, and learning condition in 2 areas of the ventral striatum (F-values > 12.0, p-values < 0.001, cluster size >10 voxels; see Fig. 4A). Separate contrasts for the 2 age groups showed significant interactions between performance group and learning condition only for OA (t-scores > 4.0, p-values < 0.001, cluster size >10 voxels). As shown in Fig. 4A older high performers show enhanced ventral striatal BOLD activity in the delayed compared the immediate reward condition. To provide a continuous analysis of these effects, we performed a whole-brain analysis of covariance using performance in the delayed reward condition as a between-subject covariate. This analysis revealed a significant interaction between age group, learning condition, and performance (t-score > 3.0, p-value < 0.005, cluster size >20 voxels) in a very similar area in the striatum as the median split approach (see Fig. 4B). Following up on this result, we correlated activity in this area with performance (separately for the 2 age groups). As shown in Fig. 4B in OA striatal activity correlated positively with performance ($r = 0.57$, $p < 0.001$), whereas in YA striatal activity correlated negatively with performance ($r = -0.49$, $p < 0.01$).

3.2.1. Performance-matched subgroups

To control for performance differences between groups, we performed an additional analysis by matching subgroups of YA and OA ($N = 12$ per group) in terms of overall performance (see Fig. 5). Similar to the overall analysis, for the performance-matched subgroups we found a significant interaction between age group and learning condition in the lateral and medial PFC (t-scores > 4.0, p-values < 0.05). Separate analyses for the 2 age groups showed a significant main effect of learning condition in YA (t-scores > 4.0, p-values < 0.05) but not in OA.

3.2.2. Behavioral change point analysis

To examine age differences in learning dynamics in the delayed reward condition, we performed a change point analysis using CUSUM plots (see Section 2 and Durstewitz et al., 2010; Gallistel et al., 2004). As shown in Fig. 6A, we found that behavioral change points happened significantly earlier and were more pronounced in YA than OA $F(1, 48) = 20.43$, $p < 0.001$, $\eta^2 = 0.30$. Furthermore, the analysis showed a significant main effect of performance group $F(1, 50) = 7.83$ $p = 0.007$, $\eta^2 = 0.14$, as well as an interaction between age group and performance group $F(1, 50) = 5.94$ $p = 0.02$, $\eta^2 = 0.11$. As shown in Fig. 6A change points occurred significantly earlier in younger high compared with younger low performers ($p < 0.001$, $\eta^2 = 0.40$). No such effect was observed in OA ($p = 0.81$).

3.2.3. Reaction time change point analysis

To analyze the effects of change points on reaction times, we computed reaction times for trials before and after change points and subjected them to an ANOVA involving the factors age group, performance group, and change point (before vs. after change point). The analysis revealed significant main effects for age group, performance group, and change point (p's < 0.001, η^2's > 0.22) as well as a significant interaction between age group and change point $F(1,48) = 7.05$, $p < 0.01$, $\eta^2 = 0.04$. As shown in Fig. 6B, reaction times dropped substantially after behavioral change points and this effect was significantly more pronounced in YA compared with OA.

3.2.4. fMRI change point analysis

To investigate change points in the fMRI data, we subdivided the time series from the delayed reward condition into periods before and after behavioral change points (separately for each individual and learning block). This analysis revealed a significant interaction between age group and change point in the left dlPFC ($t > 4.5$, $p < 0.05$). Separate analyses for the 2 age groups showed more enhanced BOLD activity before than after change points for YA in the dlPFC ($t > 4.5$, $p < 0.05$; see Fig. 6B). No such effect was observed for OA.

To examine the temporal dynamics of dlPFC activity in the 2 age groups, we performed a change point analysis on the BOLD signal time series in a structural ROI in the left dlPFC (for details see Section 2). As shown in Fig. 6C the CUSUM plots for the BOLD data show the opposite pattern as those for the behavioral data. That is, in YA, the values increase until the change point (CUSUM maxima) is reached and then decrease. As shown in Fig. 6C, change points in the dlPFC BOLD time series occurred significantly earlier in YA than OA $F(1, 48) = 6.35$, $p = 0.02$, $\eta^2 = 0.12$. Furthermore, we found a significant effect of performance group $F(1, 48) = 6.08$, $p = 0.02$, $\eta^2 = 0.11$, showing that dlPFC change points happened significantly earlier in high performing compared with low performing individuals (see Fig. 6). To investigate the relationship between behavioral and neural change points, we performed correlation analyses. As shown in Fig. 6D we found a significant positive correlation between behavioral and neural change points in YA ($r = 0.53$, $p = 0.005$), but not in OA ($p = 0.43$). A comparison of correlation coefficients using Fisher z-transformation showed that correlations were significantly different from each other (z-score $= 2.55$, $p < 0.01$), indicating that in YA, but not in OA earlier neural change points were associated with earlier behavioral change points.

4. Discussion

Foresighted and deliberate decisions depend on the ability to learn the value of future outcomes and the sequential choices that are necessary to achieve them. In this study, we investigated age differences in the ability to extract sequential state transition structures while learning to predict future reward using a modified 3-state Markov decision task (Tanaka et al., 2004) in combination with fMRI.

4.1. Age-related and individual differences in learning to predict future reward

Consistent with our predictions, the behavioral results show pronounced age-related impairments in learning to predict future reward but no age differences in learning from immediate outcomes (see Fig. 2A). Moreover, we found substantial individual differences in learning abilities in the two age groups: A median split for performance showed that high-performing YA learn almost as rapidly in the delayed as in the immediate reward condition. In contrast, high performing OA show slower and more gradual learning in the delayed reward condition (see Fig. 2B). Consistent with these results, in YA, we found a positive association between learning in the delayed reward condition and measures of fluid intelligence. In contrast, in OA we found that higher reward sensitivity (as reflected in BAS scores) was predictive of better learning from future reward. Taken together, the current behavioral findings suggest that OA have substantial deficits in learning sequential task structures in the delayed reward condition. The absence of age differences in learning from immediate reward is consistent with several previous findings, indicating that OA show similar performance as YA when learning from deterministic (immediate) reward (Eppinger et al., 2008; Hämmerer et al., 2011; Pietschmann et al., 2011). The fact that individuals differ so drastically in their ability to learn to predict future reward may suggest that different underlying mechanisms contribute to learning in different subgroups of YA and OA. Rapid learning in high-performing YA may be driven by insights into the transition structure of the task (the Markov property). In contrast, slower and more gradual learning in high-performing older individuals may reflect a habitual learning strategy that relies on repeated experiences of stimulus-reward contingencies (Daw et al., 2011). The results of the correlational analysis nicely support this view by showing that in YA learning to predict future reward depends on fluid abilities (McClure et al., 2004; Shamosh et al., 2008), whereas in OA enhanced reward sensitivity is associated with better learning from future reward (Smillie et al., 2007).

4.2. Neural systems involved in learning to predict future reward

Previous findings showed that the PFC is involved in learning the value of future reward and in mediating foresighted decisions (McClure et al., 2004; Shamosh et al., 2008; Tanaka et al., 2004). Given these findings we hypothesized that learning to predict future reward would be associated with enhanced PFC activity. Furthermore, we expected that learning deficits in OA might result from an under-recruitment of the PFC (Nyberg et al., 2010). Consistent with these predictions YA showed enhanced BOLD activity in the delayed than the immediate reward condition in the dorsolateral, rostrolateral, and medial PFC. In OA, we found diminished BOLD responses and no significant differences between conditions in these areas (see Fig. 3). A control analysis comparing performance-matched subgroups (see Fig. 5) revealed similar results, showing an enhanced recruitment of the lateral and medial PFC in the delayed compared with the immediate reward condition in YA but no such effect in OA. Thus, these results show that the observed under-recruitment of the lateral PFC in OA is not simply due to differences in performance or obtained reward. Interestingly, as for the behavioral data, the fMRI results revealed substantial individual differences in the neural systems involved in learning to

predict future reward. A median split for performance in the delayed reward condition revealed a significant 3-way interaction between the factors age, performance, and learning condition in the ventral striatum. Follow-up analyses showed that this effect was due to enhanced ventral striatal activity during learning to predict future reward in high-performing OA (see Fig. 4A). Moreover, a covariance analysis showed that in OA enhanced striatal activity was associated with better performance in the delayed reward condition whereas the reverse pattern was observed in YA. Together, these findings suggest that OA may rely more on (reward-related) striatal mechanisms during learning to predict future reward.

To summarize, our results show enhanced PFC recruitment during learning to predict future reward in YA. The prefrontal activity in YA may be associated with insights into the transition structure of the task and my thus reflect the learning of a representation (or "model") of the decision states. These findings are nicely consistent with previous findings that point to a role of the PFC in the rapid learning of sequential contingencies across events (Durstewitz et al., 2010; Gläscher et al., 2010; Lee et al., 2014). In line with our hypothesis, age-related deficits in learning to predict future reward are associated with an under-recruitment of the PFC in OA. These findings are consistent with several previous results, suggesting that functional deficits in the PFC, as well as decline in DA projections to the PFC, may contribute to age-related impairments in executive control (Braskie et al., 2008; Caetano et al., 2012; Landau et al., 2009; Li et al., 2001). Moreover, we found that better learning to predict future reward in the elderly was associated with enhanced activity in the ventral striatum. Given the well-established role of the ventral striatum in model-free RL (Daw et al., 2011; Niv et al., 2012), these results may indicate that high-performing OA engage in a habitual learning strategy that relies on repeated exposure to stimulus-action-reward associations. This interpretation is supported by 2 behavioral findings: (1) older high performers show slow and gradual learning consistent with habitual learning. (2) In OA higher reward sensitivity predicts better learning performance.

4.3. Behavioral and neural dynamics of learning to predict future reward

Our final hypothesis was that the lateral PFC has a specific role in learning sequential contingencies. Based on previous findings (Durstewitz et al., 2010; Gläscher et al., 2010; Yoshida and Ishii, 2006), we predicted that PFC activity should reflect abrupt shifts in choice behavior during learning (change points). To examine behavioral change points, we calculated CUSUM plots for accuracy in the delayed reward condition (Durstewitz et al., 2010; Gallistel et al., 2004). As shown in Fig. 6A, we found clearly identifiable behavioral change points in YA. In contrast, in OA change points occurred later and were less pronounced. Furthermore, we found earlier change points in high-performing compared with low-performing YA, whereas no such effect was observed in OA (see Fig. 6A). This finding is nicely consistent with the idea that in high-performing YA learning is associated with abrupt shifts in choice behavior, which might reflect insights into the transition structure.

In the next step, we analyzed the fMRI data as a function of change points. As expected, we found enhanced dlPFC activity before compared with after change points in YA, but not in OA (see Fig. 6B). That is, in YA periods before behavioral change points are characterized by enhanced PFC activity, whereas PFC involvement drops after the transition structure has been learned.

Given these findings our next prediction was that changes in dlPFC activity across time should resemble the behavioral dynamics that we observed in the performance-based change point analysis. To test this prediction, we performed an analogous CUSUM analysis for the fMRI time series in the left dlPFC (BA 9) as for the choice data. This analysis showed a similar (although inverted) pattern as for the behavioral CUSUM curves (see Fig. 6C). That is, dlPFC activity is enhanced in the beginning of learning and then decreases rapidly. Similar to the behavioral data, dlPFC change points occurred earlier and were more pronounced in YA than OA. Moreover, we found that shifts in dlPFC dynamics happened significantly earlier in high-performing compared with low-performing groups (see Fig. 6C). Finally, we examined whether behavioral and dlPFC change points are related to each other. Consistent with our predictions, in YA dlPFC change points were predictive of behavioral change points, which was not the case in the elderly (see Fig. 6D). Taken together, these findings show that in YA the dlPFC is critically involved in mediating insights into the transition structure of the task. These insights are reflected in abrupt shifts in dlPFC activity as well as performance (Boettiger and D'Esposito, 2005; Durstewitz et al., 2010). In OA reduced dlPFC recruitment seems to lead to deficits in the extraction of sequential task structures and hence to impairments in learning to predict future reward.

4.4. Computational mechanisms of model-based learning

Our data lend themselves to the interpretation that YA may rely more on a model-based learning strategy, whereas OA may engage in a model-free way of learning associations between state actions and reward in the delayed reward condition. However, it could also be argued that the underlying learning mechanism is similar (model-free) in both groups but YA use different learning parameters. For example, one could assume that YA have a higher learning rate, which should speed up learning. We, however, think that this latter interpretation is not sufficient to explain our findings because higher learning rates should enhance learning of the optimal action that leads to the big reward as well the suboptimal action that leads to small rewards. Thus, higher learning rates per se are unlikely to drive the faster learning in YA. Another possible alternative explanation would be to assume that YA discount future rewards less than OA. Given several findings that point to reduced discounting in OA than YA in descriptive tasks this interpretation seems relatively implausible (Eppinger et al., 2012; Green et al., 1994). However, even if it were true, reduced discounting of delayed reward may explain the fact that both age groups learn the optimal action in the delayed reward condition, but learning would still be relatively slow because it relies on a sufficient sampling of the environment. This is inconsistent with the behavioral results in YA, which point to a rapid learning of the underlying task structure.

Several recent studies in YA used computational RL approaches to investigate model-based learning (e.g., Gläscher et al., 2010; Lee et al., 2014). In these studies participants had to learn a forward model of a tree-like task structure based on state prediction errors. These state prediction errors reflect how predicted an upcoming state (stimulus) is, given the current estimate of the state transition probability (see Gläscher et al., 2010). To provide opportunity for this type of learning the state space has to involve unique transitions between states. The current task design does not involve such a tree-like structure. Rather, the 2 actions lead to a different order of transitions between the same states (see Fig. 1). That is, the state transition structure is ambiguous and optimal behavior depends on a representation of the (deterministic) action outcome relationships across the 3 stimuli. Therefore, model-based RL approaches that rely on the learning via state prediction errors are not amenable for modeling the current task design.

Behavioral findings from a study using a hybrid RL model in combination with a 2-stage Markov decision task point to an age-related shift from model-based to model-free decision-making

(Eppinger et al., 2013b). Whether this shift is due to deficits in integrating model-based and model-free decision information, whether it is due to deficits state-prediction error signaling, or whether there is a more general problem of OA in representing state spaces of experimental tasks are important open questions for future research. To tackle these research questions, future studies will have to use formal modeling approaches in combination with suitable tasks and neuroimaging (electroencephalogram, fMRI)

To conclude, our results show that in YA the dlPFC plays a critical role in linking subsequent states, actions, and outcomes while learning to predict future reward. That is, the dlPFC might be involved in mediating insights into sequential transition structures. In OA deficits in dlPFC function seem to lead to impairments in the learning of state transition structures and hence to impoverished predictions of future reward. Apart from the age differences in prefrontal recruitment, we found that better learning to predict future reward in OA was associated with enhanced activity in the ventral striatum as well as greater reward sensitivity (as measured using the BIS-BAS questionnaire). This finding suggests high-performing OA may engage in a habitual learning strategy that relies on repeated exposure to stimulus-reward associations.

We think that our results are relevant in a broader societal context because many of our everyday decision problems involve new learning about underlying (partially observable) structures and may only be insufficiently solved by a model-free learning strategy. That is, deficits in the ability to learn sequential state structures (such as in OA) may lead to inflexible behavior in situations in which one can not draw on previous experience (Mata et al., 2011; Samanez-Larkin and Knutson, 2015). This is particularly relevant in situations in which previously learnt structures are not applicable any more (such as when using a new technology or device [e.g., new mobile device, or TV] or a new software). With respect to financial decisions deficits in model-based behavior may be particularly relevant when policy changes implicate the need to shift from predescribed benefit plans to individually tailored personal investments. To the degree that such investment plans rely on the learning of underlying structures and complex dependencies they may draw on a limiting resource in OA.

Disclosure statement

The authors have no conflicts of interest to disclose.

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References

Arnsten, A.F.T., Wang, M.J., Paspalas, C.D., 2012. Neuromodulation of thought: flexibilities and vulnerabilities in prefrontal cortical network synapses. Neuron 76, 223–239.
Ashburner, J., 2007. A fast diffeomorphic image registration algorithm. Neuroimage 38, 95–113.
Ashburner, J., Friston, K.J., 2005. Unified segmentation. Neuroimage 26, 839–851.
Bäckman, L., Nyberg, L., Lindenberger, U., Li, S.C., Farde, L., 2006. The correlative triade among aging, dopamine, and cognition. Neurosci. Biobehavioral Rev. 30, 791–807.
Baddeley, A.D., Emslie, H., Nimmo-Smith, I., 1992. The Speed and Capacity of Language Processing (SCOLP) Test. Thames Valley Test Company, Bury St. Edmunds, Suffolk, England.
Bennett, I.J., Madden, D.J., Vaidya, C.J., Howard, J.H.J., Howard, D.V., 2011. White matter integrity correlates of implicit sequence learning in healthy aging. Neurobiol. Aging 32, 2317.e1–2317.e12.
Boettiger, C.A., D'Esposito, M., 2005. Frontal networks for learning and executing arbitrary stimulus–response associations. J. Neurosci. 25, 2723–2732.
Braskie, M.N., Wilcox, C.E., Landau, S.M., O'Neil, J.P., Baker, S.L., Madison, C.M., Kluth, J.T., Jagust, W.J., 2008. Relationship of striatal dopamine synthesis capacity to age and cognition. J. Neurosci. 28, 14320–14328.
Caetano, M.S., Horst, N.K., Harenberg, L., Liu, B., Arnsten, A.F.T., Laubach, M., 2012. Lost in transition: aging-related changes in executive control by the medial prefrontal cortex. J. Neurosci. 32, 3765–3777.
Carver, C.S., White, T.L., 1994. Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: the BIS/BAS scales. Jounral Personal. Social Psychol. 67, 319–333.
Chowdhury, R., Guitart-Masip, M., Lambert, C., Dayan, P., Huys, Q., Duezel, E., Dolan, R.J., 2013. Dopamine restores reward prediction errors in old age. Nat. Neurosci. 16, 648–653.
Cox, R.W., 1996. AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. Comput. Biomed. Res. Int. J. 29, 162–173.
Daw, N.D., Gershman, S.J., Seymour, B., Dayan, P., Dolan, R.J., 2011. Model-based influences on humans' choices and striatal prediction errors. Neuron 69, 1204–1215.
Dreher, J.C., Meyer-Lindenberg, A., Kohn, P., Berman, K.F., 2008. Age-related changes in midbrain dopaminergic regulation of the human reward system. Proc. Natl. Acad. Sci. U. S. A. 105, 15106–15111.
Durstewitz, D., Vittoz, N.M., Floresco, S.B., Seamans, J.K., 2010. Abrupt transitions between prefrontal neural ensemble states accompany behavioral transitions during rule learning. Neuron 66, 438–448.
Eppinger, B., Haemmerer, D., Li, S.C., 2011. Neuromodulation of reward-based learning and decision making in human aging. Ann. N. Y. Acad. Sci. 1235, 1–17.
Eppinger, B., Kray, J., Mock, B., Mecklinger, A., 2008. Better or worse than expected? Aging, Learning, and the ERN. Neuropsychologia 46, 521–539.
Eppinger, B., Nystrom, L., Cohen, J.D., 2012. Reduced sensitivity to immediate reward during decision-making in older than younger adults. PLoS One 7, 1–10.
Eppinger, B., Schuck, N.W., Nystrom, L.E., Cohen, J.D., 2013a. Reduced striatal responses to reward prediction errors in older compared to younger adults. J. Neurosci. 33, 9905–9912.
Eppinger, B., Walter, M., Heekeren, H.R., Li, S.C., 2013b. Of goals and habits: age-related and individual differences in goal-directed decision-making. Front. Decis. Neurosci. 7, 1–14.
Gallistel, C.R., Fairhurst, S., Balsam, P., 2004. The learning curve: Implications of a quantitative analysis. Proc. Natl. Acad. Sci. U. S. A. 101, 13124–13131.
Gläscher, J., Daw, N.D., Dayan, P., O'Doherty, J.P., 2010. States versus rewards: dissociable neural prediction error signals underlying model-based and model-free reinforcement learning. Neuron 66, 585–595.
Green, L., Fry, A.F., Myerson, J., 1994. Discounting of delayed rewards. a life-span comparison. Psychol. Sci. 5, 33–36.
Hagberg, G., Zito, G., Patria, F., Sanes, J.N., 2001. Improved detection of event-related MRI signals using probability functions. Neuroimage 14, 1193–1205.
Hämmerer, D., Li, S.C., Mueller, V., Lindenberger, U., 2011. Lifespan differences in electrophysiological correlates of monitoring gains and losses during probabilistic reinforcement learning. J. Cogn. Neurosci. 23, 579–592.
Harris, K.C., Dubno, J.R., Keren, N.I., Ahlstrom, J.B., Eckert, M.A., 2009. Speech recognition in younger and older adults: a dependency on low-level auditory cortex. J. Neurosci. 29, 6078–6087.
Iacobucci D., Posavac S.S., Kardes F.R., Schneider M.J. and Popovich D.L., 2014. Toward a more nuanced understanding of the statistical properties of a median split, *J. Consumer Psychol.* (in press)
Landau, S.M., Lal, R., O'Neil, J.P., Baker, S.L., Jagust, W.J., 2009. Striatal dopamine and workin memory. Cereb. Cortex 19, 445–454.
Lee, S.W., Shimojo, S., O'Doherty, J.P., 2014. Neural computations underlying arbitration between model-based and model-free learning. Neuron 81, 687–699.
Li, S.-C., Lindenberger, U., Hommel, B., Aschersleben, G., Prinz, W., Baltes, P.B., 2004. Transformations in the couplings among intellectual abilities and constituent cognitive processes across the lifespan. Psychol. Sci. 15, 155–163.
Li S.-C., U., Lindenberger, U., Sikström, S., 2001. Aging cognition: From neuromodulation to representation. Trends Cogn. Sci. 5, 479–486.
Lindenberger, U., Baltes, P.B., 1997. Intellectual functioning in old and very old age: cross-sectional results from the Berlin Aging Study. Psychol. Aging 12, 410–432.
MacCullum, R.C., Zhang, S., Preacher, K.J., Rucker, D.D., 2002. On the practice of dichotomization of quantitative variables. Psychol. Methods 7, 19–40.
Mata, R., Josef, A.K., Samanez-Larkin, G.R., Hertwig, R., 2011. Age differences in risky choice: a meta-analysis. Ann. N. Y. Acad. Sci. 1235, 18–29.
McClure, S.M., Laibson, D.I., Loewenstein, G., Cohen, J.D., 2004. Separate neural systems value immediate and delayed monetary rewards. Science 306, 503–507.
Mell, T., Wartenburger, I., Marschner, A., Villringer, A., Reischies, F.M., Heekeren, H.R., 2009. Altered function of ventrtal striatum during reward-based decision-making in old age. Front. Hum. Neurosci. 3, 1–10.
Nagel, I.E., Preuschhof, C., Li, S.C., Baeckman, L., Lindenberger, U., Heekeren, H.R., 2009. Performance level modulates adult age differences in brain activation during spatial working memory. Proc. Natl. Acad. Sci. U. S. A. 106, 22552–22557.
Niv, Y., Edlund, J.A., Dayan, P., O'Doherty, J.P., 2012. Neural prediction errors reveal a risk-sensitive reinforcement-learning process in the human brain. J. Neurosci. 32, 551–562.
Nyberg, L., Salami, A., Andersson, M., Eriksson, J., Kalpouzos, G., Kauppi, K., Lind, J., Pudas, S., Persson, J., Nilsson, L.G., 2010. Longitudinal evidence for diminished frontal cortex function in aging. Proc. Natl. Acad. Sci. U. S. A 107, 22682–22686.
Pietschmann, M., Endrass, T., Czerwon, B., Kathmann, N., 2011. Aging, probabilistic learning and performance monitoring. Biol. Psychol. 86, 74–82.
Raven, J.C., Raven, J.E., Court, J.H., 1998. Progressive Matrices. Oxford Psychologists Press, Oxford, England.

Raz, N., 2005. The aging brain observed in vivo: differential changes and their modifiers. In: Cabeza, R., Nyberg, L., Park, D. (Eds.), Cognitive Neuroscience of Aging: Linking Cognitive and Cerebral Aging. Oxford University Press, New York, p. 400.
Saad, Z.S., Glen, D.R., Chen, G., Beauchamp, M.S., Rutvik, D., Cox, R.W., 2009. A new method for improving functional-to-structural MRI alignment suing local Pearson correlations. Neuroimage 44, 839–848.
Samanez-Larkin, G.R., D'Esposito, M., 2008. Group comparisons: imaging the aging brain. Soc. Cogn. Affective Neurosci. 3, 290–297.
Samanez-Larkin, G.R., Knutson, B., 2015. Decision making in the ageing brain: changes in affective and motivational circuits. Nat. Rev. Neurosci. 16, 278–289.
Samanez-Larkin, G.R., Levens, S.M., Perry, L.M., Dougherty, R.F., Knutson, B., 2012. Frontostriatal white matter integrity mediates adult age differences in probabilistic reward learning. J. Neurosci. 32, 5333–5337.
Samanez-Larkin, G.R., Worthy, D.A., Mata, R., McClure, S.M., Knutson, B., 2014. Adult age differences in frontostriatal representation of prediction error but not reward outcome. Cogn. Affective Behav. Neurosci. 14, 672–682.
Shamosh, N.A., DeYoung, C.G., Green, A.E., Deidre, L.R., Johnson, E.J., Conway, A.R.A., Engle, R.W., Braver, T.S., Gray, J.R., 2008. Individual differences in delay discounting. Relation to intelligence, working memory, and anterior prefrontal cortex. Psychol. Sci. 19, 904–911.
Smillie, L.D., Dalgleish, L.I., Jackson, C.J., 2007. Distinguishing between learning and motivation in behavioral tests of the reinforcement sensitivity theory of personality. Personal. Social Psychol. Bull. 33, 476–489.
Tanaka, S.C., Doya, K., Okada, G., Ueda, K., Okamoto, Y., Yamawaki, S., 2004. Prediction of immediate and future rewards differentially recruits cortico-basal ganglia loops. Nat. Neurosci. 7, 887–893.
Volkow, N.D., Gur, R.C., Wang, G.J., Fowler, J.S., Mpberg, P.J., Ding, Y.S., Hitzemann, R., Smith, G., Logan, J., 1998. Association between decline in brain dopamine activity with age and cognitive and motor impairment in healthy individuals. Am. J. Psychiatry 155, 344–349.
Volkow, N.D., Logan, J., Fowler, J.S., Wang, G.J., Gur, R.C., Wong, C., Felder, C., Gatley, S.J., Ding, Y.S., Hitzemann, R., Pappas, N., 2000. Association between age-related decline in brain dopamine activity and impairment in frontal and cingulate metabolism. Am. J. Psychiatry 157, 75–80.
Yoshida, W., Ishii, S., 2006. Resolution of uncertainty in the prefrontal cortex. Neuron 50, 781–789.