Published in final edited form as:

Neurobiol Aging. 2018 September ; 69: 185–198. doi:10.1016/j.neurobiolaging.2018.05.019.

Age-related differences in striatal, medial temporal, and frontal involvement during value-based decision processing

Yu-Shiang Su^{a,b}, Jheng-Ting Chen^a, Yong-Jheng Tang^a, Shu-Yun Yuan^a, Anna C. McCarrey^c, and Joshua Oon Soo Goh^{a,d,e,f,g,*}

^aGraduate Institute of Brain and Mind Sciences, College of Medicine, National Taiwan University, Taipei, Taiwan

^bTaiwan International Graduate Program in Interdisciplinary Neuroscience, National Taiwan University and Academia Sinica, Taipei, Taiwan

^cDepartment of Psychology, Idaho State University, Pocatello, ID, USA

^dDepartment of Psychology, National Taiwan University, Taipei, Taiwan

^eNeurobiology and Cognitive Science Center, National Taiwan University, Taipei, Taiwan

^fCenter for Artificial Intelligence and Advanced Robotics, National Taiwan University, Taipei, Taiwan

^gLaboratory of Behavioral Neuroscience, Intramural Research Program, National Institute on Aging, Baltimore, MD, USA

Abstract

Appropriate neural representation of value and application of decision strategies are necessary to make optimal investment choices in real life. Normative human aging alters neural selectivity and control processing in brain regions implicated in value-based decision processing including striatal, medial temporal, and frontal areas. However, the specific neural mechanisms of how these age-related functional brain changes modulate value processing in older adults remain unclear. Here, young and older adults performed a lottery-choice functional magnetic resonance imaging experiment in which probabilities of winning different magnitudes of points constituted expected values of stakes. Increasing probability of winning modulated striatal responses in young adults, but modulated medial temporal and ventromedial prefrontal areas instead in older adults. Older adults additionally engaged higher responses in dorso-medio-lateral prefrontal cortices to more unfavorable stakes. Such extrastriatal involvement mediated age-related increase in risk-taking decisions. Furthermore, lower resting-state functional connectivity between lateral prefrontal and striatal areas also predicted lottery-choice task risk-taking that was mediated by higher functional

*Corresponding author at: Graduate Institute of Brain and Mind Sciences, College of Medicine, National Taiwan University, No. 1 Ren-Ai Rd. Section 1, RM 1554, Zhongzheng District, Taipei, Taiwan 10051. Tel: +886 2 2312 3456 x88022; fax: +886 2 2322 4814. joshuagoh@ntu.edu.tw (J.O.S. Goh).

Disclosure statement

The authors have no actual or potential conflicts of interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.neurobiolaging.2018.05.019>.

connectivity between prefrontal and medial temporal areas during the task, with this mediation relationship being stronger in older than younger adults. Overall, we report evidence of a systemic neural mechanistic change in processing of probability in mixed-lottery values with age that increases risk-taking of unfavorable stakes in older adults. Moreover, individual differences in age-related effects on baseline frontostriatal communication may be a central determinant of such subsequent age differences in value-based decision neural processing and resulting behaviors.

Keywords

Aging; Brain function; Value-based decision-making; fMRI

1. Introduction

Real life investments typically entail an expected gain proportional to the invested resource but also a possible loss, depending on outcomes. For instance, one spends money to buy an apple expecting to eat a juicy fruit but there is always a probability that there is a worm in the apple and the money spent is wasted. To maximize investments and minimize losses during such mixed lottery situations, neural networks in the human brain must be able to represent information about stimuli value, such as the expected value (EV) of investments, as accurately as possible with respect to physical outcomes. Neural processing of mixed lotteries might also engage relevant strategies or beliefs where necessary or effective (Kahneman and Tversky, 1979), such as noting past negative experiences at a particular grocery store, or prioritizing physical or mental health over money, or using only partial information to simplify decisions. Aging changes human brain functions such that neural representations of different stimuli are less distinctive (Goh et al., 2010; Park et al., 2004; Yassa et al., 2011) and the flexible engagement of goal-directed control and strategic processing is diminished (Ardiale and Lemaire, 2012; Hakun et al., 2015; Harris and Wolbers, 2014; Konishi et al., 2013). Older adults also display distinct decision behaviors compared with young adults that, across different experimental contexts, reflect more variable decision criteria, such as not always choosing options with higher EVs, and more reactive decision strategies, such as being more sensitive to recent outcomes (Pachur et al., 2017; Rutledge et al., 2016; Tymula et al., 2013; Worthy et al., 2016). These brain and behavioral differences between young and older adults motivate the need to determine the mechanistic links between changes in human neural processing of value and decision-making behavior as a person ages, particularly in light of the aging world demographic (Vaupel, 2010). Here, we reconcile how age effects on neural operations that selectively process information and apply goal-directed strategies impact assessment of EV in a risky lottery choice task (LCT).

In the LCT (Goh et al., 2016), which tests mixed lottery decisions, different probabilities (P) of winning (and simultaneously, losing; $1-P$) are combined with different magnitudes (M) of points such that $EV = P \times M + (1-P) \times (-M)$ for any given trial (Fig. 1A). Stakes and outcomes are independent across trials so that the optimal approach is to decide to accept or reject the given stakes based solely on the objective information about EV provided in each trial. Moreover, because for any given magnitude of points, the probability of winning also

determines the probability of losing the points, risk-neutral agents should have an acceptance decision threshold (DT) or certainty equivalence set at $EV = 0$ (or $p = 50\%$) (Dohmen et al., 2011). DTs greater or less than $EV = 0$ indicate risk-averse or risk-taking preferences, respectively.

Performance in this task might, in principle, rely on neural representations of EV (or even more simply, P) in ventral striatum (VS) that shows sensitivity to different levels of expected rewards or losses (Berns et al., 2001; Knutson et al., 2001; Preuschoff et al., 2006; Schultz, 2000; Tom et al., 2007). Differential sensitivity to value underlies the role of VS in gating and selecting adaptive motor responses to obtain rewards or avoid losses (Nicola, 2007). However, the main neurotransmitter that operates in this region, dopamine, has reduced efficacy with age (Dreher et al., 2008; Erixon-Lindroth et al., 2005; Kaasinen et al., 2000; Wong et al., 1997). Neuro-computational theory projects that reduced dopaminergic efficacy results in lower signal-to-noise ratio during information processing that underlies less distinctive neuronal responses (or lower neural sensitivity) to different stimuli in target brain areas (Bäckman et al., 2010; Li and Sikström, 2002). In older adults then, we expect less neural sensitivity to valuative information in VS. This increases the likelihood that decisions will be less influenced by objective EV information and more influenced by more subjective processes in other brain regions that bias decision criteria.

Experiments have shown dissociable age-related biases in loss processing compared with gains (Mather et al., 2012; Pachur et al., 2017; Samanez-Larkin et al., 2007, 2010). This is consistent with socioemotional selectivity theory (Carstensen, 2006; Carstensen et al., 1999; Mather and Carstensen, 2005) that posits a shift in life goals toward senescence such that maintenance of well-being or positive affect has greater influence on older than younger adult decision-making. Two extensions are made in relation to EV processing. First, there should be enhanced affective reactions to prospects in general in older compared with younger adults, who should be more apathetic. Specifically, neural responses that track the desirability of EVs should be more evident in older than young adults in brain areas involved in affective processing. In our whole-brain analysis, we focus on affective responses in the amygdala and anterior medial temporal lobe (MTL) and ventromedial prefrontal cortex (VMPFC) as these have previously been implicated during LCT processing (Goh et al., 2016) and other value-related experiments (Berns et al., 2001; Knutson et al., 2003; Phelps, 2004; Phelps et al., 2014). Second, older adults should engage greater down-regulation processing in response to situations that induce negative affect because positive affective reactions should not require regulation. As such, dorsomedial and dorsolateral frontal (DMPFC and DLPFC) engagement to down-regulate negative affect associated with unfavorable EVs should be more enhanced in older than younger adults (Mather and Knight, 2005). Overall, we expect that neural engagement in young and older adults during mixed lotteries should shift from an emphasis on veridical EV responses in the VS to more affective-like and regulatory responses in MTL and frontal regions. Given our previous finding of an overall risk-taking preference in older adults as a group during the LCT (Goh et al., 2016), we also expect here that greater expression of such affective-like neural responses should be associated with greater propensity to accept loss-dominant mixed lotteries in the older age group. Specifically, we expected age differences in risk-taking

behavior to be mediated by age differences in VS, MTL, and frontal neural responses to EV during choice processing in value-based decisions.

Finally, if indeed there is a systemic alteration of brain regions involved in valuate processing with age, a more network approach to evaluate how age modulates the associations between brain inter-regional functional connectivity and risk-taking behavior might provide further complementary support for the aforementioned considerations based on regional neural responses. Evidence shows that lower white matter structural connectivity between frontal and striatal areas is an important determinant of the ability of older adults to process probabilistic reward (Samanez-Larkin et al., 2012). In addition, antecedent reduction in frontal white matter tissue integrity is a hallmark of normative age-related structural brain changes that have been associated with cognitive decline, particularly in tests of executive function (Borghesani et al., 2013; Fjell et al., 2017; Gazes et al., 2016; Head et al., 2004; Hedden et al., 2016; Kennedy and Raz, 2009; Madden et al., 2017, 2009; Sullivan et al., 2010a,b). At least one study has also shown links between age differences in white matter structural connectivity, functional connectivity, and cognitive performance (Davis et al., 2012), albeit focusing on callosal connections between prefrontal homologs. Thus, age-related changes in frontal white matter tissue integrity suggests that age differences in baseline frontostriatal functional communication (as indicated by resting-state functional connectivity) should play a central role in older adult value-based decision neural processing and behavior.

We reasoned that neural functional communication during LCT processing (or LCT-related functional connectivity) might reflect a mediatory response to a primary effect of frontostriatal baseline resting-state functional connectivity on LCT risk-taking behavior. Specifically, disruption of frontostriatal baseline functional connectivity with age should drive altered functional communication in other neural networks engaged during decision processing tasks in older relative to younger adults that then influences older adult task-related decision behavior. In this light, we also examined functional connectivity between the frontal, striatal, and medial temporal areas during LCT performance and during resting-state in the same young and older individuals. We expected that if frontostriatal baseline connectivity is an important determinant of older adult value-based decision processing, then LCT-related functional connectivity between these brain regions should mediate between frontostriatal resting-state functional connectivity and LCT decision behavior, and that this mediation should be moderated by age.

2. Materials and methods

2.1. Participants

A total of 44 younger and 54 older adults volunteered for this study. Exclusion criteria were presence or history of neurological or psychiatric disorder, artificial implants, or other counterindications for MRI scanning. All participants underwent the MRI session followed by a neuropsychological test session on a separate day within 1 month. All participants gave written informed consent on the day of the MRI session for this study, which was approved by National Taiwan University Hospital Research Ethics Committee. From all volunteers, we excluded 2 younger and 6 older adults because of excessive head motion (>3.4375 mm

translation or $>3^\circ$ rotation; on the basis of the size of 1 voxel) during functional scanning, 1 younger and 4 older adults because of having null responses for more than 15 trials in the LCT (the total number of trials in 1 condition), 3 older adults who showed equal acceptance of all choice conditions or greater acceptance of loss-dominant than gain-dominant conditions (indicating failure to understand the task), and 1 younger and 1 older adult who dropped out of neuropsychological testing (precluding assessment of cognitive status). The remaining participants entered into the analysis were 40 younger (mean age: 23.3 years; SD: 1.97 years; age range: 20.2–28.5 years; 14/26 males/females) and 40 older adults (mean age: 67.9 years; SD: 4.93 years; age range: 59.2–77.7 years; 12/28 males/females) (Supplementary Table S1). Mini-Mental State Exam scores for these participants were greater than 26 except for 1 older adult who scored 25, and 1 who scored 24, which were still within the normal range based on local age-adjusted norms (Sun et al., 2014). Participants were remunerated for their time in the study. One older participant did not contribute resting-state functional magnetic resonance imaging (fMRI) data due to technical failure while scanning.

2.2. fMRI LCT stimuli, procedures, and behavioral analyses

The LCT task has been described in detail in Goh et al. (2016) involving a larger sample study of older individual differences. In this present LCT fMRI experiment, we adopted an expanded version to yield more robust estimates of neural response differences between young and older adults. Briefly here, each trial in the LCT was divided into choice and outcome phases (Fig. 1A). The choice phase presented text depicting the win/lose probability and points magnitude. While probabilities and magnitudes varied continuously, choice conditions were treated as discretized ranges to facilitate counterbalancing during stimuli generation, presentation ordering, and also specific aspects of data analysis below. Supplementary Table S2 details the means and ranges of probabilities, magnitudes, and resulting EVs of each condition. There were 5 levels of win probability (low-low, LL*; middle-low, ML*; middle-middle, MM*; middle-high, MH*; high-high, HH*) and 3 levels of magnitude (low, *L; middle, *M; high, *H) comprising the 15 choice conditions (LLL, LLM, LLH, MLL, MLM, MLH, MML, MMM, MMH, MHL, MHM, MHH, HHL, HHM, HHH). Note, participants were agnostic to these discrete choice conditions and stimuli probabilities and magnitudes were continuously distributed from their perspective.

Choice text stimuli remained on the screen for 4 seconds, within which subjects decided to accept or reject the stakes with assigned button presses in the right hand. The choice phase was followed by a fixation (with interstimulus interval [ISI] ranging from 1 to 5 seconds; jittered across trials) after which the outcome phase was presented for 2 seconds. Note that each trial presents a mixed lottery so that the magnitude at stake to be gained is also the same magnitude at stake to be lost. Outcomes were stochastically predetermined based on actual stakes of each trial with the limitation that no condition could have only winning or only losing predetermined outcomes across all trials of that condition. If participants accepted the stakes, depending on the predetermined outcome, the outcome phase feedback would be either a gain or a loss with increased or decreased accumulated points, respectively. If participants rejected the stakes, outcomes would also be presented within parenthesis with no change in the accumulated points. Null responses also resulted in no

change in points but with a reminder message to respond. Participants were given the goal to maximize their total accumulated points across 225 LCT trials. A fixation (ISI ranging from 1 to 5 seconds; jittered across trials) then followed outcome phases before the beginning of the next trial. No combinations of probability and magnitude were repeated throughout the experiment.

Participants underwent a familiarization practice version of the LCT before MRI scanning. fMRI experimental stimuli were presented using E-Prime software version 2.0 (Psychology Software Tools, Sharpsburg, PA, USA) back-projected onto a screen at the front of the scanner that participants viewed using a mirror mounted on the head coil. There were a total of 5 runs of fMRI scanning each consisting of 45 trials (3 trials per choice condition in each run). Trial conditions were presented in pseudorandom order such that there were no more than 2 consecutive trials with the same choice condition.

Analyses of behavioral responses were conducted using R version 3.3.1 (www.r-project.org). To obtain an individual index of risk preferences, logistic regression was applied on each participant's binary accept/reject responses using trialwise EV as the independent variable [$\log(\text{Response}) = \beta_0 + \beta_1 EV + \epsilon$] to yield DTs [$-(\beta_0/\beta_1)$] for each individual. DT is thus the estimated EV at which a participant's acceptance rate ($AR = N_{\text{accepted trials}}/N_{\text{responded trials}}$) was at chance (0.5) (Supplementary Fig. S1) (Dohmen et al., 2011). ARs for each participant were also evaluated for the different discretized levels of probability of winning and magnitude comprising the 15 choice conditions. ARs for all choice conditions were submitted as the dependent variable in a 3-way repeated measures mixed-effects analysis of variance (ANOVA) with probability and magnitude as within-subject independent variables and age as a between-subjects independent variable. To interrogate simple effects from the omnibus ANOVAs, post hoc comparisons were conducted using the "emmeans" package version 1.1 in R with Satterthwaite estimation of degrees of freedom. Specifically, pairwise comparisons of mean ARs between young and older adults for each choice condition were further conducted to evaluate significant interactions associated with age based on the ANOVA with significance thresholded at $p < 0.05$ with Bonferroni correction for multiple comparisons. Similarly, response times (RTs) across the 15 choice conditions were also submitted to a 3-way ANOVA with post hoc evaluation of simple effects using the emmeans package in R.

2.3. Brain imaging acquisition protocol

Brain imaging was performed using a 32-channel head coil with a 3T Skyra System (Siemens Medical Solutions, Erlangen, Germany) located at National Cheng-Chi University, Taipei, Taiwan. For each participant, functional images were acquired using an echo-planar pulse sequence with TR = 2000 ms, TE = 24 ms, FA = 90°, 38 axial slices, 64 × 64 matrix, and 3.4375 × 3.4375 × 4 mm voxel resolution. Slices were aligned in parallel to the anterior-posterior commissural plane and positioned for whole-brain coverage. Two hundred eighteen volumes were acquired in each of the 5 functional experimental task runs and 180 volumes were acquired for 1 run of a resting-state fMRI experiment (rs-fMRI; eyes open focusing on a fixation). A coplanar individual gradient field map with short TE = 4.92 ms, long TE = 7.38 ms, and TR = 500 ms, was acquired for distortion correction and better spatial

registration of the functional images. A coplanar T2-weighted structural image with TR = 7480 ms, TE = 102 ms, FA = 150°, 38 axial slices, 256 × 256 matrix, and 1 × 1 × 4 mm voxel resolution was also acquired for coregistration of functional to anatomical images. A high-resolution T1-weighted magnetization prepared rapid acquisition gradient echo sequence with TR = 2000 ms, TE = 2.98 ms, FA = 9°, 192 sagittal slices, 256 × 256 matrix, and 1 × 1 × 1 mm voxel resolution, was acquired for normalization to template space.

2.4. LCT fMRI data preprocessing and analysis

Preprocessing and analyses of brain imaging data were conducted using SPM12 revision 6906 (Statistical Parametric Mapping, Wellcome Trust Centre for Neuroimaging, UK). We created a study-specific template to minimize biasing of effects due to age differences in brain structure. The high-resolution T1-weighted images for each participant were segmented and submitted to the Diffeomorphic Anatomical Registration Through Exponentiated Linear Algebra procedure (Ashburner, 2007). This resulted in individual deformation field maps that were subsequently applied to the functional data during the normalization step. For the functional images for each participant, we performed slice-time correction followed by head motion correction with unwarping based on the gradient field map. Corrected functional images were then coregistered to the T2 then T1 structural images, and spatially normalized to the study-specific template with resampling at 3 × 3 × 3 mm voxels. Normalized functional images were then affine-transformed to standard Montreal Neurological Institute space and smoothed with a 3D 8 mm full width at half maximum Gaussian kernel.

Our main whole-brain analysis of the functional imaging data applied an exploratory approach to identify brain regions in which there were any age-related differences in neural responses to the different probability and magnitude conditions. Note that in the LCT experimental design, where each trial had a choice and an outcome phase, these phases were interleaved by jittered ISIs so that first-level general linear models (GLMs) of voxel blood oxygen level—dependent signal timecourses separately modeled choice and outcome responses for each trial, albeit within the same model. Thus, in this main whole-brain analysis, the first-level GLM included 18 primary regressors based on the onsets of the 15 discrete choice phase conditions (5 levels of probability × 3 levels of magnitude; Supplementary Table S2) and 3 outcome phase conditions (gain, loss, reject; see aforementioned Behavioral Methods), convolved with the canonical hemodynamic response function (HRF). Temporal derivatives of the aforementioned regressors to account for age-related delay of blood oxygen level—dependent signals, null response choice and outcome phases (if present; onsets convolved with HRF), and 6 motion parameters were additionally used as covariates (model equation is shown in Supplementary Methods). At the group-level, first-level whole-brain voxelwise neural response estimates for the 15 choice conditions of each individual were submitted to a whole-brain voxelwise 3-way repeated-measures ANOVA with probability and magnitude as within-subject independent variables and age as a between-subjects independent variable. We focused on age × probability, age × magnitude, and age × probability × magnitude interactions to identify voxels across the whole brain in which any responses to probability or magnitude were significantly modulated by age during

the choice phase. Because our focus in this study was on choice-related neural processes, outcome responses are not presently evaluated further.

We also conducted a second supplementary whole-brain analysis using model-based fMRI analysis that evaluated neural responses to probability and magnitude as continuous variables. Studies have shown that responses to probability show linear effects reflecting value processing as well as quadratic trends reflecting more uncertainty (Knutson et al., 2005; Preuschoff et al., 2006; Tobler et al., 2007). Thus, we applied this more specific model-based fMRI approach as a means to corroborate resulting age differences in whole-brain activity patterns from the general exploratory approach aforementioned, and to obtain voxelwise summary coefficient measures of neural sensitivity to probability and magnitude for regions-of-interest (ROI) analyses below. In addition, this supplementary analysis further qualified whether neural responses in brain regions showing age-related differences in the main exploratory analysis were driven by linear probability or magnitude effects reflecting value processing or quadratic effects reflecting more uncertainty. A P^2 regressor was included to account for the contribution of neural processing related to uncertainty, which should peak when $p = 0.5$. As aforementioned, choice and outcome phase responses were assigned separate regressors within the same model. Different from the aforementioned model, the first-level GLM for this supplementary approach included 9 primary regressors that included the onsets of all choice phases as 1 regressor convolved with the HRF, 5 regressors that modulated the choice phase regressor by trialwise probabilities in a linear (P) and quadratic (P^2) manner, magnitudes (M), and their interactions ($P \times M$, $P^2 \times M$), and as in the main approach previously mentioned, 3 regressors for outcome phase conditions (gain, loss, reject) also convolved with the HRF. Temporal derivatives of the aforementioned regressors, null response trials (if present; convolved with HRF), and 6 motion parameters were included as covariates (see Supplementary Methods). Regressors that modulated the choice phase regressor were nonorthogonal. In sum, this model-based first-level GLM yielded whole-brain coefficient images reflecting each individual's voxelwise neural sensitivity to trialwise changes in P , P^2 , M , and their interaction $P \times M$, $P^2 \times M$ during the choice phase. At the group-level supplementary analysis, these first-level whole-brain coefficient images were submitted to one sample t-test to identify voxels showing significant neural sensitivity to the respective choice phase parameters across the whole brain in young and older adult age groups.

Significance thresholds for all whole-brain analyses were set at $p < 0.001$ (uncorrected) with cluster size >15 for cortical regions and $p < 0.005$ with cluster size >20 for subcortical regions. Similar separate criteria for cortical and subcortical regions was used in our previous publication using this same LCT task (Goh et al., 2016) and was a means to adapt to effect sizes in the smaller volumes of subcortical tissue. Both criteria fulfilled a whole-brain clusterwise false discovery rate (FDR) of $p < 0.05$ based on Monte-Carlo simulation with 10,000 iterations (<https://www2.bc.edu/sd-slotnick/scripts.htm>; Slotnick, 2017; Slotnick et al., 2003).

2.5. ROI analysis

ROIs were defined as 8 mm spheres around peak contrast voxels showing significant interaction effects of age $\times$ probability and age $\times$ probability $\times$ magnitude from the main exploratory whole-brain analysis approach (age $\times$ magnitude did not yield significant voxels, see results in the following). Neural functional response estimates for the 15 discrete choice conditions from the main whole-brain analysis were then extracted from ROIs for each individual participant. Response estimates were submitted as the dependent variable in mixed-effects linear regression analyses using R running the “lme4” package version 1.1—12 and ‘lmerTest’ package version 2.0—32. Independent variables in the mixed-effects linear model included probability (Prob; 5 levels), magnitude (Mag; 3 levels), age (2 levels; coded young = 1, old = -1), the interactions between these prior variables (4 in total), and sex as fixed effects, and the intercepts for each subject as well as for probability and magnitude nested in each subject as random effects. Satterthwaite approximations were used to obtain denominator degrees of freedom for hypothesis testing of model coefficients. Polynomial contrasts of the model coefficients were specified and evaluated to interrogate the discrete linear effect of probability (Prob_{linear}), and the quadratic effect of probability (Prob_{quadratic}) and their interactions with magnitude separately for young and older adults as well as comparing between age groups. Effects of Mag and age differences in Mag responses were not evaluated in ROIs as the whole-brain age $\times$ magnitude contrast did not yield significant voxels, see results in the following. Individual neural sensitivity coefficients for continuous trialwise changes in P from the supplementary whole-brain model-based approach were also extracted from ROIs and used in correlation analyses and the analysis of their role in mediating the effect of age on DT.

For ROIs that presented significant correlations between neural sensitivity to probability (P) or magnitude (M) with DT, we further assessed their joint mediatory contribution in the effect of age on DT. Mediation analyses were conducted using the “lavaan” package version 0.5–23.1097 under the R environment. The mediation model assessed the effect of age (young vs. old; 1 vs. -1, respectively) on DT via neural sensitivity to P (based on the model-based fMRI analysis) in ROIs as multiple mediators (M_j), with the causal events formulated in the following equations.

$$DT = i_{DT} + cAge + \varepsilon_{DT}$$

$$M_j = i_{M_j} + a_j Age + \varepsilon_{M_j}$$

$$DT = i_{DT} + c'Age + \sum_j b_j M_j + \varepsilon_{DT}$$

In the aforementioned equations, i denote the respective model intercepts, c and c' denote coefficients for the effect of age on DT before and after accounting for the contribution of multiple mediators, respectively, a is the coefficient for the effect of age on the j th mediator, b is the coefficient for the j th mediator's effect on DT, and ε denotes the respective model

residual. Inference regarding the mediations is then evaluated by significance testing of the indirect effects $a_j \times b_j$ (Hayes, 2015; Hayes and Rockwood, 2017). Note, although DT is indicated in the aforementioned equations, all analyses of DT with respect to brain responses were based on square root—adjusted values (see results in the following).

2.6. Functional connectivity preprocessing and analysis

To assess functional connectivity, brain imaging data from the LCT experiment and rs-fMRI scans were first adjusted for slice timing, head motion, field distortion, and coregistered to T1-weighted images as with the aforementioned preprocessing procedures. Spatial normalization and smoothing were not conducted for functional connectivity analysis. Preprocessed images were then filtered to remove linear signal drifts and frequencies higher than 0.08 Hz and lower than 0.009 Hz from voxel timecourses. Finally, voxelwise regression was used to remove the effects of 6 dimensions of head motion, the mean signal within white matter, and mean signal within cerebrospinal fluid, and for the LCT experiment, the task contributions of the 15 choice and 3 feedback conditions. The resulting residual timecourses for each individual participant's processed functional data were retained to assess functional connectivity between ROIs. ROIs from the aforementioned main whole-brain approach were deformed to each individual participant's native space using the inverse individual flow fields generated from the Diffeomorphic Anatomical Registration Through Exponentiated Linear Algebra procedure. For each participant, mean residual timecourses from each ROI were cross-correlated to obtain inter-ROI Pearson correlation coefficients. Correlation coefficients were subjected to Fisher transformation to yield z-scores for subsequent analyses.

Moderated mediation models were constructed to assess the modulatory influence of age (young vs. old; 1 vs. -1, respectively) on the mediatory role of LCT functional connectivity between ROIs (M_j) in the effect of resting-state functional connectivity (RSFC) between ROIs on DT (adjusted), which is formulated in the following equations.

$$DT = i_{DT} + cRSFC + \epsilon_{DT}$$

$$M_j = i_{M_j} + a_{RSFC} j^{RSFC} + a_{Age} j^{Age} + a_{RSFC \cdot Age} j^{RSFC \cdot Age} + \epsilon_{M_j}$$

$$DT = i_{DT} + c'RSFC + \sum b_j M_j + \epsilon_{DT}$$

In the aforementioned equations, i denote the respective model intercepts, c and c' denote coefficients for the effect of RSFC on DT before and after accounting for the contribution of multiple mediators (LCT functional connectivity), respectively, a is the coefficient for the effect of age with its interaction with RSFC for the j th mediator, b is the coefficient for the j th mediator's effect on DT, and ϵ denotes the respective model residual. The indirect effect of mediators for young and older adult age groups are computed as $a_{RSFC_j} \times b_j + a_{RSFC \cdot Age_j} \times b_j \times Age$. Inference regarding the moderated mediation is then evaluated by significance

testing of the $a_{RSFC \cdot Age_j} \times b_j$ estimates relative to zero for the age effect on the mediation (Hayes, 2015; Hayes and Rockwood, 2017).

3. Results

3.1. Higher risk-taking in older than younger adults in lottery choice decisions

Older adults showed lower DTs than younger adults (old: $\overline{DT}$ (SD) = -14.9 (22.9); young: $\overline{DT}$ (SD) = -2.56 (7.20); $t_{78} = 3.24$, $p = 0.002$, Fig. 1B) indicating more risk-taking behavior in the former. Square root adjustment of absolute DT to account for the skewed distribution yielded the same statistical result (old: $\sqrt{DT}$ (SD) = -2.66 (2.99); young: $\sqrt{DT}$ (SD) = -0.98 (1.88); $t_{78} = 3.01$, $p = 0.003$, Fig. 1C) and this adjusted DT is used for subsequent correlations against neural responses. Removing the 4 older individuals with the lowest DTs did not change the overall results (Supplementary Results) so that these were considered within representative performance range (see also Goh et al., 2016).

Analysis of AR across the 15 choice conditions further revealed that age differences were present from middle to lower probability conditions (Fig. 1D). Specifically, a repeated measures ANOVA yielded significant interaction effects between probability, magnitude, and age group ($F_{8,624} = 2.12$, $p = 0.032$) on AR, between probability and age group ($F_{4,312} = 6.18$, $p < 0.001$), between magnitude and age group ($F_{2,156} = 7.76$, $p < 0.001$), and between probability and magnitude ($F_{8,624} = 15.18$, $p < 0.001$), as well as significant main effects of age group ($F_{1,78} = 5.90$, $p = 0.017$), probability ($F_{4,312} = 848.67$, $p < 0.001$), and magnitude ($F_{2,156} = 5.86$, $p = 0.003$). Post hoc comparisons parsing out the 3-way interaction effect showed significantly higher ARs in older than younger adults in the MMM ($t_{603.58} = 3.44$, $p = 0.009$), MMH ($t_{603.58} = 3.39$, $p = 0.011$), MLM ($t_{603.58} = 3.99$, $p = 0.001$), MLH ($t_{603.58} = 3.80$, $p = 0.002$), LLM ($t_{603.58} = 3.17$, $p = 0.024$), and LLH ($t_{603.58} = 3.76$, $p = 0.003$) conditions. Thus, while young adults reduced ARs to increasing probabilities of losing and higher magnitudes of cost constituting the trial EVs, older adults accepted more middle to lower probability stakes than younger adults particularly as the magnitude of points became more tempting, albeit unfavorable.

Analysis of RTs also revealed age differences particularly in lower probability conditions (Supplementary Fig. S2). Repeated measures ANOVA yielded significant interactions between probability and age group ($F_{4,312} = 3.42$, $p = 0.009$), and between probability and magnitude ($F_{8,624} = 4.53$, $p < 0.001$), but showed no interaction between magnitude and age group ($F_{2,156} = 1.15$, $p = 0.320$) and no 3-way interaction ($F_{8,624} = 1.09$, $p = 0.368$). Main effects were significant for age group ($F_{1,78} = 20.62$, $p < 0.001$), probability ($F_{4,312} = 79.75$, $p < 0.001$), but not magnitude ($F_{2,156} = 1.01$, $p = 0.366$). Because, not surprisingly, older adults showed typical general slowing of RTs compared with younger adults, and there were no age interaction effects with magnitude, post hoc evaluations focused on within-group pairwise comparisons of probability effects. These showed significant RT increases from low to middle probabilities (ML*—MM*: $t_{312} = -4.13$, $p < 0.001$; LL*—ML*: $t_{312} = -2.86$, $p = 0.046$) and RT decreases from middle to high probabilities (MM*—MH*: $t_{312} = 7.01$, $p < 0.001$; MH*—HH*: $t_{312} = 5.19$, $p < 0.001$) in younger adults. By contrast, older adults showed less RT differences from low to middle probabilities (ML*—MM*: $t_{312} =$

–2.12; $p = 0.346$; LL*—ML*: $t_{312} = -1.19$, $p = 1.000$) although RTs did significantly decrease from middle to high probabilities (MM*—MH*: $t_{312} = 8.13$, $p < 0.001$; MH*—HH*: $t_{312} = 3.23$, $p = 0.014$). Thus, younger adults reduced RTs when stakes were more certain (toward low or high probability conditions), whereas older adults evinced additional deliberation time for taking risks on unfavorable stakes.

3.2. Probability modulated young VS but older VMPFC and MTL

Repeated measures ANOVA of whole-brain functional responses (the main exploratory whole-brain analysis) identified significant interaction effects of age by probability in the right VS, right MTL, VMPFC, DMPFC, and bilateral DLPFC, and age by probability by magnitude in the left putamen, but no age by magnitude effects (Fig. 2A; Supplementary Table S3). Note that the left putamen region is substantially dorsally and laterally displaced in the striatum relative to the right VS region so we treated these as 2 separate functional brain areas. ROI analysis with polynomial contrasts applied in linear mixed models (see Methods) further detailed the specific age differences in responses to probability and magnitude in these brain areas (Fig. 2B—G; Supplementary Table S4). Consistent with less distinctive responses to value, we found an interaction between age and the linear effect of probability (Prob_{linear}; $t_{316} = 2.73$, $p = 0.007$; Fig. 2B) in the right VS due to a positive linear trend in younger ($t_{158} = 2.45$, $p = 0.015$) but not older adults ($t_{476} = -1.20$, $p = 0.233$), whose right VS responses were not modulated by probability. Instead, older adults evinced greater sensitivity to increasing probability in right MTL and VMPFC. Specifically, we found age by Prob_{linear} interactions (right MTL: $t_{316} = -2.61$, $p = 0.009$; Fig. 2C; VMPFC: $t_{316} = -1.96$, $p = 0.0513$; Fig. 2D) driven by linear increases in neural responses to increasing probability in older (right MTL: $t_{158} = 3.12$, $p = 0.002$; VMPFC: $t_{158} = 3.43$, $p < 0.001$) but not younger (right MTL: $t_{158} = -0.80$, $p = 0.426$; VMPFC: $t_{158} = 0.07$, $p = 0.941$) adults.

3.3. Higher responses to unfavorable choices in older adult DLPFC and DMPFC

Bilateral DLPFC and DMPFC responded with higher neural activity as probability of losing increased (or as probability of winning decreased in the mixed lotteries) in older but not younger adults (Fig. 2E—G). Specifically, bilateral DLPFC and DMPFC showed age by Prob_{linear} interactions (left DLPFC: $t_{316} = 3.35$, $p < 0.001$; right DLPFC: $t_{316} = 2.24$, $p = 0.026$; DMPFC: $t_{316} = 2.51$, $p = 0.013$) qualified by negative Prob_{linear} response trends indicating increasing neural activity to increasing probability of losing in older adults (left DLPFC: $t_{158} = -3.89$, $p < 0.001$; right DLPFC: $t_{158} = -2.52$, $p = 0.013$; DMPFC: $t_{158} = -4.14$, $p < 0.001$) but not younger (left DLPFC: $t_{158} = 1.25$, $p = 0.213$; right DLPFC: $t_{158} = 1.05$, $p = 0.295$; DMPFC: $t_{158} = 0.280$, $p = 0.781$) adults. Supplementary model-based fMRI analysis treating probability and magnitude as continuous and performed separately for each age group corroborated the previously mentioned findings on age differences in brain areas showing neural sensitivity to probability. Specifically, linear probability-related neural responses shifted from the VS in younger adults to MTL and frontal areas in older adults (Supplementary Fig. S3A).

Interestingly, we found interaction effects between the quadratic neural responses to probability (Prob_{quadratic}) and age in bilateral DLPFC ROIs such that younger adults showed

inverted U-shaped responses across probability conditions in contrast to linearly increasing neural responses to lower probability conditions in older adults (young vs. old; left DLPFC: $t_{316} = -2.28$, $p = 0.023$; right DLPFC: $t_{316} = -2.89$, $p = 0.004$; Fig. 2E—F, Supplementary Table S3 and Supplementary Fig. S3A, C). Analysis of the left putamen ROI also yielded similar results as in the DLPFC ROIs. Specifically, left putamen responses showed enhanced inverted U-shaped $\text{Prob}_{\text{quadratic}}$ neural responses particularly to increasing magnitudes, in young but not older adults, who again showed less distinctive responses across choice EV conditions in this striatal area (young vs. old: $t_{794} = -2.09$, $p = 0.037$; young: $t_{397} = -2.87$, $p = 0.004$; old: $t_{555} = -0.526$, $p = 0.599$; Supplementary Fig. S4B). Note, unlike the right VS, the left putamen did not evince significant $\text{Prob}_{\text{linear}}$ neural responses at the group level (Supplementary Table S4), supporting our approach to treat these brain areas as functionally distinct. Thus, bilateral DLPFC and left putamen responses reflect more neural engagement during middle (relative to high and low) probability conditions in younger adults, particularly at higher stake magnitudes. Such a neural response profile is consistent with greater decision difficulty inducing greater cognitive control when relying on a $p = 50\%$ (or EV = 0) strategy, especially when stakes increase. This neural response profile is also in contrast to the linear increase in DLPFC and DMPFC neural responses as probability to lose increased in older adults, indicative of a different decision strategy compared with younger adults. Modulation of neural activity in relation to the main effect of magnitude was observed in several brain areas but these were minimally affected by age (Supplementary Table S3 and Fig. S3B).

3.4. Frontostriatal neural sensitivity to probability mediates age effects on risk-taking

Correlations between ROI neural sensitivity to P (regression coefficients for P from the supplementary model-based fMRI analysis) and decision behavior were evaluated (Fig. 3). In both age groups, separately as well as the sample as a whole, individuals who had greater neural sensitivity to linear increases in probability of losing (negative linear neural sensitivity to probability of winning) in right VS, DMPFC, and left DLPFC demonstrated more risk-taking behavior, with lower adjusted DT scores (greater acceptance for more loss dominant stakes) (Fig. 3A—C). This correlation between greater linear neural sensitivity to probability of losing with lower DT across individuals was additionally significant in the right DLPFC and left putamen in young adults, with the right DLPFC correlation also significant for the sample as a whole (Fig. 3D, Supplementary Fig. S4C). However, linear regressions performed for each ROI failed to yield any significant interaction effects of linear neural probability sensitivity and age on DT (right VS: $t_{76} = -1.10$, $p = 0.277$; DMPFC: $t_{76} = -0.95$; $p = 0.343$; left DLPFC: $t_{76} = -0.79$; $p = 0.435$; right DLPFC: $t_{76} = 0.51$; $p = 0.614$; left putamen: $t_{76} = 1.37$; $p = 0.176$). Thus, individual linear neural sensitivity to probability in these ROIs was associated with DT, and age did not modulate these brain-behavior correlations.

We then evaluated whether greater linear negative neural sensitivity to probability in these ROIs during the LCT mediated the effect of age on DTs. We applied a mediation model to test the indirect effect of age on DT via simultaneous multiple ROI linear neural probability sensitivities (see Section 2.5; Fig S5, Supplementary Table S5A). Significant indirect effects of age on DT were found for left DLPFC ($Z = 2.74$, $p = 0.006$) and right VS ($Z = 2.18$, $p =$

0.029) with a marginal negative effect of right DLPFC ($Z = -1.86$, $p = 0.063$). Note that indirect effects of age on DT were also all significant except for left putamen even when ROIs were considered in separate mediation models (Supplementary Table S5B). Thus, greater risk-taking with age operated through greater negative neural probability sensitivity in the right VS and left DLPFC with somewhat reduced right DLPFC involvement in older compared with younger adults.

3.5. Associations between resting-state and LCT functional connectivity of ROIs with risk-taking behavior in young and older adults

Given the aforementioned age differences in brain regions engaged for processing probability during the LCT, we further evaluated how baseline resting-state and task-related functional communication between the different neural networks in young and older adults were associated with LCT performance. We first examined young and older adult DT associations with baseline RSFC between the ROIs identified in the main whole-brain analysis previously mentioned (Supplementary Fig. S6). During resting state (Fig. 4A, B), in younger adults, lower DT was associated only with lower functional connectivity between left putamen and left DLPFC. By contrast, in older adults, lower DT correlated with lower functional connectivity between left putamen and left DLPFC, between right VS and left DLPFC, and between right VS and right DLPFC. Linear regression analysis revealed a significant interaction effect of age with right VS and left DLPFC RSFC on DT ($t_{75} = -2.36$, $p = 0.021$). Specifically, higher individual baseline RSFC between the right VS and left DLPFC was associated with higher DTs in older but not in younger adults. Furthermore, note that right VS and left DLPFC were functionally disconnected (mean RSFC was not significantly different from zero) in older adults as a group during baseline resting state (see Supplementary Fig. S6).

We then examined young and older adult DT associations with functional connectivity during the LCT task (LCTFC) between the same identified ROIs (Supplementary Fig. S6; Fig. 4C, D). In young adults, lower DT was associated with lower functional connectivity between left putamen and right MTL. By contrast, in older adults, lower DT correlated with lower functional connectivity between the left and right DLPFC, and between DMPFC and right MTL. Linear regressions revealed a marginal interaction effect of age with bilateral DLPFC LCTFC on DT ($t_{76} = -1.80$, $p = 0.075$). Note that LCT functional connectivity between bilateral DLPFC was significantly lower in older than younger adults with aging (Supplementary Fig. S6).

3.6. Age modulates the effect of DLPFC-VS RSFC on LCT risk-taking behavior via mediation by LCT task functional connectivity

That frontostriatal RSFC modulated individual decision behavior more in older than younger adults suggests age effects on baseline functional communication in this network that may underlie the changes in the broader network engaged by older adults during the LCT task. Thus, we applied a moderated mediation analysis to evaluate age modulation of the effect of baseline resting-state frontostriatal functional connectivity on LCT decision behavior mediated by network functional connectivity during the LCT task. We focused on functional connections with any evidence for age differences in associations with DT from the

aforementioned correlation analyses that included RSFC between right VS and left DLPFC as the primary causal effect, and LCTFC between left DLPFC and right DLPFC, between right MTL and DMPFC (where correlations reached significance in older but not younger adults), and between left putamen and right MTL (where correlations reach significance in younger but not older adults) as mediators. We also hypothesized that older adults should have stronger mediation than younger adults of MTL and frontal processing during the LCT.

Results and details of the moderated mediation coefficients are shown in Fig. 5 and Supplementary Table S6 (coefficient means (SEM) of key effects are highlighted here in the main text). As expected, the model showed a significant direct effect of right VS and left DLPFC RSFC on DT (mean (SEM) = 2.97 (1.13); $Z = 2.62$, $p = 0.004$, 1-tailed; see Supplementary Table S6, c'). To provide an anchor then, a unit change in right VS and left DLPFC RSFC (which are Fisher Z-transformed correlations; see Methods) was proportional to a change in $\sqrt{DT}$ by 2.97, after accounting for the mediation variables. For young adults, there was only a marginal further negative indirect effect of the left DLPFC and right DLPFC LCTFC mediation (mean (SEM) = -0.517 (0.402); $Z = -1.29$, $p = 0.099$, 1-tailed; Supplementary Table S6, indirect effect for young adults for M_2) of the aforementioned direct effect. In older adults, the aforementioned direct effect was significantly positively mediated by left DLPFC and right DLPFC LCTFC (mean (SEM) = 0.909 (0.540); $Z = 1.68$, $p = 0.046$, 1-tailed) and a marginal effect of DMPFC and right MTL LCTFC (mean (SEM) = 0.941 (0.622); $Z = 1.51$, $p = 0.066$, 1-tailed) (Supplementary Table S6, indirect effects for older adults for M_2 and M_3). Critically, age (young vs. older) significantly moderated the mediation effects of the LCTFC between the left and right DLPFC (mean (SEM) = -0.713 (0.370); $Z = -1.93$, $p = 0.027$, 1-tailed), and between DMPFC and right MTL (mean (SEM) = -0.771 (0.424); $Z = -1.82$, $p = 0.035$, 1-tailed) (Supplementary Table S6, effect of moderated mediation for M_2 and M_3). Evaluation of the aforementioned moderated mediation model based on simultaneous multiple mediators using separate models for each mediator yielded similar results (Supplementary Table S7).

4. Discussion

Our findings demonstrate a systemic neurofunctional difference in the way the older human adult brain approaches mixed-lottery choice decisions relative to young adults. Instead of directly engaging a more rudimentary VS-based stimulus-response selection in reaction to EV as in young adults, older adults evinced greater involvement across MTL, ventral and dorsal medial prefrontal, and bilateral lateral prefrontal areas that implicate more affective-like reactions and higher regulatory control. Critically, comprehensive analyses of various aspects of our brain and behavioral data provide support for the notion that age-related shift to involve more MTL and frontal processing of mixed-lottery choices underlies greater behavioral propensity to accept unfavorable stakes in older compared with younger adults. Specifically, altered neural sensitivity to losing stakes in bilateral DLPFC and right VS mediated the effect of greater age in increasing LCT risktaking. In addition, the engagement of LCT functional connectivity between left and right DLPFC and between right MTL and DMPFC in mediating the effect of baseline frontostriatal RSFC on risk-taking was more evident in older than in younger adults.

Several results in this present study comparing older (aged 59–78 years old) with younger (aged 20–29 years old) adult age groups are consistent with our previous study focusing on older individuals aged 55–80 years old (Goh et al., 2016). In both studies, mean LCT DTs in older adults as a group were in the negative EV range indicating an overall risk-taking preference, with this present study also showing that the DT was significantly lower compared with that for younger adults. RTs were also slower for both older adult groups as EVs became more negative in both studies, particularly for more extreme risk-taking older individuals in Goh et al. (2016). Neural activity during older adult choice processing in this study increased with increasing stake probability in VMPFC and with increasing stake magnitude (but not probability) in bilateral ventral striatal areas, similar to our previous finding of increasing neural activity with increasing EV in these same brain areas. Finally, in both studies, older adult neural activity in bilateral lateral and dorsomedial prefrontal areas increased to decreasing EV or increasing probability of losing. Such replication of older adult behavioral and frontostriatal responses to valiative information in mixed-lottery choices further accentuates the differences in comparison with younger adults in this present study, who showed more risk-neutral behavior and ventral striatal sensitivity to stake probability.

Interestingly, although our previous study showed older adult MTL neural activity during the LCT decreased with increasing EV (and also increasing probability), MTL responses in this present study increased with increasing probability. We suggest that this difference in mean neural sensitivity to valiative information across older adult groups reflects the substantial heterogeneity of individual differences in MTL responses. Indeed, the previous study found MTL responses ranged from having positive to negative associations with increasing EV across a much larger sample of risk-averse to risk-taking older individuals, respectively. Critically, evaluation of older individuals in that study revealed that although individuals with extreme risk-taking preferences showed negative neural sensitivity to EV in MTL responses, more moderately risktaking individuals showed minimum to positive MTL neural EV sensitivity. Thus, the negative mean MTL sensitivity to EV in the previous study may have been driven by more individuals with extreme risk-taking preferences sampled in that larger cohort in contrast to the positive mean MTL sensitivity to probability in older adults in this study, which might reflect relatively moderate risk-taking preferences in this present older adult sample. Nevertheless, in both studies, MTL sensitivity to value plays a more prominent role in older adult risk-taking decisions compared with younger adults. Taken together, the findings from these 2 studies provide complementary views of young and older adult group differences in neural responses associated with valiative processing of choices as well as older adult individual differences in these age-related effects.

Previous studies on age differences in value-based decisionmaking have reported mixed-findings on whether older adults are more or less risk-taking compared with younger adults. Metaanalysis across studies revealed that the mixed findings were largely due to task differences in the dependence on learning and memory, and framing of the decision context (Best and Charness, 2015; Mata et al., 2011). Not surprisingly, age differences are generally detected when the decision task required retrieval of past outcome histories. Importantly, in studies where probabilities are made explicit and learning from past outcomes are not required, the effects of age in risk preferences also differed if current choices are framed as

potential gains, potential losses, or mixed (Pachur et al., 2017; Rutledge et al., 2016; Tymula et al., 2013). Specifically, for gain-only probabilistic lotteries, older adults showed greater risk-aversion than younger adults (Rutledge et al., 2016; Tymula et al., 2013). By contrast, for loss-only lotteries, older adults evinced greater risk-taking than younger adults (Tymula et al., 2013; albeit Rutledge et al., 2016 found no age differences). Critically, Rutledge et al. (2016) also evaluated mixed lotteries similar to our LCT in which choices in each trial were between a sure outcome or a simultaneous chance of gain or loss (with no null outcomes) and found higher risk-taking in older than younger adults, consistent with our results. It should be noted, however, that older adults may have a higher preference for certainty compared with younger adults in choices that involve sure versus probabilistic outcomes as in the previously mentioned studies, perhaps due to the reduced cognitive effort to process the former (Mather et al., 2012). Controlling for this, Pachur et al. (2017) presented young and older adults with 2 lottery options in each trial with different variable magnitudes and probabilities constituting EV and risk differences between the options. Computational modeling of their behavioral decision data revealed lower loss aversion (overweighting of losing EVs) and greater optimism of potential gains (overweighting of the probability of winning; see Hess, 2015) in older compared with younger adults, consistent with the higher acceptance rates for unfavorable mixed lotteries (low probability of winning high magnitudes) in older than younger adults in our study. In light of these prior studies, we highlight that our LCT task stimuli were straightforward texts that bypassed the need to translate from graphical representations of value as might be used in other studies, given age effects on perceptual processing (Goh et al., 2010; Park et al., 2004). The zero outcome for rejected lotteries also allows us to determine a more neutral certainty equivalence using estimated individual DTs. Finally, the LCT task favors decisions made solely on information given during each trial and discourages reliance on past reward history. Thus, although our paradigm favors more objective and risk-neutral decisions, we still find that older adults display greater risk-taking behavior than younger adults. Overall, the emergent finding integrating across past studies and ours is that, barring cognitive demand and reward framing influences, older adults engage greater risk-taking behavior than younger adults particularly for unfavorable stakes in mixed lottery decisions. Critically, we add to extant behavioral literature by showing that this age-related change in risky behavior for mixed-lotteries is associated with a shift in brain central processing of value from striatal areas in younger adults to more medial temporal and frontal areas in older adults.

It may be counter-intuitive that increased medial temporal and frontal activity that we interpret to reflect greater affective-like modulation and control is associated with greater risk-taking in older adult decision-making. We note, however, that increased control-related neural activity in older adults has been indicative of the heightened need for compensatory neural recruitment to cope with underlying declines in more primary neural processes (Goh, 2013; Hakun et al., 2015; Schneider-Garces et al., 2010; Zhu et al., 2014) (5, 35–37). In line with a positivity bias (Mather and Carstensen, 2005) and the behavioral findings in Pachur et al. (2017), increased frontal and medial temporal activity for unfavorable lotteries in older adults is also consistent with greater neural processing engaged to regulate negative affect associated with losing prospects compared with the positive affect for more favorable prospects. Alternatively, higher medial temporal and frontal activity in older adults may

reflect different motivations than younger adults, such as greater salience for winning under unfavorable rather than favorable odds, when making lottery decisions. These cases are not mutually exclusive and are consistent with age-related positivity bias and changes in the neural processing of goals and values (Samanez-Larkin and Knutson, 2015). We acknowledge, however, that our experiment only evaluates age-related differences in neural and behavioral responses to different probabilities and magnitudes. As such, future studies that examine neural processes associated with specific motivations behind older adult value-based decisions and direct modulations of emotional reactions during decision processing are required to elucidate this issue.

That age effects were largely seen in neural processing of probability but not magnitude in our results agrees with studies that found age effects using tasks involving probability in decisions (Dreher et al., 2008), and those that found preservation in neural responses in older adults using tasks that did not involve probability (Lorenz et al., 2014; Samanez-Larkin et al., 2007, 2014). We speculate that such modulation of neural responses to probability but not magnitude reflects the specific influence of age on certainty processing in older adult value-based decisions (Mather et al., 2012) as well as distinct neuronal firing patterns to different components of EV (Fiorillo et al., 2003). Specifically, in our experiment, neural coding of increasing magnitude might be more concrete and can be directly instantiated via increases in neuronal population activity that thereby scale the salience of other concurrent neural processes. By contrast, apart from such quantitative modulation of neuronal population activity, neural coding of the probability of winning or losing likely also involves more qualitative access to different beliefs about probability (Ma and Jazayeri, 2014). For this reason, neural coding of probability might be more susceptible to age-related changes in the use of strategies that emphasize the subjective meaning, and thus framing (e.g., 10% chance of winning vs. 90% chance of losing), of a given probability.

In our study, baseline RSFC between the left DLPFC and right VS predicted older adult DTs during the LCT more than younger adults. This finding supports the association between older adult reward learning and ventromedial prefrontal to striatal structural connectivity (Samanez-Larkin et al., 2012), and suggests that the baseline efficacy of frontostriatal communication is an important determinant of older adult decision neural processing and decision behavior. Indeed, the role functional connectivity between left and right DLPFC and between right MTL and VMPFC during the LCT in mediating the effect of frontostriatal baseline RSFC on DTs was more evident in older than younger adults. Thus, apart from the influence of psychological differences in motivation and affective processing between young and older adults, we also provide evidence on more neurobiological aspects of brain aging that jointly contribute to older adult decision-making as well. Further work that comprehensively integrate white-matter tract and fMRI data in longitudinal studies are required to more precisely characterize how age changes in brain structural connections conduct dynamic functional communication between frontal and striatal brain regions that then bear on older adult information processing associated with decision behaviors.

Finally, and more broadly, it is intriguing to consider whether responding to veridical EV is always the optimal approach when interacting with the environment from the perspective of the human species as a whole. With age comes wisdom (Worthy et al., 2011) and extended

prior subjective experiences with the environment. For humans, relative to other species, this experience can be communicated via stable and also complex means within and across generations. This suggests that as a species with rich social tools, humans can more effectively harness information about longterm environmental contingencies compared with more instantaneous snapshots of immediate contexts. Thus, the neural processes underlying the change in goals with age jointly reflect the effects of senescent neural functioning as well as cohort-wise assessments of environmental utilities. Individual differences across older adult value-based decision-making (Goh et al., 2016) then stand as critical indicators of the effects of the environment in relation to specific biological limitations. For instance, the human species did not much have to contend with issues of Alzheimer's Disease (and other age-related cognitive declines implicated in frontal, striatal, and medial temporal functioning) until recent increases in life expectancy (Vaupel, 2010). In this light, we recommend that longitudinal studies are critical for investigations on broader economic implications surrounding aging human neural processing of value-based decisions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The Taiwan Ministry of Science and Technology grant nos. 102-2410-H-002-004-MY3, 103-2410-H-002-082-MY2, 105-2420-H-002-002-MY2, and 105-2410-H-002-055-MY3 supported this work.

The Taiwan Ministry of Science and Technology grant nos. 102-2410-H-002-004-MY3, 103-2410-H-002-082-MY2, 105-2420-H-002-002-MY2, and 105-2410-H-002-055-MY3 supported this work.

The authors declare that the data contained in the article being submitted have not been previously published, have not been submitted elsewhere, and will not be submitted elsewhere while under consideration at *Neurobiology of Aging*.

All participants gave written informed consent on the day of the MRI session for this study, which was approved by National Taiwan University Hospital Research Ethics Committee.

The authors declare that that all authors have reviewed the contents of the article being submitted, approved its contents, and validated the accuracy of the data.

References

- Ardiale E, Lemaire P, 2012 Within-item strategy switching: an age comparative study in adults. *Psychol. Aging* 27, 1138–1151. [PubMed: 22563941]
- Ashburner J, 2007 A fast diffeomorphic image registration algorithm. *Neuroimage* 38, 95–113. [PubMed: 17761438]
- Bäckman L, Lindenberger U, Li S-C, Nyberg L, 2010 Linking cognitive aging to alterations in dopamine neurotransmitter functioning: recent data and future avenues. *Neurosci. Biobehav. Rev.* 34, 670–677. [PubMed: 20026186]
- Berns GS, McClure SM, Pagnoni G, Montague PR, 2001 Predictability modulates human brain response to reward. *J. Neurosci.* 21, 2793–2798. [PubMed: 11306631]
- Best R, Charness N, 2015 Age differences in the effect of framing on risky choice: a meta-analysis. *Psychol. Aging* 30, 688–698. [PubMed: 26098168]
- Borghesani PR, Madhyastha TM, Aylward EH, Reiter MA, Swamy BR, Warner Schaie K, Willis SL, 2013 The association between higher order abilities, processing speed, and age are variably

mediated by white matter integrity during typical aging. *Neuropsychologia* 51, 1435–1444. [PubMed: 23507612]

Carstensen LL, 2006 The influence of a sense of time on human development. *Science* 312, 1913–1915. [PubMed: 16809530]

Carstensen LL, Isaacowitz DM, Charles ST, 1999 Taking time seriously. A theory of socioemotional selectivity. *Am. Psychol.* 54, 165–181. [PubMed: 10199217]

Davis SW, Kragel JE, Madden DJ, Cabeza R, 2012 The architecture of cross-hemispheric communication in the aging brain: linking behavior to functional and structural connectivity. *Cereb. Cortex.* 22, 232–242. [PubMed: 21653286]

Dohmen T, Falk A, Huffman D, Sunde U, Schupp J, Wagner GG, 2011 Individual risk Attitudes: measurement, determinants, and behavioral consequences. *J. Eur. Econ. Assoc.* 9, 522–550.

Dreher J-C, Meyer-Lindenberg A, Kohn P, Berman KF, 2008 Age-related changes in midbrain dopaminergic regulation of the human reward system. *Proc. Natl. Acad. Sci. U. S. A.* 105, 15106–15111. [PubMed: 18794529]

Erixon-Lindroth N, Farde L, Wahlin T-BR, Sovago J, Halldin C, Bäckman L, 2005 The role of the striatal dopamine transporter in cognitive aging. *Psychiatry Res.* 138, 1–12. [PubMed: 15708296]

Fiorillo CD, Tobler PN, Schultz W, 2003 Discrete coding of reward probability and uncertainty by dopamine neurons. *Science* 299, 1898–1902. [PubMed: 12649484]

Fjell AM, Sneve MH, Grydeland H, Storsve AB, Walhovd KB, 2017 The disconnected brain and executive function decline in aging. *Cereb. Cortex.* 27, 2303–2317. [PubMed: 27073220]

Gazes Y, Bowman FD, Razlighi QR, O'Shea D, Stern Y, Habeck C, 2016 White matter tract covariance patterns predict age-declining cognitive abilities. *Neuroimage* 125, 53–60. [PubMed: 26477658]

Goh JO, Su YS, Tang YJ, McCarrey AC, Tereshchenko A, Elkins W, Resnick SM, 2016 Frontal, striatal, and medial temporal sensitivity to value distinguishes risk-taking from risk-Aversive older adults during decision making. *J. Neurosci.* 36, 12498–12509. [PubMed: 27927964]

Goh JOS, 2013 Aging of neural circuits underlying decision-making behavior. *J. Neurosci. Neuroengineering* 2, 3–13.

Goh JOS, Suzuki A, Park DC, 2010 Reduced neural selectivity increases fMRI adaptation with age during face discrimination. *Neuroimage* 51, 336–344. [PubMed: 20139012]

Hakun JG, Zhu Z, Johnson NF, Gold BT, 2015 Evidence for reduced efficiency and successful compensation in older adults during task switching. *Cortex.* 64, 352–362. [PubMed: 25614233]

Harris MA, Wolbers T, 2014 How age-related strategy switching deficits affect wayfinding in complex environments. *Neurobiol. Aging* 35, 1095–1102. [PubMed: 24239438]

Hayes AF, 2015 An index and test of linear moderated mediation. *Multivar. Behav. Res.* 50, 1–22.

Hayes AF, Rockwood NJ, 2017 Regression-based statistical mediation and moderation analysis in clinical research: observations, recommendations, and implementation. *Behav. Res. Ther* 98, 39–57. [PubMed: 27865431]

Head D, Buckner RL, Shimony JS, Williams LE, Akbudak E, Conturo TE, McAvoy M, Morris JC, Snyder AZ, 2004 Differential vulnerability of anterior white matter in nondemented aging with minimal acceleration in dementia of the Alzheimer type: evidence from diffusion tensor imaging. *Cereb. Cortex.* 14, 410–423. [PubMed: 15028645]

Hedden T, Schultz AP, Rieckmann A, Mormino EC, Johnson KA, Sperling RA, Buckner RL, 2016 Multiple brain markers are linked to age-related variation in cognition. *Cereb. Cortex.* 26, 1388–1400. [PubMed: 25316342]

Hess TM, 2015 A prospect theory-based evaluation of dual-process influences on aging and decision making: support for a contextual perspective In: Hess TM, Strough J, Löckenhoff C (Eds.), *Aging and Decision Making*. Academic Press, San Diego, pp. 189–212.

Kaasinen V, Vilkmann H, Hietala J, Nagren K, Helenius H, Olsson H, Farde L, Rinne J, 2000 Age-related dopamine D2/D3 receptor loss in extrastriatal regions of the human brain. *Neurobiol. Aging* 21, 683–688. [PubMed: 11016537]

Kahneman D, Tversky A, 1979 Prospect theory: an analysis of decision under risk. *Econometrica* 47, 263–291.

- Kennedy KM, Raz N, 2009 Aging white matter and cognition: differential effects of regional variations in diffusion properties on memory, executive functions, and speed. *Neuropsychologia* 47, 916–927. [PubMed: 19166865]
- Knutson B, Adams CM, Fong GW, Hommer D, 2001 Anticipation of increasing monetary reward selectively recruits nucleus accumbens. *J. Neurosci.* 21, Rc159. [PubMed: 11459880]
- Knutson B, Fong GW, Bennett SM, Adams CM, Hommer D, 2003 A region of mesial prefrontal cortex tracks monetarily rewarding outcomes: characterization with rapid event-related fMRI. *Neuroimage* 18, 263–272. [PubMed: 12595181]
- Knutson B, Taylor J, Kaufman M, Peterson R, Glover G, 2005 Distributed neural representation of expected value. *J. Neurosci.* 25, 4806–4812. [PubMed: 15888656]
- Konishi K, Etchamendy N, Roy S, Marighetto A, Rajah N, Bohbot VD, 2013 Decreased functional magnetic resonance imaging activity in the hippocampus in favor of the caudate nucleus in older adults tested in a virtual navigation task. *Hippocampus* 23, 1005–1014. [PubMed: 23929534]
- Li S-C, Sikström S, 2002 Integrative neurocomputational perspectives on cognitive aging, neuromodulation, and representation. *Neurosci. Biobehav. Rev.* 26, 795–808. [PubMed: 12470691]
- Lorenz RC, Gleich T, Beck A, Pöhland L, Raufelder D, Sommer W, Rapp MA, Kühn S, Gallinat J, 2014 Reward anticipation in the adolescent and aging brain. *Hum. Brain Mapp.* 35, 5153–5165. [PubMed: 24801222]
- Ma WJ, Jazayeri M, 2014 Neural coding of uncertainty and probability. *Annu. Rev. Neurosci.* 37, 205–220. [PubMed: 25032495]
- Madden DJ, Bennett IJ, Song AW, 2009 Cerebral white matter integrity and cognitive aging: contributions from diffusion tensor imaging. *Neuropsychol. Rev.* 19, 415–435. [PubMed: 19705281]
- Madden DJ, Parks EL, Tallman CW, Boylan MA, Hoagey DA, Cocjin SB, Packard LE, Johnson MA, Chou Y, Potter GG, Chen N, Siciliano RE, Monge ZA, Honig JA, Diaz MT, 2017 Sources of disconnection in neurocognitive aging: cerebral white-matter integrity, resting-state functional connectivity, and white-matter hyperintensity volume. *Neurobiol. Aging* 54, 199–213. [PubMed: 28389085]
- Mata R, Josef AK, Samanez-Larkin GR, Hertwig R, 2011 Age differences in risky choice: a meta-analysis. *Ann. N Y Acad. Sci.* 1235, 18–29. [PubMed: 22023565]
- Mather M, Carstensen LL, 2005 Aging and motivated cognition: the positivity effect in attention and memory. *Trends Cogn. Sci.* 9, 496–502. [PubMed: 16154382]
- Mather M, Knight M, 2005 Goal-directed memory: the role of cognitive control in older adults' emotional memory. *Psychol. Aging* 20, 554–570. [PubMed: 16420131]
- Mather M, Mazar N, Gorlick MA, Lighthall NR, Burgeno J, Schoeke A, Ariely D, 2012 Risk preferences and aging: the “certainty effect” in older adults' decision making. *Psychol. Aging* 27, 801–816. [PubMed: 23066800]
- Nicola SM, 2007 The nucleus accumbens as part of a basal ganglia action selection circuit. *Psychopharmacology (Berl)* 191, 521–550. [PubMed: 16983543]
- Pachur T, Mata R, Hertwig R, 2017 Who dares, who Errs? Disentangling cognitive and motivational roots of age differences in decisions under risk. *Psychol. Sci.* 28, 504–518. [PubMed: 28406375]
- Park DC, Polk TA, Park R, Minear M, Savage A, Smith MR, 2004 Aging reduces neural specialization in ventral visual cortex. *Proc. Natl. Acad. Sci. U. S. A.* 101, 13091–13095. [PubMed: 15322270]
- Phelps EA, 2004 Human emotion and memory: interactions of the amygdala and hippocampal complex. *Curr. Opin. Neurobiol.* 14, 198–202. [PubMed: 15082325]
- Phelps EA, Lempert KM, Sokol-Hessner P, 2014 Emotion and decision making: multiple modulatory neural circuits. *Annu. Rev. Neurosci.* 37, 263–287. [PubMed: 24905597]
- Preuschoff K, Bossaerts P, Quartz SR, 2006 Neural differentiation of expected reward and risk in human subcortical structures. *Neuron* 51, 381–390. [PubMed: 16880132]
- Rutledge RB, Smittenaar P, Zeidman P, Brown HR, Adams RA, Lindenberger U, Dayan P, Dolan RJ, 2016 Risk taking for potential reward decreases across the lifespan. *Curr. Biol.* 26, 1634–1639. [PubMed: 27265392]

- Samanez-Larkin GR, Gibbs SEB, Khanna K, Nielsen L, Carstensen LL, Knutson B, 2007 Anticipation of monetary gain but not loss in healthy older adults. *Nat. Neurosci.* 10, 787–791. [PubMed: 17468751]
- Samanez-Larkin GR, Knutson B, 2015 Decision making in the ageing brain: changes in affective and motivational circuits. *Nat. Rev. Neurosci.* 16, 278–289. [PubMed: 25873038]
- Samanez-Larkin GR, Kuhnen CM, Yoo DJ, Knutson B, 2010 Variability in nucleus accumbens activity mediates age-related suboptimal financial risk taking. *J. Neurosci.* 30, 1426–1434. [PubMed: 20107069]
- Samanez-Larkin GR, Levens SM, Perry LM, Dougherty RF, Knutson B, 2012 Frontostriatal white matter integrity mediates adult age differences in probabilistic reward learning. *J. Neurosci.* 32, 5333–5337. [PubMed: 22496578]
- Samanez-Larkin GR, Worthy DA, Mata R, McClure SM, Knutson B, 2014 Adult age differences in frontostriatal representation of prediction error but not reward outcome. *Cogn. Affect. Behav. Neurosci.* 14, 672–682. [PubMed: 24853269]
- Schneider-Garces NJ, Gordon BA, Brumback-Peltz CR, Shin E, Lee Y, Sutton BP, Maclin EL, Gratton G, Fabiani M, 2010 Span, CRUNCH, and beyond: working memory capacity and the aging brain. *J. Cogn. Neurosci.* 22, 655–669. [PubMed: 19320550]
- Schultz W, 2000 Multiple reward signals in the brain. *Nat. Rev. Neurosci.* 1, 199–207. [PubMed: 11257908]
- Slotnick SD, 2017 Cluster success: fMRI inferences for spatial extent have acceptable false-positive rates. *Cogn. Neurosci.* 8, 150–155. [PubMed: 28403749]
- Slotnick SD, Moo LR, Segal JB, Hart J, 2003 Distinct prefrontal cortex activity associated with item memory and source memory for visual shapes. *Brain Res. Cogn. Brain Res.* 17, 75–82. [PubMed: 12763194]
- Sullivan EV, Rohlfing T, Pfefferbaum A, 2010a Quantitative fiber tracking of lateral and interhemispheric white matter systems in normal aging: relations to timed performance. *Neurobiol. Aging* 31, 464–481. [PubMed: 18495300]
- Sullivan EV, Rohlfing T, Pfefferbaum A, 2010b Longitudinal study of callosal microstructure in the normal adult aging brain using quantitative DTI fiber tracking. *Dev. Neuropsychol.* 35, 233–256. [PubMed: 20446131]
- Sun Y, Lee HJ, Yang SC, Chen TF, Lin KN, Lin CC, Wang PN, Tang LY, Chiu MJ, 2014 A nationwide survey of mild cognitive impairment and dementia, including very mild dementia, in Taiwan. *PLoS One* 9, e100303. [PubMed: 24940604]
- Tobler PN, O'Doherty JP, Dolan RJ, Schultz W, 2007 Reward value coding distinct from risk attitude-related uncertainty coding in human reward systems. *J. Neurophysiol.* 97, 1621–1632. [PubMed: 17122317]
- Tom SM, Fox CR, Trepel C, Poldrack RA, 2007 The neural basis of loss aversion in decision-making under risk. *Science* 315, 515–518. [PubMed: 17255512]
- Tymula A, Belmaker LAR, Ruderman L, Glimcher PW, Levy I, 2013 Like cognitive function, decision making across the life span shows profound age-related changes. *Proc. Natl. Acad. Sci. U. S. A.* 110, 17143–17148. [PubMed: 24082105]
- Vaupel JW, 2010 Biodemography of human ageing. *Nature* 464, 536–542. [PubMed: 20336136]
- Wong DF, Young D, Wilson PD, Meltzer CC, Gjedde A, 1997 Quantification of neuroreceptors in the living human brain: III. D2-like dopamine receptors: theory, validation, and changes during normal aging. *J. Cereb. Blood Flow Metab.* 17, 316–330. [PubMed: 9119905]
- Worthy DA, Davis T, Gorlick MA, Cooper JA, Bakkour A, Mumford JA, Poldrack RA, Todd Maddox W, 2016 Neural correlates of state-based decision-making in younger and older adults. *Neuroimage* 130, 13–23. [PubMed: 26690805]
- Worthy DA, Gorlick MA, Pacheco JL, Schnyer DM, Maddox WT, 2011 With age comes wisdom: decision making in younger and older adults. *Psychol. Sci.* 22, 1375–1380. [PubMed: 21960248]
- Yassa MA, Lacy JW, Stark SM, Albert MS, Gallagher M, Stark CEL, 2011 Pattern separation deficits associated with increased hippocampal CA3 and dentate gyrus activity in nondemented older adults. *Hippocampus* 21, 968–979. [PubMed: 20865732]

Zhu Z, Hakun JG, Johnson NF, Gold BT, 2014 Age-related increases in right frontal activation during task switching are mediated by reaction time and white matter microstructure. *Neuroscience* 278, 51–61. [PubMed: 25130561]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Fig. 1.

(A) Sample trial from the LCT showing the percentage probability of winning (or losing) a given magnitude of points during the choice phase. If participants decide to accept the given stake, the outcome points are given (outcome top number; example depicts a winning trial outcome) with the accumulated points (outcome bottom number) updated accordingly. If the participants decide to reject the stake, the missed outcome is given in parentheses with no change in accumulated points. (B, C) Violin plots depicting probability density distributions of young and older adult DT EVs and adjusted DTs ($\sqrt{DT}$). White circles are individual data points. (D) Acceptance rates across the different levels of probability to win (or lose) and points magnitudes (see Supplementary Table S2) for young and older adults. * denote $p < 0.05$ with Bonferroni correction for multiple comparisons. Error bar indicates SEM. Abbreviations: DT, decision threshold; EV, expected value; ISI, interstimulus interval; LCT, lottery choice task.

Fig. 2.

(A) Brain regions in which neural responses to probability were modulated by age. Whole-brain significance threshold was set at $p < 0.05$ (adjusted for FDR). Neural response estimates across probability levels were extracted from ROI identified from the whole-brain statistical volume that included (B) the right VS, (C) the right MTL, (D) the VMPFC, (E, F) bilateral DLPFC, and (G) the DMPFC. Contrasts testing linear ($\text{Probi}_{\text{linear}}$; solid black lines) and quadratic ($\text{Probi}_{\text{quadratic}}$; dashed black lines) effects of increasing probability on neural responses are shown where they significantly differed across age. Error bar indicates SEM.; LL, ML, MM, MH, HH indicate different probability levels (see Supplementary Table S2). Abbreviations: DMPFC, dorsomedial prefrontal cortex; DLPFC, dorsolateral prefrontal cortex; FDR, false discovery rate; HH, high-high; MTL, medial temporal lobe; ML, middle-

low; MM, middle-middle; MH, middle-high; LL, low-low; ROI, regions-of-interest; VS, ventral striatum; VMPFC, ventromedial prefrontal cortex.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Fig. 3.

Scatterplots depicting correlations between individual neural sensitivity to linear increases in probability (regression coefficient for P from model-based fMRI analysis) and adjusted DTs ($\sqrt{DT}$) in (A) the right VS, (B) DMPFC, (C) left DLPFC, and (D) right DLPFC in young (orange) and older adults (blue). Correlation coefficients (r) are shown for young (Y), old (O), and for both age groups together (All), along with the slope coefficients (β with SEM in parentheses) of regression lines. * denotes $p < 0.05$ (uncorrected), ** denotes $p < 0.05$ (adjusted for FDR). Abbreviations: DMPFC, dorsomedial prefrontal cortex; DLPFC, dorsolateral prefrontal cortex; DT, decision threshold; FDR, false discovery rate; VS, ventral

striatum. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Fig. 4.

(A) Heatmaps depicting functional connections that correlated with adjusted DTs ($\sqrt{DT}$) in young and older adults during resting-state fMRI (rs-fMRI). Warm and cool colors denote positive and negative correlations, respectively. (B) Scatterplots detailing the significant correlations between individual $\sqrt{DT}$ and functional connections during the rs-fMRI experiment. Correlation coefficients (r) are shown for young (Y), old (O), and for both age groups together (All), along with the slope coefficients (β with SEM in parentheses) of regression lines. (C, D) Heatmaps and scatterplots for the LCT experiment. * denote $p <$

0.05 (uncorrected). Abbreviations: DT, decision threshold; LCT, lottery choice task. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Fig. 5.

(A) Graphical visualization highlighting key effects in the simultaneous mediation analysis results evaluating the moderating effect of age (see Methods; see Supplementary Table S6 for full coefficient details). Age moderated the mediation roles (M_j) of left DLPFC–right DLPFC (M_2) and DMPFC–right MTL (M_3) LCT functional connectivities in the direct effect (c') of left DLPFC–right VS resting-state functional connectivity (RSfC) on LCT behavioral DTs ($\sqrt{DT}$). Significant coefficients ($p < 0.05$, 1-tailed) are denoted in bold with thick lines. (B) Mean indirect effect estimates ($a_{\text{RSFC}j} b_j + a_{\text{RSFC}, \text{Age}j} b_j \times \text{Age}$) for each of the

3 mediators in the model across age for young (coded 1) and older (coded -1) adult groups. Note, moderated mediation effects are the differences in indirect effect between young and older adults ($a_{\text{RSFC.Agej}} \cdot b_j = 0.5[[a_{\text{RSFCj}} \cdot b_j + a_{\text{RSFC.Agej}} \cdot b_j \times (1)] - [a_{\text{RSFCj}} \cdot b_j + a_{\text{RSFC.Agej}} \cdot b_j \times (-1)]]$). * denotes $p < 0.05$ (1-tailed); † denotes $p < 0.10$ (1-tailed). Error bar indicates SEM. Abbreviations: DMPFC, dorsomedial prefrontal cortex; DLPFC, dorsolateral prefrontal cortex; DT, decision threshold; LCT, lottery choice task; MTL, medial temporal lobe; VS, ventral striatum.