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Better the devil you know than the devil you don't: Neural processing of risk and ambiguity

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A R T I C L E I N F O

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A B S T R A C T

Risk and ambiguity are inherent in virtually all human decision-making. Risk refers to a situation in which we know the precise probability of potential outcomes of each option, whereas ambiguity refers to a situation in which outcome probabilities are not known. A large body of research has shown that individuals prefer known risks to ambiguity, a phenomenon known as ambiguity aversion. One heated debate concerns whether risky and ambiguous decisions rely on the same or distinct neural circuits. In the current meta-analyses, we integrated the results of neuroimaging research on decision-making under risk (n = 69) and ambiguity (n = 31). Our results showed that both processing of risk and ambiguity showed convergence in anterior insula, indicating a key role of anterior insula in encoding uncertainty. Risk additionally engaged dorsomedial prefrontal cortex (dmPFC) and ventral striatum, whereas ambiguity specifically recruited the dorsolateral prefrontal cortex (dlPFC), inferior parietal lobe (IPL) and right anterior insula. Our findings demonstrate overlapping and distinct neural substrates underlying different types of uncertainty, guiding future neuroimaging research on risk-taking and ambiguity aversion.

1. Introduction

Uncertainty is inherent in virtually all human endeavours. Individuals seldom make decisions with absolute certainty, as complete knowledge of the alternatives and consequences is not possible or practical. When you choose a course from a menu or contemplate a retirement plan, you are facing the uncertainties that pervade daily life. How individuals cope with uncertainty determines the quality of their decision-making and affects their well-being. Intolerance of uncertainty has been linked to a range of psychiatric disorders (Boswell et al., 2013), including anxiety disorders, obsessive-compulsive disorder, and posttraumatic stress disorder.

Risk and ambiguity are two widely studied conditions in which the possible outcomes of an action are uncertain. Risk refers to a situation in which we know the precise probability of potential outcomes in each option (Stearns, 2000). In most risky decisions, participants must decide between a safe choice and a risky choice with a known probability of the potential outcome. The basis of rational choice in decision-making under risk is axiomatized in expected utility theory, which holds that rational decision-makers will choose the option that will result in the highest expected utility, being the sum of the products of possible outcome with the probability of occurrence of the events (Von Neumann and Morgenstern, 1945). In contrast, decision-making under ambiguity occurs in situations where the probability of a specific outcome is unknown. Individuals generally prefer to take a risk when they know the specific odds rather than when the odds are ambiguous, a preference known as ambiguity aversion (Ellsberg, 1961). Ambiguity aversion can lead to suboptimal choices that contradict expected utility theories (Ellsberg, 1961).

Previous research on risk-taking has typically focused on the contrast of higher risk versus lower or no risk. Several popular paradigms, such as the Ellsberg Paradox Task (Hsu et al., 2005; Levy et al., 2009), Wheel of Fortune (Roy et al., 2011; Smith et al., 2009), Iowa Gambling Task (IGT, Brevers et al., 2013; Fukui et al., 2005; Sun et al., 2017) and Balloon Analogue Risk Task (BART, Lei et al., 2017; Qi et al., 2015;

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Rao et al., 2018) have been widely used to investigate decision making under risk. In the Ellsberg Paradox Task and Wheel of Fortune, individuals are presented with a gambling option with a relatively lower probability of winning but a bigger reward magnitude, and another option with relatively higher winning probability but a smaller reward. In contrast to these descriptive risk, the probabilities of outcomes in both IGT and BART are not stated but rely on participants' ability to learn from experience (Mata et al., 2011). Risk-seeking is measured by the average number of selections from advantageous (high reward but also higher punishment) minus disadvantageous (low reward but also lower punishment) decks in the IGT, or the number of pumps in unexploded balloons for the BART. The higher the number, the greater the risk-tasking. In these cases, people can know the probability of outcomes through learning. For high and low risk conditions, the levels of ambiguity are comparable.

Neuroimaging studies on risk-taking have identified risk-associated activity in reward processing regions, including the ventral striatum and ventral medial prefrontal cortex (vmPFC; Critchley et al., 2001; Hsu et al., 2005). Moreover, the anterior insula also plays a key role in encoding risk prediction and in behavioural adaptions to risk (Baek et al., 2017; Congdon et al., 2013; Jung et al., 2013; Sun et al., 2017). A recent meta-analysis study used the activation likelihood estimation (ALE) method and found that dorsolateral prefrontal cortex (dlPFC), parietal cortex, and anterior insula were activated when decisions were made in risk-related situations (Mohr et al., 2010). However, this study lumped all risk-related processes together, leaving the neural correlates of specific sub-types of risk unknown, such as descriptive risk and experienced risk.

It has been proposed that processing of ambiguity and risk engage distinct neural networks. Using fMRI, Hsu et al. found that processing of ambiguity was associated with greater activation in OFC, dmPFC and amygdala, relative to the processing of risk. Since processing of ambiguity elicits stronger activity in the neural system involved in evaluating general uncertainty, this suggests that the degree of uncertainty is higher in the ambiguous condition. Moreover, other studies have found that, relative to risk-taking, decision-making under ambiguity elicits stronger activity in the orbitofrontal cortex (OFC), inferior frontal gyrus (IFG), anterior insula, and posterior parietal cortex (Bach et al., 2009; Fujino et al., 2016; Huettel, 2006; Levy et al., 2009), suggesting that these areas are especially crucial in processing ambiguity. Additionally, it has been observed that processing of ambiguity activates a response from other regions, such as the superior and inferior parietal lobe, postcentral gyrus, dlPFC, and ACC (Bach et al., 2011; Causse et al., 2013; Guo et al., 2013; Payzan-LeNestour et al., 2013).

Decision-making under risk and ambiguity may also rely on similar underlying neural mechanisms, as both entail making choices under uncertainty. It has been found that the subjective value of both conditions was represented in the same brain regions, including the striatum and the vmPFC (Levy et al., 2009). One possibility is that there is no reliable difference between risk and ambiguity related information when processed at the neural level. Consistent with this possibility, one study found that unlike the healthy controls who were risk- and ambiguity-averse, patients with orbitofrontal cortex (OFC) lesions were risk- and ambiguity-neutral (Hsu et al., 2005), suggesting that OFC plays an important role in processing both risk and ambiguity. Another possibility is that processing of risk and ambiguity recruit the same brain regions but the activity associated with the processing of ambiguity is stronger. Also, the previous meta-analysis found that making choices in risky tasks was associated with OFC activation while making choices in ambiguous tasks was associated with dorsolateral PFC (dlPFC) activity (Krain et al., 2006). However, Krain et al. did not make a quantitative comparison between different types of uncertainty. Notably, they included patient studies, which biased the results (Paulus et al., 2003a, 2002a, 2002b; Paulus et al., 2003b). Whether processing of risk and ambiguity are supported by distinguishable neural networks remains a hotly debated question.

Though previous researchers have utilised the ALE method to explore the neural processing of risk in decision-making, the question of whether the neural activity profiles in risk processing are similar to or distinct from those of ambiguity processing was still left untouched (Mohr et al., 2010). To this end, we integrated findings from relevant neuroimaging literatures using quantitative meta-analyses to examine whether processing of risk and ambiguity engage the same or distinct neural mechanisms. Local differentiation and global integration are complementary profiles of brain organization, as each brain area is characterized by its regional functions and its specific interactions with other regions (Eickhoff et al., 2018; Toga et al., 2006). To explicitly test and confirm the different characteristics between processing of risk and ambiguity in independent datasets, we further employed functional decoding to study the functional characterisation and connectivity-based meta-analytic coactivations profiles of the resulting regions, as performed in previous studies (Camilleri et al., 2018; Gu et al., 2019). The key idea behind functional decoding is to allow statistical inference on the type of tasks that evoke activation in a particular region of interest. Functional connectivity analyses, including meta-analytic connectivity modelling (MACM) and resting-state functional connectivity (RSFC), were also conducted to test how risk and ambiguity related regions are linked to other brain regions. MACM analysis relies on identifying the conjointly co-activation patterns on a specific seed region of interest (ROI seed) across experiments without any selection biases (Cieslik et al., 2016; Robinson et al., 2016) and hence reflects task-based functional connectivity. RSFC analysis, on the other hand, captures the functional connectivity based on the synchronized spontaneous signal fluctuation in the absence of an actual task (Barkhof et al., 2014). Given that the functional role of a region is supposed to be crucially related to and interacted with the neural network, these functional connectivity analyses can provide new insight into large-scale communication and functional specialization of the human brain.

We expected to find activity in the anterior insula to be associated with the processing of both risk and ambiguity, given the predominant role of the anterior insula in encoding uncertainty in general (Gorka et al., 2016). We predicted that reward-related neural networks are involved specifically in the processing of risk. We further hypothesized that undertaking ambiguous tasks would elicit more activity in cognitive control regions, including OFC, dlPFC, and parietal regions. Hsu and colleagues (2005) found stronger OFC activity in response to ambiguity compared with risk, and patients with OFC lesions did not show either risk or ambiguity aversion. It is possible that some regions may signal how much is unknown and how much cognitive resources are needed to be employed to resolve uncertainty. As less information about reward probability is known in ambiguity than risk, higher activity in these regions is expected for ambiguous compared with risky situations. Moreover, although reward probability information is more available under risk, individuals may attempt to estimate probabilities and ponder on probabilities of potential outcomes while reflecting choice options. This process of guessing and assigning probabilities may additionally recruit brain regions implicated in deliberation. Importantly, we further examine whether and how task characteristics, such as decision stage (anticipation vs. choose phase), type of contrast (linear regression or binary contrast), reward type (win, loss, win/loss domains), and risk type (descriptive vs. learning related), influence the neural patterns. The functional connectivity profiles associated with key regions were also examined to illustrate the brain networks that are potentially linked with risk/ambiguity.

2. Methods

2.1. Meta-analysis

2.1.1. Literature search and selection

The Boolean search on neuroimaging literature was conducted in January 2020 for two separate meta-analyses in PubMed, Web

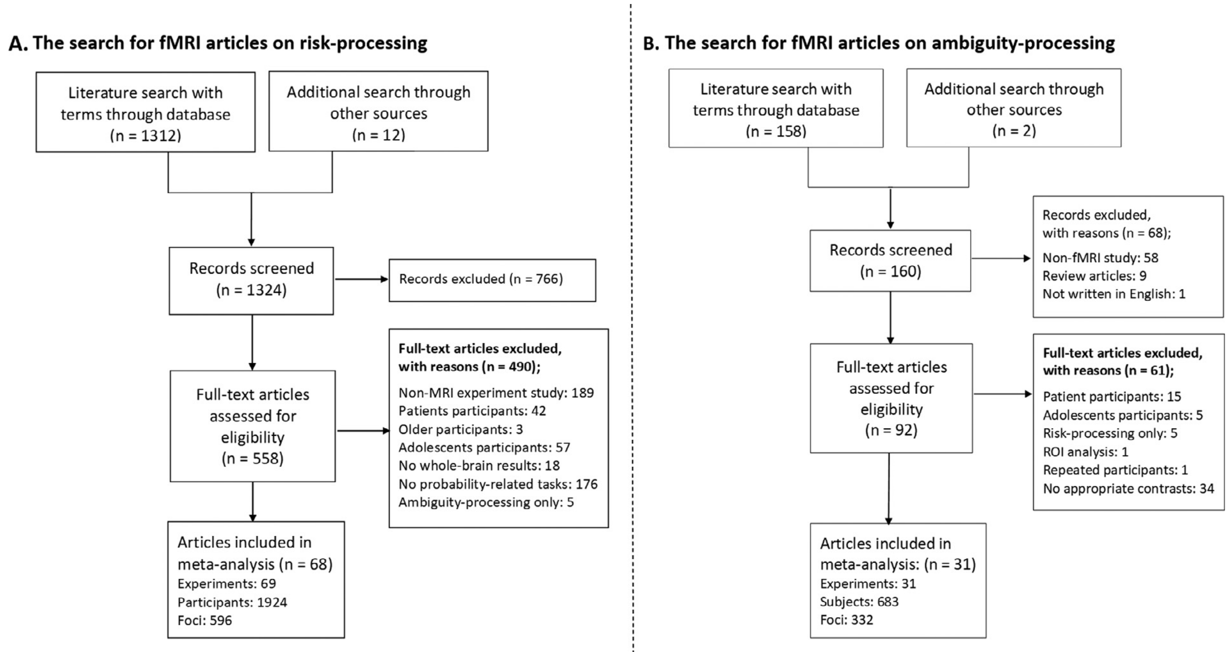

Fig. 1. Flow chart of the study selection process for the meta-analysis on the processing of risk (A) and ambiguity (B).

of Science and Google scholar by adopting the PRISMA-guidelines (Shamseer et al., 2015). One search for fMRI articles on risk-processing was identified using terms: ("risk" OR "risky") AND ("decision making" OR "choice") AND ("fMRI" OR "neuroimaging"). Another search for fMRI articles on ambiguity-processing, was performed using terms: ("ambiguity" OR "ambiguous" OR "estimation uncertainty") AND ("decision making" OR "choice") AND ("fMRI" OR "neuroimaging"). In addition, the reference lists in published meta-analysis reviews (Krain et al., 2006; Mohr et al., 2010) were screened. These searches yielded 558 articles on risk-processing and 158 articles on ambiguity-processing that were then screened for eligibility.

After reading each article, we implemented the following inclusion criteria: (1) data were obtained from healthy adults population; (2) whole-brain rather than region of interest (ROI) analysis; (3) activations were presented in a standardized stereotaxic space, such as Talairach or Montreal Neurological Institute (MNI); (4) results were based on either a binary contrast (e.g., high > low risk/ambiguity, risky/ambiguous > safe, or risk > ambiguity) or parametric modulation analyses; and (5) outcomes were probabilistic, but probabilities regarding outcome were known to the participants in risk-processing and unknown in ambiguity-processing. The final dataset included 69 eligible experiments related to risk-processing and 31 eligible experiments related to ambiguity-processing. Data exaction and synthesis were initially performed by S. Wu and then verified by R. Yu.

Fig. 1 displays a flowchart representing the steps taken to screen and identify eligible articles for both meta-analyses. Talairach coordinates were converted to the MNI coordinates using an icbm2tal algorithm (Lancaster et al., 2007). In the meta-analysis on risk-taking, the 68 articles reported on 69 experiments (11 experiments did not report gender; of the remaining experiments, 56.22% male) and yielded a total of 596 foci, involving 1926 participants. Two studies did not give the exact age range. The age of the remaining participants ranged from 18 to 67 years. In the meta-analysis on ambiguity-processing, the 31 articles reported on 31 experiments (three experiments did not report gender; of the remaining experiments, 43.31% male) and yielded a total of 332 foci, involving 683 participants. The age of participants ranged from 18 to 53 years and the mean is 28.95 ± 7.71 years. See Tables 1 and 2 for a list of demographic information, and contrasts selected for each meta-analysis across eligible experiments.

2.1.2. *ALE meta-analyses*

The ALE algorithm was used for the coordinate-based meta-analyses, which determines the convergence of foci reported by testing if the clustering is significantly higher than expected under the null-distribution of a random spatial association across given experiments (Turkeltaub et al., 2012). The ALE method treats reported foci as spatial probability distributions. The widths are based on empirical estimates of the spatial uncertainty which depends on sample sizes and between-template variability (Eickhoff et al., 2009). Specifically, larger sample sizes are modelled with smaller Gaussian distributions. Such weighting assumes that larger samples generate more reliable approximations of the real activation (Eickhoff et al., 2009).

For each contrast, an individual activation map was created from the maximum probability associated with each reported coordinate. These activation maps were then jointly computed to obtain an overall ALE map across all experiments (Turkeltaub et al., 2002). To distinguish signal from noise and allow for inference of random effects, ALE scores were assessed against the null-distribution of random spatial association between experiments (Eickhoff et al., 2012, 2009). For correcting multiple comparisons, the significance was set at the threshold of $p < 0.05$ using a cluster-level family-wise error (cFWE) correction (10,000 permutations, 50 mm^3 minimum cluster-size) with a cluster forming threshold at $p < 0.001$. For the selection of significant clusters, additional criteria were applied where each cluster must have contributions from at least two experiments to minimize the influence of outliers, with the average contribution of the most dominant experiment (MDE) not exceeding of 50% and the two most dominant experiments (2MDEs) not exceeding of 80% (Eickhoff et al., 2017).

2.1.3. *Contrast and conjunction analyses*

To further explore distinct and common neural bases of risk-processing and ambiguity-processing, we conducted contrast and conjunction analyses. Specifically, differences between these two forms of uncertainty were compared by computing the voxel-wise difference between the two independent ALE maps. All experiments were then pooled and randomly divided into two groups of the same size (Eickhoff et al., 2011; Gu et al., 2019; Langner et al., 2018). For these two randomly assembled groups, two sets of ALE values were computed. For each voxel,

Table 1
List of studies included in the meta-analysis of risk processing.

Article	N(male)	Mean age (SD) / age range	Paradigm	Contrast type	Category of tasks	Context	Domain	Foci	Software	Data source
Abidi et al. (2018)	14(7)	23.5/18–29	Probability Discounting Task	High > Low Risk	Descriptive	DR	/	5	SPM12	Table 1
Abler et al. (2009)	15(15)	N.A./23–27	Monetary Incentive Task	Risky Parametric	Descriptive	whole	+	5	SPM5	Table 1
Aridan et al. (2019)	40(19)	22.6(2.9)	Mixed Gambles Risk Task	Risky Parametric	Descriptive	DR	+ / -	13	FMRIPREP	Table S1
Bach et al. (2009)	20(10)	27.4(5.8)	Pavlovian Conditioning Task	Risky > Safe	Experienced	AR	/	2	SPM12	Table S2
Baek et al. (2017)	75(46)	25.4(4.6)	Risk Aversion Task	Risky > Safe	Descriptive	DR	+ / -	4	SPM5	Table S2&S3
Behrens et al. (2007)	18(9)	N.A./18–32	Probability-Tracking Task	Risky Parametric	Experienced	DR	+ / -	1	FSL	Material P14
Berns and Bell (2012)	30(9)	N.A./18–45	Risk Safe Task	Risky Parametric	Descriptive	AR	+	4	SPM5	Table 1
Blankenstein et al. (2017)	50(25)	23.71 (2.56)	Wheel of Fortune Task	Risk > Ambiguity	Descriptive	DR	+	14	SPM8	Table 1
Brevers et al. (2015)	10(8)	36.2(13.0)	Card-Deck Paradigm	Risky > Safe	Descriptive	DR	+	6	Brain Voyager QX	Table 3
Brevers et al. (2016)	15(6)	22.1(1.67)	Iowa Gambling Task	Risk > Ambiguity	Experienced	DR	+ / -	5	FSL	Table 2
Chark and Chew (2015)	16(N.A.)	N.A.	Ellsberg Paradox Task	Risk > Ambiguity	Descriptive	DR	+	2	SPM2	Table 1
Christopoulos et al. (2009) study1	13(8)	24.5(N.A.)	Two-choice Gambling Task	High > Low Risk	Descriptive	DR	+	1	SPM2	Page 12,578
Christopoulos et al. (2009) study2	14(N.A.)	N.A.		High > Low Risk	Descriptive	DR	+	1	SPM2	Page 12,578
Cohen et al. (2005)	16(9)	N.A./20–27	Two-choice Gambling Task	High > Low Risk	Experienced	DR	+	5	SPM99	Table 1
Congdon et al. (2013)	23(10)	25.7(4.43)	Angling Risk Task	Risky Parametric	Descriptive	DR	+	3	FSL	Table 2
Dong et al. (2015)	22(N.A.)	22.2(1.8)	Two-options Risky Task	High > Low Risk	Descriptive	DR	+ / -	2	SPM5	Table 1
Dreher et al. (2005)	31(16)	27.6(5.7)	Slot-machine Task	High > Low Risk	Descriptive	AR	+ / -	4	SPM99	Table 2
Engelmann and Tamir (2009)	10(7)	N.A./18–31	Wheel of Fortune Task	Risky Parametric	Descriptive	DR	+	17	AFNI	Table 2
Ernst et al. (2004)	17(N.A.)	N.A./20–40	Wheel of Fortune Task	Risk > Ambiguity	Descriptive	DR	+	19	SPM99	Table 1
Fukui et al. (2005)	14(13)	24.4(1.45)	Iowa Gambling Task	Risky > Safe	Experienced	DR	+	1	SPM99	Table 1
Fukunaga et al. (2012)	16(8)	20.19/ (N.A.)	Balloon analogue Risk Taking Task	Risky Parametric	Experienced	O	+	4	SPM5	Page 485–486
Gilman et al. (2012)	20(8)	26.1(2.8)	Risk-taking Task	Risky > Safe	Experienced	AR	+ / -	3	AFNI	Table 1
Gorka et al. (2016)	37(10)	31.8 (12.4)	Slot-machine Task	Risky > Safe	Descriptive	AR	+ / -	6	SPM8	Table 2
Gowin et al. (2014)	40(26)	35.6(11.5)	Risky Gains Task	Risky > Fixation	Descriptive	DR	+ / -	38	AFNI	Table S3
Grinband et al. (2006)	10(5)	N.A./18–34	Stimulus-categorization Task	Parametric	Experienced	DR	/	8	FSL	Table S2
Guo et al. (2013)	15(N.A.)	29.3(8.7)	Poker Cards Task	Risky > Safe	Descriptive	DR	+	18	SPM8	Table 2
Häusler et al. (2018)	165 (N.A.)	39.0(6.4)	Real-life Stock Trading	Risky > Safe	Experienced	DR	+ / -	3	SPM12	Table S3
Helfinstein et al. (2014)	108 (N.A.)	21–50	Balloon analogue Risk Taking Task	Risky > Safe	Experienced	DR	+ / -	7	FSL	Table 1
Hsu et al. (2005)	16(13)	23.5(6.2)	Ellsberg Paradox Task	Risk > Ambiguity	Descriptive	DR	+	12	SPM2	Table S9
Hsu et al. (2009)	21(10)	29.6(7.5)	Ellsberg Paradox Task	Risky Parametric	Descriptive	DR	+	25	SPM2	Table 2
Huettel et al. (2005)	12(9)	N.A./20–33	Probabilistic Guessing Task	Risky Parametric	Descriptive	DR	+	10	SPM99	Table 1
Huettel (2006)	12(6)	N.A./18–29	Different Probability Reinforcement Task	Risk > Certainty & Ambiguity	Descriptive	DR	+	15	SPM99	Table 2

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Table 1 (*continued*)

Article	N(male)	Mean age (SD) / age range	Paradigm	Contrast type	Category of tasks	Context	Domain	Foci	Software	Data source
Kohno et al. (2015)	60(33)	N.A./18–51	Balloon Analogue Risk-Taking Task	Risky Parametric	Experienced	DR	+	8	FSL	Table 1
Kuhnen and Knutson (2005)	19(9)	27(N.A.) /24–39	The behavioural Investment Allocation Strategy Task	Risky Parametric	Descriptive	AR	+ / -	2	AFNI	Page 765
Labudda et al. (2008)	16(8)	62.3(4.81)	Game of Dice Task	High > Low risk	Descriptive	DR	+ / -	6	SPM2	Table 2
Lawrence et al. (2008)	15(15)	32.7/22–57	Iowa Gambling Task	Risky > Safe	Experienced	DR	+	10	SPM2	Table 2
Lee et al. (2007)	12(12)	29.9(6.2)	Risk-taking Task	Risky > Safe	Descriptive	DR	+ / -	4	SPM2	Table 2
Lei et al. (2017)	37(37)	23.1(1.9)	Balloon Analogue Risk-Taking Task	Risky > Safe	Experienced	DR	+	1	AFNI	Table 2
Levy et al. (2009)	20(N.A.)	20–41	Ellsberg Paradox	Risky Parametric	Descriptive	DR	+	2	Brain Voyager QX	Table 1
Luigjes et al. (2016)	13(2)	34(8.4)	Two Gambles	High > Low risk	Descriptive	DR	+	1	SPM8	Table 3
Matthews et al. (2004)	12(7)	34/20–56	Lane Risk Task	Risky > Safe	Descriptive	DR	+ / -	4	AFNI	Table 2
Minati et al. (2012)	22(12)	36(7)	Gambling Task	Risk > Ambiguity	Descriptive	AR	+/-	5	SPM8	Table 2, P87
Mohr et al. (2010b)	19(8)	N.A./18–35	Risk Perception and Investment Decision Task	Risky > Safe	Descriptive	DR	+ / -	2	FEAT(FSL)	Table S7
Nagel et al. (2017)	18(N.A.)	26 (6.28)	Strategy Lottery Choices	Risky Parametric	Descriptive	DR	+	4	SPM8	Page 58
Pan et al. (2019)	35(17)	26/19–40	Balloon analogue Risk Taking Task	Risky Parametric	Experienced	O	+	9	SPM8	Table 1
Paulus et al. (2003b)	17(11)	38.3(1.4)	Risky-Gains Task	Risky > Safe	Descriptive	DR	+ / -	5	AFNI	Table 1
Preuschoff et al. (2006)	19(10)	21.4/18–30	Card Gambling Guessing	Risky Parametric	Descriptive	AR	+/-	9	Brain Voyager v1.26	Table S2
Rao et al. (2008)	14(8)	25.4/21–35	Balloon analogue Risk Taking Task	Risky Parametric	Experienced	O	+	15	SPM2	Table 2
Rao et al. (2018)	222 (114)	19.1(1.35)	Balloon analogue Risk Taking Task	Risky Parametric	Experienced	DR	+	16	SPM8	Table 3
Rigoli et al. (2019)	23(10)	37/20–60	Two-choice Risk Task	Risky > Safe	Descriptive	AR	+/-	7	SPM12	Table S3
Rolls et al. (2007)	13(8)	N.A./23–35	Probabilistic Monetary Reward Decision Task	Risky Parametric	Experienced	DR	+	3	SPM2	Page 656- 657
Roy et al. (2011)	23(8)	27.6 (7.9)	Wheel of Fortune Task	Risky > Safe	Descriptive	DR	+ / -	51	FSL	Table 1
Schonberg et al. (2012)	16(6)	23.6(2.9)	Balloon analogue Risk Taking Task	Risky Parametric	Experienced	DR	+	5	FEAT (FSL)	Table 2
Smith et al. (2009)	25(13)	29.1(5.5)	Wheel of Fortune Task	Risky > Safe	Descriptive	DR	+	2	AFNI	Table 3
Stern et al. (2014)	17(8)	21.6/18–32	Incentive Card Task	High >Low Risk	Descriptive	O	+ / -	4	SPM5	Table 1
Sun et al. (2017)	18(9)	40.3(4.14)	Iowa Gambling Task	Risky > Safe	Experienced	DR	+	15	AFNI	Table 2
Suzuki et al. (2016)	24(14)	29.50/ 22–38	Wheel of Fortune Task	Risky > Safe	Descriptive	DR	+	2	SPM8	Table S1
Symmonds et al. (2010)	16(N.A.)	N.A./22–36	Single-shot lottery Task	Risky Parametric	Descriptive	AR	+	13	SPM5	Table S3
van Leijenhorst et al. (2006)	26(9)	21.5(2.2)	The probability risk cake Task	High > Low Risk	Descriptive	DR	+	16	SPM2	Table 1
Vorobyev et al. (2015)	34(34)	N.A./18–19	Stoplight Game	Risky > Safe	Descriptive	DR	/	24	SPM8	Table 2
Wang et al. (2015)	30(27)	23.6(2.34)	Four card guessing Task	Risky Parametric	Descriptive	AR	+/-	5	AFNI	Table 2
Weber and Huettel (2008)	23(12)	23/19–36	Preference Elicitation Task	Risky > Safe	Descriptive	DR	+	16	FEAT (FSL)	Table 2

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Table 1 (*continued*)

Article	N(male)	Mean age (SD) / age range	Paradigm	Contrast type	Category of tasks	Context	Domain	Foci	Software	Data source
Wright et al. (2013a)	22(6)	22/18–32	Wheel of Fortune Task	Risky > Safe	Descriptive	DR	+/-	18	SPM8	Table 2
Wright et al. (2013b)	26(N.A.)	24/18–33	Wheel of Fortune Task	Risky > Safe	Descriptive	DR	+/-	15	SPM8	Table S1
Xue et al. (2008)	13(8)	23.6(6)	Cups Task	Risky Parametric	Descriptive	DR	+/-	6	FSL	Table S1
Xue et al. (2010)	14(7)	23.8/22–29	Modified Cups Task	Risky > Safe	Descriptive	DR	+/-	8	FSL	Table S5
Yazdi et al. (2019)	20(20)	39.4/24–57	Cambridge Gambling Task	Risky Parametric	Experienced	O	+	7	Brain Voyager	Table 1
Yoshida and Ishii (2006)	13(11)	N.A./23–28	Back-track Task	Risky > Safe	Experienced	DR	/	3	SPM99	Table S1
Zhang et al. (2019)	25(11)	20.64/18–25	Modified Cups Task	Risky > Safe	Descriptive	DR	+/-	10	SPM8	Table 1

Note: DR=decision risk; AR=Anticipation risk; *O*=outcome; whole= whole trial; +/-: both domain(gain & loss); +: gain only domain; /:non-monetary domain; Experienced: decisions from experience; Descriptive: decisions from description.

the differences between the ALE values were calculated. By repeating this process 25,000 times, a null-distribution of differences in ALE values between the two conditions was generated. To control for false positives, the ALE maps were set to a threshold posterior probability of $p > 95\%$. For the conjunction analyses, we identified the intersection between two corrected ALE results (Nichols et al., 2005). That is, the ALE maps for each condition were already corrected as mentioned above, and the conjunction analysis simply involved an assessment of the correspondence between both ALE contrasts.

2.2. *Investigation of putative moderators*

To examine whether results were biased by different types of contrasts, we divided the studies into parametric modelling (24 contrasts on risk-processing, 8 contrasts on ambiguity-processing) and categorical modelling (i.e., risky > safe, high > low risk, 45 contrasts on risk-processing, 23 contrasts on ambiguity-processing). Due to the number of contrasts on ambiguity parametric modulation ($N = 8$) being too small for the ALE algorithm, ambiguity parametric sub-ALE analysis was not conducted.

We also analysed together, neural representations of risk-processing at the times of decision-making and at anticipation of the outcome. Studies have indicated that there are distinct networks involved in different stages of reward processing (Liu et al., 2011; Richards et al., 2013). To assess the influence of the decision-making stage for risky choices, in a follow-up analysis, we limited our subsequent ALE analysis to contrasts that are time-locked to the onset of making decisions ($N = 53$). For ambiguity, some studies focused on the stage of making choices (14 contrasts), some on the anticipation stage (13 contrasts), and some use block design covering the whole period (3 contrasts). Not enough studies are available for a sub -analysis.

It is possible that risky decisions from description versus experience involve distinct neural underpinnings, given the function of learning impacts the processing for unknown but estimable probabilities of payoffs (Hertwig et al., 2004; Mata et al., 2011). But there has as yet been little examination of the common and dissociable neural responses between decision from description and experience. Here, we performed a sub-analysis for risk-taking with two separate groups replying on participants' ability to obtain the probabilities of outcomes, such as decisions from experience (termed as "experienced", $N = 21$) and decisions from description (termed as "descriptive", $N = 48$). Again, we ran an additional analysis for investigating differences between gains gambles ($N = 36$) and mixed gambles ($N = 28$) for risk. As the number of studies in two separate domains (Gains, $N = 11$; Mix, $N = 4$) is too small, we did not consider further a sub-analysis for ambiguity.

2.3. *Validation analysis*

To validate our current findings using conventional main ALE meta-analysis, we implemented additional leave-one-experiment-out (LOEO) analyses. We conducted LOEO analyses for the ALE meta-analyses of risk-processing and ambiguity-processing. In LOEO analysis, independent subsets of subjects called folds are created. One experiment was excluded for each ALE meta-analysis (on each fold), leaving behind N-1 experiments.

Given the unbalanced number of contrasts for risk-processing (69 contrasts) and ambiguity-processing (31 contrasts) included in the meta-analyses, it might be a lot easier to obtain consistent results in the former than the latter. To allow comparison of the experiments, we added 1000 rounds of the repeated re-subsampling approach for the main analysis and conjunction analysis to address any issue that could influence differences in statistical power. Specifically, twenty-nine experiments were randomly selected from the datasets of risk-processing and ambiguity-processing in each round of the main analysis. A conjunction analysis of the maps of all folds was done to identify brain regions that engaged in both risk-processing and ambiguity-processing. We also made a comparison between the results of primary analysis and those of re-subsampling analysis. We confirmed that averaged re-subsampling results of all rounds represented and validated our findings from the primary meta-analysis well.

All ALE maps were obtained at a threshold of cFWE correction ($p < 0.05$) with a cluster-forming threshold of $p < 0.001$ using 10,000 permutations for correcting multiple comparisons. Images are available from the NeuroVault: https://neurovault.org/collections/9175/.

2.4. *Functional decoding*

Using each cluster of brain regions revealed by contrast analyses, we implemented cluster-based functional characterization for each region based on the behavioural domains available for each neuroimaging experiment included in the BrainMap database (Turner and Laird, 2012). Compared with the automated large-scale synthesis of the neuroimaging literature database (i.e., Neurosynth), the BrainMap organizes published coordinate-based human neuroimaging literature and allows researchers to identify brain regions that are associated with certain cognitive features (Chawla and Miyapuram, 2015). Behevarioural domains in the Brainmap were categorized into 60 sub-domains, such as action, cognition, emotion, interoception and perception. A list of domains is available at https://brainmap.org/taxonomy/paradigms.html.

Both forward and reverse inference approaches were performed to identify the individual functional profile corresponding to each cluster (Camilleri et al., 2018; Lieberman and Eisenberger, 2015). The forward inference is theory-dependant, which emphasises the probability

Table 2
List of studies included in the meta-analysis of ambiguity processing.

Article	N(male)	Mean age (SD)/ age range	Paradigm	Contrast type	Type of tasks	Context	Domain	Foci	Software	Data Source
Bach et al. (2009)	20(10)	27.4(5.8)	Pavlovian Fear Condition	Ambiguous > Certain	Descriptive	Anticipation	/	13	SPM12	Table 1
Bach et al. (2011)	20(12)	22.9(2.5)	Preceding Learning Task	Ambiguous > Risky	Descriptive	Anticipation	/	3	SPM8	Table 2
Blackwood et al. (2004)	8(8)	38/18–53	Two-alternative-choice Tasks	Ambiguous > Certain	Descriptive	Decision	/	6	SPM99	Table 1
Blankenstein et al. (2017)	50(25)	23.71 (2.6)	Wheel of Fortune Task	Ambiguity > Fixation	Descriptive	Decision	+	4	SPM8	Table 4
Causse et al. (2013)	15(N.A.)	25.4 (2.5)	Plausible Aviation Task	High > Low Ambiguity	Descriptive	Decision	+/-	24	SPM8	Table 2
Chumbley et al. (2012)	14(8)	N.A./19–31	Two-choice Guessing	Ambiguous Parametric	Descriptive	Decision	/	6	SPM8	Fig. 4(b)
Elliott et al. (1999)	5(3)	N.A./29–41	Card-playing Task	Ambiguous > Certain	Descriptive	Block-based	/	12	SPM97	Table 1
Guo et al. (2013)	15(6)	N.A./23–50	Poker Cards Task	Ambiguous > Certain	Descriptive	Decision	+	15	SPM8	Table 3
Hsu et al. (2005)	16(13)	23.5(6.2)	Card-deck Task	Ambiguity > Risk	Descriptive	Decision	+	24	SPM2	Table S7
Ikink et al. (2019)	24(24)	23.83/18–34	Delay-discounting Task (time-ambiguous)	Ambiguity > Fixation	Descriptive	Decision	+	7	SPM12	Table 2
Jung et al. (2013)	24(16)	47(11.6)	Odd-Even-Pass Task	Ambiguous > Certain	Descriptive	Decision	+/-	7	SPM8	Table 1
Kano et al. (2017)	29(14)	22.5(2.8)	Cue Prediction Task	Ambiguous > Certain	Descriptive	Anticipation	/	10	SPM8	Table 4
Kobayashi and Hsu (2017)	17(N.A.)	21.7/N.A.	Auxiliary Tasks	Ambiguous Parametric	Descriptive	Anticipation	+	11	SPM8	Table 2
Krug et al. (2014)	64(37)	34.7(9.8)	Probabilistic Guessing	Ambiguous > Certain	Descriptive	Decision	/	29	SPM5	Table 3
Levy et al. (2009)	20(N.A.)	N.A./20–41	Ellsberg Paradox	Ambiguous Parametric	Descriptive	Decision	+	5	Brain Voyager QX	Table 1
Lopez Paniagua and Seger (2013)	14(5)	26.8/N.A.	Risky Lottery	Ambiguous > Certain	Descriptive	Anticipation	+	18	Brain Voyager QX	Table 1
Mestres-Missé et al. (2017)	22(11)	25.5(3.1)	Sequences Elements	Ambiguous > Certain	Descriptive	Decision	/	8	SPM12	Table S2
Motzkin et al. (2014)	19(11)	51.7(9.9)	Subsequent Predicting task	Ambiguous > Certain	Descriptive	Anticipation	/	2	AFNI & FSL	Table 2
Paulus et al. (2001)	12(10)	40(20.0)	Two-choice Prediction task	Ambiguous > Certain	Descriptive	Block-based	/	8	AFNI	Table 1
Paulus et al. (2002a)	16(12)	38.9(1.8)	Two-choice Prediction Task	Ambiguous > Certain	Descriptive	Block-based	/	6	AFNI	Table 1
Payzan-LeNestour et al. (2013)	18(9)	22.5(2.8)	Cue Probability	Ambiguous Parametric	Descriptive	Anticipation	+/-	29	SPM5	Table S2
Preuschoff et al. (2008)	19(10)	21.4/18–30	Card Gambling Guessing	Ambiguous Parametric	Descriptive	Anticipation	+/-	10	Brain Voyager v1.26	Table S5
Pushkarskaya et al. (2010)	38(20)	24.6/N.A.	Three-card Gamble	Ambiguous > certain	Descriptive	Decision	+	1	AFNI	Table 2
Pushkarskaya et al. (2015)	32(16)	25.2(5.6)	Three-card Gamble	Ambiguity > Risk	Descriptive	Anticipation	+	15	Brain Voyager QX 2.2	Table S6
Sarinopoulos et al. (2009)	40(22)	20.65 (1.5)	Cue-picture Pairings	Ambiguous > Certain	Descriptive	Anticipation	/	4	AFNI 2.41	Table S1
Shankman et al. (2014)	19(6)	30.1 (12.8)	Counting-ups Game	High > Low Ambiguity	Descriptive	Decision	/	8	SPM8	Table 1
Tobler et al. (2006)	22(9)	27/19–50	Pavlovian Blocking Paradigm	Parametric	Descriptive	Anticipation	+	11	SPM2	Table 2
Verney et al. (2003)	17(7)	36.2(7.8)	Two-choice Prediction Task	Ambiguous Parametric	Descriptive	Decision	/	12	AFNI	Table 1
Volz et al. (2003)	16(11)	24.9/21–35	Two-card Prediction	Ambiguous Parametric	Descriptive	Anticipation	/	7	LIPSIA	Table 2
Volz et al. (2004)	12(5)	25.1/20–31	Two-card Prediction	Ambiguous Parametric	Descriptive	Anticipation	/	5	LIPSIA	Table 4
Yarkoni et al. (2005)	26(N.A.)	22.4(3.6)	Maze exploration task	Ambiguous > Certain	Descriptive	Outcome	+	10	N.A.	Table 3

Note: +/-: both domain(gain & loss); +: gain only domain; /:non-monetary domain; N.A.: not available; Descriptive: decisions from description.

of observing activations in a particular brain region/cluster when given a psychological process (Henson, 2006), whereas reverse inference is a kind of reasoning, which refers to the probability of a psychological process being present from the observed activations in a particular brain region/cluster (Gu et al., 2019; Kohn et al., 2014). As such, the reverse inference approach allows a statistical inference on a particular region that is likely to be recruited by the type of tasks (Hutzler, 2014). A significant threshold was set at $p < 0.05$, using the false discovery rate (FDR) for multiple comparisons.

2.5. Meta-analytic connectivity modelling (MACM) analyses

MACM allows to assess co-activation across numerous neuroimaging studies in databases and delineate pre-defined ROIs based on functional connectivity maps (Langner et al., 2014). To examine the co-activation patterns of distinct activations derived from different contrasts, we selected the clusters that survived both the main ALE analysis and contrast analyses (i.e., right putamen and left anterior insula in the risk versus ambiguity contrast, left inferior frontal gyrus, right inferior parietal lobe and right dlPFC in the reverse contrast, see the Results section) and these clusters-based ROIs were put into the BrainMap database (http://www.brainmap.org/) as separated seeds to search for studies that reported activations within each cluster (Laird et al., 2009). For our analyses, only whole-brain neuroimaging studies with activations reported in the standard stereotaxic space in healthy participants were included. All experiments that feature at least one focus of activation in a particular seed region were identified in BrainMap. For clusters from the contrast of risk versus ambiguity, there are 129 experiments (2064 subjects, 2299 foci) reporting activations in right putamen and 147 experiments (2391 subjects, 204 foci) in left anterior insula. While for clusters from the contrast of ambiguity versus risk, there are 274 experiments (4254 subjects, 4101 foci) reporting activations in left IFG, 67 experiments (1096 subjects, 886 foci) in right IPL and 84 experiments (1167 subjects, 1124 foci) in right dlPFC.

Next, the retrieved experiments were subjected to a quantitative meta-analysis using the revised activation likelihood estimation (ALE) algorithm (as described above) to detect areas of convergence of co-activation with each seed. Importantly, convergence was assessed across all the activation foci reported in these experiments. Statistical significance was assessed at $p < 0.05$ after correction for multiple comparisons.

2.6. Resting-state functional connectivity (RSFC) analyses

In addition to the co-activation patterns from functional connectivity analyses, we implemented whole brain task-free connectivity analyses using brain regions identified in our contrast analyses as ROI seeds (risk vs. ambiguity: right putamen and left anterior insula, ambiguity vs. risk: left IFG, right IPL and right dlPFC). Resting-state functional connectivity analyses were based on the enhanced Nathan Kline Institute-Rockland Sample (NKI-RS,), where we obtained the resting-state MRI maps from 192 healthy adults (65% female, 20–75 years old, mean [± SD] age = 46.4 ± 16.7 years) (Nooner et al., 2012).

Images acquisition. The data were acquired on a Siemens TimTrio 3T scanner using BOLD contrast and gradient-echo EPI pulse sequence with the following parameters: TR, 1.4 s; TE, 30 ms; flip angle, 6; voxel size, 2.0 mm × 2.0 mm × 2.0 mm; slice number, 64 slices. The local ethics committee of the Heinrich-Heine University in Düsseldorf approved the data re-analysis. During data acquisition, participants were instructed not to fall asleep and not to think about anything, but to look at a fixation cross instead.

Images pre-processing. To remove physiological and movement artifacts that are common in the resting MRI data, we decomposed the data into independent components (ICs) and identified noise components using a large number of distinct spatial and temporal features via pattern classification with FIX (FMRIB's ICA-based Xnoiseifier) (Griffanti et al., 2014; Salimi-Khorshidi et al., 2014). Consistent with previous approaches (Satterthwaite et al., 2013), the unique variance related to the identified artificial ICs was then regressed from the data together with 24 movement parameters (including derivatives and 2nd order effects). After the first four scans were excluded, the remaining scans were corrected for head movement. The mean EPI image was segmented and the deformation was applied to the individual EPI images (Ashburner and Friston, 2005). A 5-mm FWHM Gaussian kernel smoothing was applied.

Seed-to-Voxel connectivity. To implement the seed-based analysis, the parameters presenting functional connectivity (bivariate correction) between the average BOLD signals from given seed clusters and other voxels in the whole brain were computed. The correlation coefficient based on the voxel-wise analysis was transformed into Fisher's Z-scores and then employed in the subjects-wise consistent analysis.

Table 3
ALE meta-analysis results for processing of risk, ambiguity, their conjunctions and contrasts.

Cluster #	Brain regions	BA	MNI coordinate (mm) X	Y	Z	Peak Z score	Volume
Risk processing							
1	Anterior Insula (R)	13	36	24	−2	7.46	5440
2	dmPFC (R)	8	4	24	42	6.11	4560
3	Anterior Insula (L)	13	−32	16	−8	5.56	2296
4	Ventral Striatum (R)	/	12	2	−4	4.74	1760
5	Ventral Striatum (L)	/	−10	0	−6	4.01	1080
Ambiguity processing							
1	Anterior Insula (R)	13	36	22	2	5.53	1872
2	IPL (R)	40	50	−54	40	4.53	976
3	MFG (L)	44	−48	8	38	4.98	968
4	dlPFC (R)	9	42	28	34	4.73	872
Conjunction (Risk ∩ Ambiguity)							
1	Anterior Insula (R)	13	36	22	2	5.53	1408
Risk > Ambiguity							
1	Anterior Insula (L)	13	−30	22	−12	2.31	472
2	Putamen (R)	/	20	10	2	2.55	224
3	FoC (R)	13	26	24	−2	1.89	104
Ambiguity > Risk							
1	IPL (R)	40	48	−56	38	2.88	800
2	MFG (L)	44	−50	10	38	3.41	776
3	dlPFC (R)	9	40	30	32	2.72	624
4	Anterior Insula (R)	13	44	14	−6	2.27	120

Note: *L* = Left; *R* = Right; BA = Brodmann area; IPL = Inferior Parietal Lobe; dmPFC = Dorsal medial Prefrontal Cortex; dlPFC = Dorsal lateral Prefrontal Cortex; FoC = Frontal Operculum Cortex (extension of insula); All results have threshold at *P*(cluster-FWE) = 0.05 with a cluster-forming threshold of $P < 0.001$ using 10,000 permutations.

3. Results

3.1. ALE main findings

The ALE meta-analysis on risk-processing revealed significant convergence of activity in bilateral anterior insula, bilateral dmPFC and bilateral ventral striatum (Fig. 2 and Table 3). Thirty-one out of the 69 contrasts contributed to the cluster in right anterior insula (MDE = 8.04%; 2MDEs = 15.14%, Table 4). Seventeen out of 69 contrasts contributed to the cluster in left anterior insula (MDE = 9.31%; 2MDEs = 18.27%, Table 4). Sixteen out of 69 contrasts contributed to the cluster in bilateral dmPFC (MDE = 22.60%; 2MDEs = 40.92%, Table 4). Twenty-one out of 69 contrasts contributed to the cluster in right ventral striatum (MDE = 16.27%; 2MDEs = 25.80%, Table 4). Twenty-eight out of 69 contrasts contributed to the cluster in left ventral striatum (MDE = 10.96%; 2MDEs = 16.96%, Table 4).

For the processing of ambiguity, the ALE meta-analysis revealed significant convergence of activity in right anterior insula, right precuneus, and right dlPFC (Fig. 2 and Table 3). Ten out of the 31 contrasts contributed to the cluster in right anterior insula (MDE = 19.39%; 2MDEs = 37.29%, Table 5). Eight out of 31 contrasts contributed to the

Table 4
Average contribution of each experimental for significant clusters on risk-processing.

Cluster name	Study	N	Task	Contrast	No. of foci	Average contribution (%)
Anterior Insula (R)	Abidi et al. (2018)	14(7)	Probability Discounting Task	High > Low Risk	5	0.32
	Aridan et al. (2019)	40(19)	Mixed Gambles Risk Task	Risky Parametric	13	0.63
	Blankenstein et al. (2017)	50(25)	Wheel of Fortune Task	Risk > Ambiguity	14	2.81
	Brevers et al. (2015)	10(8)	Card-Deck Paradigm	Risky > Safe	6	0.49
	Cohen et al. (2005)	16(9)	Two-choice Gambling Task	High >Low Risk	5	0.08
	Dong et al. (2015)	22(N.A)	Two-options Risky Task	High >Low Risk	2	2.46
	Engelmann and Tamir (2009)	10(7)	Wheel of Fortune Task	Risky Parametric	17	0.53
	Gorka et al. (2016)	37(10)	Slot-machine Task	Risky > Safe	6	3.9
	Grinband et al. (2006)	10(5)	Stimulus-categorization Task	Parametric	8	3.25
	Guo et al. (2013)	15(N.A)	Poker Cards Task	Risky > Safe	18	2.83
	Helfinstein et al. (2014)	108 (N.A)	Balloon analogue Risk Taking Task	Risky > Safe	7	3.89
	Huettel et al. (2005)	12(9)	Probabilistic guessing	Risky Parametric	10	3.60
	Huettel (2006)	12(6)	Different Probability Reinforcement Task	Risk > Certainty & Ambiguity	15	3.84
	Kohno et al. (2015)	60(33)	Balloon Analogue Risk Taking Task	Risky Parametric	8	6.62
	Lawrence et al. (2008)	15(15)	Iowa Gambling Task	Risky > Safe	10	3.73
	Mohr et al. (2010b)	19(8)	Risk Perception and Investment Decision Task	Risky > Safe	2	2.53
	Nagel et al. (2017)	18(N.A)	Strategy lottery choices	Risky Parametric	4	2.91
	Pan et al. (2019)	35(17)	Balloon analogue Risk Taking Task	Risky Parametric	9	1.15
	Paulus et al. (2003b)	17(11)	Risky-Gains Task	Risky > Safe	5	3.82
	Preuschoff et al. (2006)	19(10)	Card gambling guessing	Risky Parametric	9	2.72
	Rao et al. (2008)	14(8)	Balloon analogue Risk Taking Task	Risky Parametric	15	0.5
	Rigoli et al. (2019)	23(10)	Two-choice Risk Task	Risky > Safe	7	3.84
	Roy et al. (2011)	23(8)	Wheel of Fortune Task	Risky > Safe	51	8.04
	Schonberg et al. (2012)	16(6)	Balloon analogue Risk Taking Task	Risky Parametric	5	3.10
	Stern et al. (2014)	17(8)	Incentive Card Task	High > Low Risk	4	2.34
	Sun et al. (2017)	18(9)	Iowa Gambling Task	Risky > Safe	15	3.47
	Symmonds et al. (2010)	16(N.A)	Single-shot lottery Task	Risky Parametric	13	7.10
	van Leijenhorst et al. (2006)	26(9)	The probability risk cake Task	High > Low Risk	16	4.02
	Weber and Huettel (2008)	23(12)	Preference elicitation Task	Risky > Safe	16	5.47
	Wright et al. (2013)	24(6)	Wheel of fortune Task	Risky > Safe	18	5.97
	Zhang et al. (2019)	25(11)	Modified Cups Task	Risky > Safe	10	3.92
Anterior Insula (L)	Gorka et al. (2016)	37(10)	Slot-machine Task	Risky > Safe	6	8.42
	Grinband et al. (2006)	10(5)	Stimulus-categorization Task	Parametric	8	0.69
	Helfinstein et al. (2014)	108 (N.A)	Balloon analogue Risk Taking Task	Risky > Safe	7	9.31
	Hsu et al. (2009)	21(10)	Ellsberg Paradox Task	Risk > Ambiguity	12	5.81
	Huettel et al. (2005)	12(9)	Probabilistic guessing	Risky Parametric	10	2.79
	Huettel (2006)	12(6)	Different Probability Reinforcement Task	Risk > Certainty & Ambiguity	15	6.00
	Lawrence et al. (2008)	15(15)	Iowa Gambling Task	Risky > Safe	10	5.16
	Nagel et al. (2017)	18(N.A)	Strategy lottery choices	Risky Parametric	4	8.82
	Preuschoff et al. (2006)	19(10)	Card gambling guessing	Risky Parametric	9	8.96
	Rao et al. (2008)	14(8)	Balloon analogue Risk Taking Task	Risky Parametric	15	8.96
	Rigoli et al. (2019)	23(10)	Two-choice Risk Task	Risky > Safe	7	6.59
	Schonberg et al. (2012)	16(6)	Balloon analogue Risk Taking Task	Risky Parametric	5	7.49
	Sun et al. (2017)	18(9)	Iowa Gambling Task	Risky > Safe	15	1.68
	Symmonds et al. (2010)	16(N.A)	Single-shot Lottery Task	Risky Parametric	13	2.95
	Wright et al. (2013)	24(6)	Wheel of Fortune Task	Risky > Safe	18	7.46
	Xue et al. (2010)	14(7)	Modified Cups Task	Risky > Safe	8	1.08
	Zhang et al. (2019)	25(11)	Modified Cups Task	Risky > Safe	10	7.56
dmPFC (L/R)	Baek et al. (2017)	75(46)	Risk Aversion Task	Risky > Safe	4	0.22
	Chark and Chew (2015)	16(N.A)	Ellsberg Paradox Task	Risk > Ambiguity	2	0.63
	Dreher et al. (2005)	31(16)	Slot-machine Task	High > Low Risk	2	0.47
	Gowin et al. (2014)	40(26)	Risky Gains Task	Risky > Fixation	38	11.25
	Grinband et al. (2006)	10(5)	Stimulus-categorization Task	Parametric	8	6.87
	Hsu et al. (2005)	16(13)	Ellsberg Paradox Task	Risk > Ambiguity	12	6.72
	Hsu et al. (2009)	21(10)	Ellsberg Paradox Task	Risky Parametric	35	22.6
	Levy et al. (2009)	20(N.A)	Ellsberg Paradox Task	Risky Parametric	2	1.39
	Matthews et al. (2004)	12(7)	Lane Risk Task	Risky > Safe	4	5.78
	Rao et al. (2008)	14(8)	Balloon analogue Risk Taking Task	Risky Parametric	15	1.44
	Rao et al. (2018)	222 (114)	Balloon analogue Risk Taking Task	Risky Parametric	16	0.31

(continued on next page)

Table 4 (*continued*)

Cluster name	Study	N	Task	Contrast	No. of foci	Average contribution (%)
	Rolls et al. (2007)	13(8)	Probabilistic Monetary Reward Decision Task	Risky Parametric	3	1.12
	Roy et al. (2011)	23(8)	Wheel of Fortune Task	Risky > Safe	51	12.43
	Symmonds et al. (2010)	16(N.A)	Single-shot lottery Task	Risky Parametric	13	6.93
	Vorobyev et al. (2015)	34(34)	Stoplight Game	Risky > Safe	24	18.32
	Wang et al. (2015)	30(27)	Four Cards Guessing	Risky Parametric	5	3.35
Ventral Striatum (R)	Abidi et al. (2018)	14(7)	Probability Discounting Task	High > Low Risk	5	0.25
	Aridan et al. (2019)	40(19)	Mixed Gambles Risk Task	Risky Parametric	13	0.14
	Baek et al. (2017)	75(46)	Risk Aversion Task	Risky > Safe	4	8.66
	Berns and Bell (2012)	30(9)	Risk Safe Task	Risky Parametric	4	4.00
	Brevers et al. (2015)	10(8)	Card-Deck Paradigm	Risky > Safe	6	1.59
	Dreher et al. (2005)	31(16)	Slot-machine Task	High > Low Risk	4	0.49
	Gowin et al. (2014)	40(26)	Risky Gains Task	Risky > Fixation	38	0.11
	Grinband et al. (2006)	10(5)	Stimulus-categorization Task	Parametric	8	6.48
	Hsu et al. (2009)	21(10)	Ellsberg Paradox Task	Risky Parametric	25	7.14
	Huettel (2006)	12(6)	Different Probability Reinforcement Task	Risk > Certainty & Ambiguity	15	4.41
	Kohno et al. (2015)	60(33)	Balloon Analogue Risk Taking Task	Risky Parametric	8	6.73
	Levy et al. (2009)	20(N.A)	Ellsberg Paradox Task	Risky Parametric	2	0.12
	Rao et al. (2008)	14(8)	Balloon analogue Risk Taking Task	Risky Parametric	15	7.88
	Rao et al. (2018)	222 (114)	Balloon analogue Risk Taking Task	Risky Parametric	16	9.53
	Rolls et al. (2007)	13(8)	Probabilistic Monetary Reward Decision Task	Risky Parametric	3	1.73
	Roy et al. (2011)	23(8)	Wheel of Fortune Task	Risky > Safe	51	16.27
	Sun et al. (2017)	18(9)	Iowa Gambling Task	Risky > Safe	15	7.72
	Vorobyev et al. (2015)	34(34)	Stoplight game	Risky > Safe	24	7.96
	Xue et al. (2008)	13(8)	Cups task	Risky Parametric	6	1.54
	Yazdi et al. (2019)	20(20)	Cambridge Gambling Task	Risky Parametric	7	6.35
	Zhang et al. (2019)	25(11)	Modified cups task	Risky > Safe	10	0.66
Ventral Striatum (L)	Behrens et al. (2007)	18(9)	Probability-Tracking Task	Risky Parametric	1	3.17
	Brevers et al. (2016)	15(6)	Iowa Gambling Task	Risk > Ambiguity	5	5.13
	Christopoulos et al. (2009)	13(8)	Two-choice Gambling Task	High >Low Risk	1	3.62
	Cohen et al. (2005)	16(9)	Two-choice Gambling Task	High > Low Risk	5	0.20
	Congdon et al. (2013)	23(10)	Angling Risk Task	Risky Parametric	3	4.38
	Ernst et al. (2004)	17(N.A)	Wheel of Fortune Task	Risk > Ambiguity	19	10.96
	Gorka et al. (2016)	37(10)	Slot-machine Task	Risky > Safe	6	3.17
	Gowin et al. (2014)	40(26)	Risky Gains Task	Risky > Fixation	38	1.29
	Grinband et al. (2006)	10(5)	Stimulus-categorization Task	Parametric	8	4.54
	Guo et al. (2013)	15(N.A)	Poker Cards Task	Risky > Safe	18	3.69
	Helfinstein et al. (2014)	108 (N.A)	Balloon analogue Risk Taking Task	Risky > Safe	7	4.39
	Huettel (2006)	12(6)	Different Probability Reinforcement Task	Risk > Certainty & Ambiguity	15	4.73
	Kohno et al. (2015)	60(33)	Balloon Analogue Risk-Taking Task	Risky Parametric	8	2.57
	Kuhnen and Knutson (2005)	19(9)	The behavioural Investment Allocation Strategy Task	Risky Parametric	2	6.00
	Labudda et al. (2008)	16(8)	Game of Dice Task	High > Low risk	6	4.31
	Minati et al. (2012)	22(12)	Gambling Task	Risk > Ambiguity	5	3.07
	Nagel et al. (2017)	18(N.A)	Strategy lottery choices	Risky Parametric	4	5.00
	Pan et al. (2019)	35(17)	Balloon analogue Risk Taking Task	Risky Parametric	9	0.19
	Rao et al. (2008)	14(8)	Balloon analogue Risk Taking Task	Risky Parametric	15	0.45
	Rao et al. (2018)	222 (114)	Balloon analogue Risk Taking Task	Risky Parametric	16	5.65
	Roy et al. (2011)	23(8)	Wheel of Fortune Task	Risky > Safe	51	4.16
	Smith et al. (2009)	25(13)	Wheel of Fortune Task	Risky > Safe	2	4.95
	Stern et al. (2014)	17(8)	Incentive Card Task	High > Low Risk	4	0.81
	Weber and Huettel (2008)	23(12)	Preference elicitation task	Risky > Safe	16	5.64
	Wright et al. (2013)	24(6)	Wheel of fortune task	Risky > Safe	18	4.14
	Xue et al. (2008)	13(8)	Cups Task	Risky Parametric	6	0.27
	Yoshida and Ishii (2006)	13(11)	Back-track Task	Risky > Safe	3	0.90
	Zhang et al. (2019)	25(11)	Modified Cups Task	Risky > Safe	10	2.48

Table 5
Average contribution of each experimental for significant clusters on ambiguity-processing.

Cluster Name	study	N	Task	Contrast	No. of foci	Average contribution (%)
Anterior Insula (R)	Bach et al. (2009a)	20(10)	Pavlovian Fear Condition	Ambiguous > Certain	13	11.43
	Chumbley et al. (2012)	14(8)	Two-choice Guessing	Ambiguous Parametric	6	0.25
	Kano et al. (2017)	29(14)	Cue Prediction Task	Ambiguous > Certain	10	6.52
	Krug et al. (2014)	64(37)	Probabilistic Guessing	Ambiguous > Certain	29	19.39
	Lopez Paniagua and Seger (2013)	14(5)	Risky Lottery	Ambiguous > Certain	18	13.46
	Paulus et al. (2001)	12(10)	Two-choice Prediction Task	Ambiguous > Certain	8	13.03
	Payzan-LeNestour et al. (2013)	18(9)	Cue Probability	Ambiguous Parametric	29	17.9
	Preuschoff et al. (2008)	19(10)	Card Gambling Guessing	Ambiguous Parametric	10	7.88
	Sarinopoulos et al. (2009)	40(22)	Cue-picture Pairings	Ambiguous > Certain	4	4.97
	Volz et al. (2003)	16(11)	Two-card Prediction	Ambiguous Parametric	7	5.14
IPL (R)	Causse et al. (2013)	15(N.A)	Plausible Aviation Task	High > Low Ambiguity	24	0.21
	Hsu et al. (2005)	16(13)	Card-deck Task	Ambiguity > Risk	24	0.42
	Kano et al. (2017)	29(14)	Cue Prediction Task	Ambiguous > Certain	10	10.49
	Krug et al. (2014)	64(37)	Probabilistic Guessing	Ambiguous > Certain	29	18.13
	Lopez Paniagua and Seger (2013)	14(5)	Risky Lottery	Ambiguous > Certain	18	19.45
	Payzan-LeNestour et al. (2013)	18(9)	Cue Probability	Ambiguous Parametric	29	15.77
	Volz et al. (2003)	16(11)	Two-card Prediction	Ambiguous Parametric	7	18.79
	Volz et al. (2004)	12(5)	Two-card Prediction	Ambiguous Parametric	5	16.57
IFG (L)	Bach et al. (2009a)	20(10)	Pavlovian Fear Condition	Ambiguous > Certain	13	27.78
	Blackwood et al. (2004)	8(8)	Two-alternative-choice Task	Ambiguous > Certain	6	12.21
	Ikink et al. (2019)	24(24)	Delay Discounting Task (time-ambiguous)	Ambiguity > Fixation	7	20.12
	Payzan-LeNestour et al. (2013)	18(9)	Cue Probability	Ambiguous Parametric	29	17.00
	Tobler et al. (2006)	22(9)	Pavlovian Blocking Paradigm	Parametric	11	18.54
	Volz et al. (2004)	12(5)	Two-card Prediction	Ambiguous Parametric	5	4.28
dlPFC (R)	Hsu et al. (2005)	16(13)	Card-deck Task	Ambiguity > Risk	24	16.76
	Jung et al. (2013)	24(16)	Odd-Even-Pass Task	Ambiguous > Certain	7	21.65
	Lopez Paniagua and Seger (2013)	14(5)	Risky Lottery	Ambiguous > Certain	18	15.77
	Paulus et al. (2001)	12(10)	Two-choice Prediction Task	Ambiguous > Certain	8	6.14
	Verney et al. (2003)	17(7)	Two-choice Prediction Task	High > Low Ambiguity	12	11.76
	Volz et al. (2003)	16(11)	Two-card Prediction	Ambiguous Parametric	7	19.21
	Volz et al. (2004)	12(5)	Two-card Prediction	Ambiguous Parametric	5	0.19
	Yarkoni et al. (2005)	26(N.A)	Card decision task	High > Low Ambiguity	10	8.48

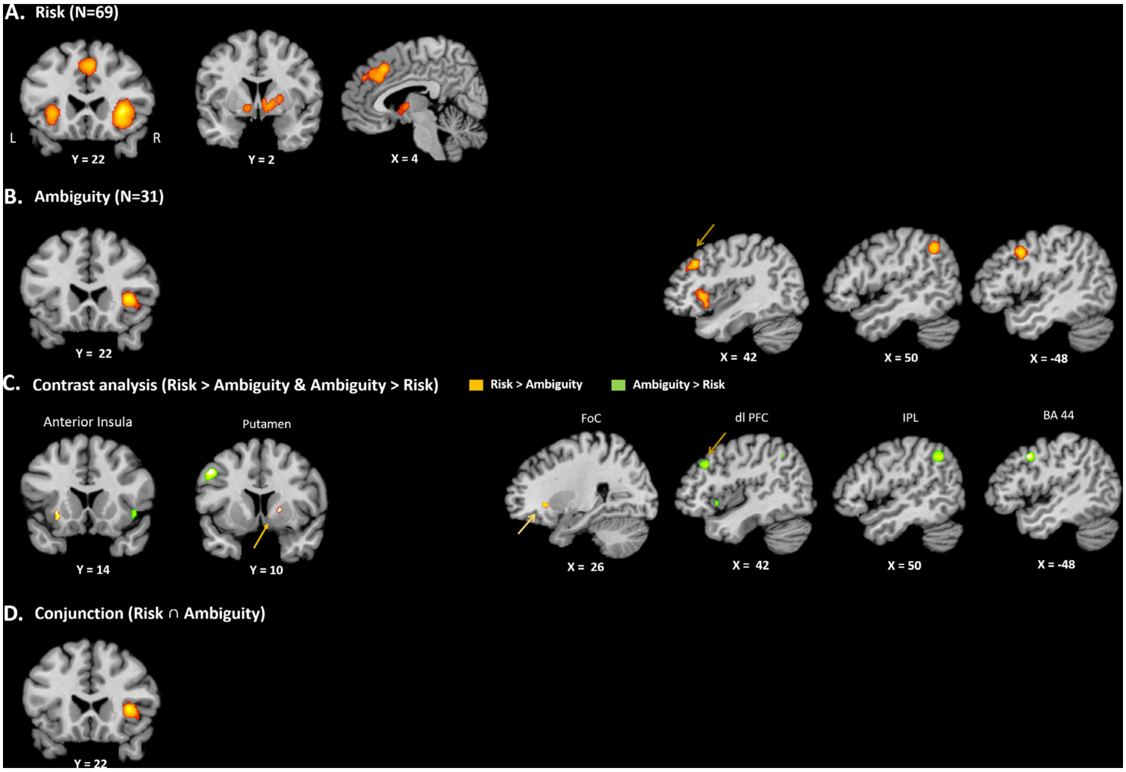

Fig. 2. Significant clusters from the main coordinate-based activation likelihood estimation meta-analysis (cluster-level family-wise error correction $p < 0.05$ with a cluster-forming threshold of $p < 0.001$ using 10,000 permutations) for risk-processing, ambiguity-processing, and their conjunction and contrasts. Consistent maximum for: (A) risk-processing; (B) ambiguity-processing; (C) the contrasts of risk- and ambiguity-processing. (D) the conjunction of risk- and ambiguity-processing. Brain regions showing higher activation in the processing of risk are illustrated in red, whereas regions showing higher activation in the processing of ambiguity are illustrated in green. L, left. R, right. N: the number of related contrasts. FoC, frontal operculum cortex (extension of Insula). dlPFC, dorsal lateral Prefrontal Cortex. IPL, inferior parietal lobule.

cluster in right IPL (MDE = 19.45%; 2MDEs = 38.24%, Table 5). Six out of 31 contrasts contributed to the cluster in left BA44 (MDE = 27.78%; 2MDEs = 47.90%, Table 5). Eight out of 31 contrasts contributed to the cluster in right dlPFC (MDE = 21.65%; 2MDEs = 40.86%, Table 5).

3.2. Conjunction and contrast analyses findings

The conjunction analysis revealed a common activation maximum in the right anterior insula, for both risk- and ambiguity-processing (Fig. 2 and Table 3). Results of contrast analysis (risk vs. ambiguity; Fig. 2 and Table 3) showed that the left anterior insula and right putamen were more activated during risk-processing than ambiguity-processing. Conversely, results showed that the right IPL, right dlPFC, right IFG and right frontal operculum cortex (FoC, also the extension of anterior insula) were more activated during ambiguity-processing than risk processing (Fig. 2 and Table 3).

3.3. Sub-analyses: moderating effects

Findings from sub-ALE analysis of risk parametric modulation contrasts (N = 24) showed significant clusters in the right anterior insula (with 10 out of 24 contributing contrasts, MDE = 29.2%; 2MDEs = 51.11%), right putamen (with 9 out of 24 contributing contrasts, MDE = 18.84%; 2MDEs = 35.7%), left anterior insula (with 12 out of 24 contributing contrasts, MDE = 16.43%; 2MDEs = 31.48%) and paracingulate gyrus (with 10 out of 24 contributing contrasts, MDE = 26.29%; 2MDEs = 50.82%). Risk binary contrasts (N = 45) revealed the convergence in the right anterior insula (with 9 out of 45 contributing contrasts, MDE = 24.57%; 2MDEs = 47.2%), right dmPFC (with 22 out of 45 contributing contrasts, MDE = 12%; 2MDEs = 19.65%), left intraparietal sulcus (IPS, with 11 out of 45 contributing contrasts, MDE = 17.13%; 2MDEs = 31.8%), left occipital cortex (with 14 out of 45 contributing contrasts, MDE = 13.99%; 2MDEs = 24.98%), and left anterior insula (with 10 out of 45 contributing contrasts, MDE = 20.06%; 2MDEs = 33.43%). In particular, the contrast of risk parametric modulation versus risk binary contrasts showed significant clusters of activation in left anterior insula and left thalamus. The reversed contrast showed activations in left occipital cortex and right IFG. These findings suggest that brain regions that encode risk levels linearly and brain regions that detect high versus low risk do not fully overlap. The results were presented in Table 6–8 and Fig. 3. Results of analysis of ambiguity binary contrasts (N = 23) showed convergence in the right anterior insula, right MFG, right occipital cortex and right IPL, largely consistent with the findings from the primary analysis with 31 contrasts. The details are presented in Table 6 and Figure S1.

The results of sub-ALE on risk-processing at the stage of decision-making (decision risk, N = 53) are largely similar to the primary analysis (N = 69), suggesting that our findings are not significantly influenced by the stage of decision-making (see Table 6 and Figure S2).

For the moderating effect of reward type, the convergence in bilateral anterior insula was revealed in both Gains gambles (N = 36, Right: with 14 out of 36 contributing contrasts, MDE = 17.9%; 2MDEs = 31.91%; Left: with 12 out of 36 contributing contrasts, MDE = 22.64%; 2MDEs = 35.08%;) and Mix gambles (N = 28, Right: with 7 out of 28 contributing contrasts, MDE = 22.23%; 2MDEs = 42.82%; Left: with 10 out of 28 contributing contrasts, MDE = 17.09%; 2MDEs = 30.39%;). The convergence in right dmPFC was also revealed in both Gains gambles (with 11 out of 36 contributing contrasts, MDE = 18.64%; 2MDEs = 35.43%) and Mix gambles (with 10 out of 28 contributing contrasts, MDE = 18.91%; 2MDEs = 36.85%).

Table 6
Findings of sub-analyses on risk-processing.

Cluster #	Brain regions	BA	MNI coordinate (mm) X	Y	Z	Peak Z score	Cluster Size (mm^3)
Gains gambles (N = 36)							
1	Anterior Insula (R)	13	34	26	0	5.6	2856
2	dmPFC (R)	8	2	24	40	5.12	2032
3	Anterior Insula (L)	13	−32	14	−8	4.8	1208
Mix gambles (N = 28)							
1	Anterior Insula (R)	13	34	22	−2	5.79	2256
2	Anterior Insula (L)	13	−32	24	−2	5.91	1112
3	dmPFC (R)	8	6	22	44	4.97	1096
Conjunctions (Gains ∩ Mix)							
1	Anterior Insula (R)	13	32	24	−2	5.27	1384
2	dmPFC (R)	8	4	24	42	4.41	536
Mix gambles (N = 28) > Gains gambles (N = 36)							
1	Anterior Insula (L)	13	−34	28	−4	2.25	448
Gains gambles (N = 36) > Mix gambles (N = 28) No activations							
Risk Parametric (N = 24)							
1	Anterior Insula (R)	13	34	22	0	4.29	1728
2	Putamen (R)	/	12	2	−2	4.30	1488
3	Anterior Insula (L)	13	−32	16	−8	5.87	1456
4	PCG (/)	6	0	24	40	4.57	1000
Risk Binary contrasts (i.e., ***Risky > Safe & High > Low risk, N = 45)***							
1	Anterior Insula (R)	13	32	24	−2	6.20	4040
2	dmPFC (R)	8	4	28	34	4.90	2312
3	IPS (L)	7	−26	−64	50	4.17	1080
4	Occipital Cortex (L)	18	−28	−88	0	4.13	944
5	Anterior Insula (L)	13	−32	24	−2	5.52	848
Risk Parametric (N = 24) > Risk Binary contrasts (N = 45)							
1	Anterior Insula (L)	13	−34	14	4	3.14	936
2	Thalamus (L)	/	−4	−2	0	3.19	576
Risk Binary contrasts (N = 45) > Risk Parametric (N = 24)							
1	Occipital Cortex (L)	18	−24	88	6	2.29	360
2	IFG (R)	13	44	32	18	2.52	256
Decision Risk (N = 53)							
1	dmPFC (R)	8	4	24	42	6.32	4400
2	Anterior Insula (R)	13	36	24	2	7.02	3736
3	Putamen (R)	/	12	2	−4	4.10	1208
4	Anterior Insula (L)	13	−32	16	−8	4.21	1080
5	Caudate (L)	/	−10	10	−4	3.94	912

Note: L = Left; R = Right; BA = Brodmann area; dmPFC = Dorsal Medial Prefrontal Cortex; PCG = Paracingulate Gyrus; IFG = Inferior Frontal Gyrus; IPS = Intraparietal sulcus; IPL = Inferior Parietal Lobe; MFG = Medial Frontal Gyrus; All results are set to a threshold at P(cluster-FWE) = 0.05 with a cluster-forming threshold of $P < 0.001$ using 10,000 permutations.

Although, both domains significantly engage the same brain clusters, significant clusters of stronger activation in left anterior insula was also observed in the comparison of Mix gambles with Gains gambles, but no significant activations were observed in the reversed contrast (See Table 6, 9, 10 and Figure S3).

The main effect regarding descriptive risk ($N = 48$) was observed in the right anterior insula, right dmPFC, left caudate, IPS and occipital cortex, while effects of experienced risk ($N = 21$) were in right anterior insula and right dmPFC. Results from the contrast of descriptive risk versus experienced risk showed significant clusters of activations in right dmPFC, left occipital cortex and left caudate (see Table S3 for more details). Of noted, results of resampling analysis revealed that significant clusters of activations in descriptive risk were limited to the right anterior insula and right dmPFC. Likewise, a similar pattern was also observed in experience risk from resampling analysis (Figure S4). There is no significant difference of activations in contrast analyses after resampling, suggesting that there is no robust difference in brain correlates between the two types of risk.

The type of contrasts included in the meta-analysis of risk/ambiguity may also influence our conjunction/contrast findings. For risk processing, the majority of studies used low risk or no risk as a baseline but some studies ($n = 6$) used ambiguity as the control condition. Hence, the results of the risk processing map already to some degree contain information about the difference between risk and ambiguity. For ambiguity processing, three studies used ambiguity > risk contrasts. The inclusion of these direct contrasts between risk and ambiguity may reduce the power to detect conjunction effect as these contrasts have already control for brain activities that are commonly elicited by the two experimental conditions. We have removed these contrasts and redone all analyses. No additional regions were identified in the conjunction analysis using the new ALE maps, see Figure S10 and S11. All main results still hold after removing risk > ambiguity and ambiguity > risk contrasts.

3.4. Validation analyses

3.4.1. LOEO findings of risk-processing and ambiguity-processing

Consistent activations maxima were found in the bilateral anterior insula, bilateral ventral striatum and dmPFC for risk-processing (Figure S5 and Table S1) and in the right anterior insula, right dlPFC, left IFG and right IPL for ambiguity-processing (Figure S6 and Table S1). In other words, the results of the LOEO approach corroborated the findings of the standard ALE meta-analysis.

3.4.2. Re-subsampling findings

The minimum conjunction of two conditions was identified in the right anterior insula and left precentral gyrus (middle frontal gyrus, IFG, Figure S7 and Table S1). The re-subsampling analyses revealed results that largely overlapped with those of the main ALE meta-analysis for risk-processing (Figure S8) and ambiguity-processing (Figure S9). Taken together, validation analyses confirmed the robustness of the findings obtained from the main ALE meta-analyses.

Table 7
Average contribution of each experimental for significant clusters on risk parametric modulation.

Cluster name	Study	N	Task	Contrast	No. of foci	Average contribution (%)
Anterior Insula (R)	Engelmann and Tamir (2009)	10(7)	Wheel of Fortune Task	Risky Parametric	17	1.35
	Grinband et al. (2006)	10(5)	Stimulus-categorization Task	Parametric	8	3
	Huettel et al. (2005)	12(9)	Probabilistic guessing	Risky Parametric	10	10.78
	Kohno et al. (2015)	60(33)	Balloon Analogue Risk-Taking Task	Risky Parametric	8	29.2
	Nagel et al. (2017)	18(N.A)	Strategy lottery choices	Risky Parametric	4	10.96
	Pan et al. (2019)	35(17)	Balloon analogue Risk Taking Task	Risky Parametric	9	0.28
	Preuschoff et al. (2006)	19(10)	Card gambling guessing	Risky Parametric	9	11.44
	Rao et al. (2008)	14(8)	Balloon analogue Risk Taking Task	Risky Parametric	15	0.77
	Schonberg et al. (2012)	16(6)	Balloon analogue Risk Taking Task	Risky Parametric	5	10.27
	Symmonds et al. (2010)	16(N.A)	Single-shot lottery Task	Risky Parametric	13	21.91
Putamen (R)	Grinband et al. (2006)	10(5)	Stimulus-categorization Task	Parametric	8	0.19
	Hsu et al. (2009)	21(10)	Ellsberg Paradox Task	Risk > Ambiguity	12	13.71
	Huettel et al. (2005)	12(9)	Probabilistic guessing	Risky Parametric	10	11.19
	Nagel et al. (2017)	18(N.A)	Strategy lottery choices	Risky Parametric	4	17
	Preuschoff et al. (2006)	19(10)	Card gambling guessing	Risky Parametric	9	18.84
	Rao et al. (2008)	14(8)	Balloon analogue Risk Taking Task	Risky Parametric	15	16.78
	Schonberg et al. (2012)	16(6)	Balloon analogue Risk Taking Task	Risky Parametric	5	16.89
	Symmonds et al. (2010)	16(N.A)	Single-shot Lottery Task	Risky Parametric	13	5.13
	Yazdi et al. (2019)	20(20)	Cambridge Gambling Task	Risky Parametric	7	0.23
Anterior Insula (L)	Berns and Bell (2012)	30(9)	Risk Safe Task	Risky Parametric	4	6.19
	Grinband et al. (2006)	10(5)	Stimulus-categorization Task	Parametric	8	9.38
	Hsu et al. (2009)	21(10)	Ellsberg Paradox Task	Risky Parametric	35	16.43
	Huettel et al. (2005)	12(9)	Probabilistic guessing	Risky Parametric	10	2.55
	Kohno et al. (2015)	60(33)	Balloon Analogue Risk-Taking Task	Risky Parametric	8	12.21
	Levy et al. (2009)	20(N.A)	Ellsberg Paradox Task	Risky Parametric	2	0.19
	Rao et al. (2008)	14(8)	Balloon analogue Risk Taking Task	Risky Parametric	15	15.05
	Rao et al. (2018)	222 (114)	Balloon analogue Risk Taking Task	Risky Parametric	16	6.61
	Rolls et al. (2007)	13(8)	Probabilistic Monetary Reward Decision Task	Risky Parametric	3	12.66
	Symmonds et al. (2010)	16(N.A)	Single-shot lottery Task	Risky Parametric	13	6.98
	Xue et al. (2008)	13(8)	Cups Task	Risky Parametric	6	11.38
	Yazdi et al. (2019)	20(20)	Cambridge Gambling Task	Risky Parametric	7	0.28
PCG (/)	Behrens et al. (2007)	18(9)	Probability-Tracking Task	Risky Parametric	1	8.83
	Congdon et al. (2013)	23(10)	Angling Risk Task	Risky Parametric	3	21.72
	Grinband et al. (2006)	10(5)	Stimulus-categorization Task	Parametric	8	0.18
	Huettel (2006)	12(6)	Different Probability Reinforcement Task	Risk > Certainty & Ambiguity	15	15.31
	Kohno et al. (2015)	60(33)	Balloon Analogue Risk-Taking Task	Risky Parametric	8	0.15
	Kuhnen and Knutson (2005)	19(9)	The behavioural Investment Allocation Strategy Task	Risky Parametric	2	26.29
	Nagel et al. (2017)	18(N.A)	Strategy lottery choices	Risky Parametric	4	24.53
	Pan et al. (2019)	35(17)	Balloon analogue Risk Taking Task	Risky Parametric	9	0.75
	Rao et al. (2008)	14(8)	Balloon analogue Risk Taking Task	Risky Parametric	15	1.85
	Rao et al. (2018)	222 (114)	Balloon analogue Risk Taking Task	Risky Parametric	16	0.33

3.5. Quantitative functional decoding for clustered-ROIs

Results on functional decoding for each ROI in the contrast analysis of risk vs. ambiguity are shown in Fig. 4. For the seed-cluster, right putamen, it was observed to have a functional association with positive emotion (reward), cognition and action (imagination). For the left anterior insula, forward and reverse inference consistently indicated an association with positive emotion (reward) and cognition (memory). For the right FoC, there was no significant association with any behavioural domain. Results on functional decoding for each ROI in the contrast analysis of ambiguity vs. risk are shown in Fig. 4. For the left IFG, the decoding analysis revealed an association with action (imagination) and cognition (working memory). For the right dlPFC, an association with cognition (reasoning and working memory) was observed. For the right

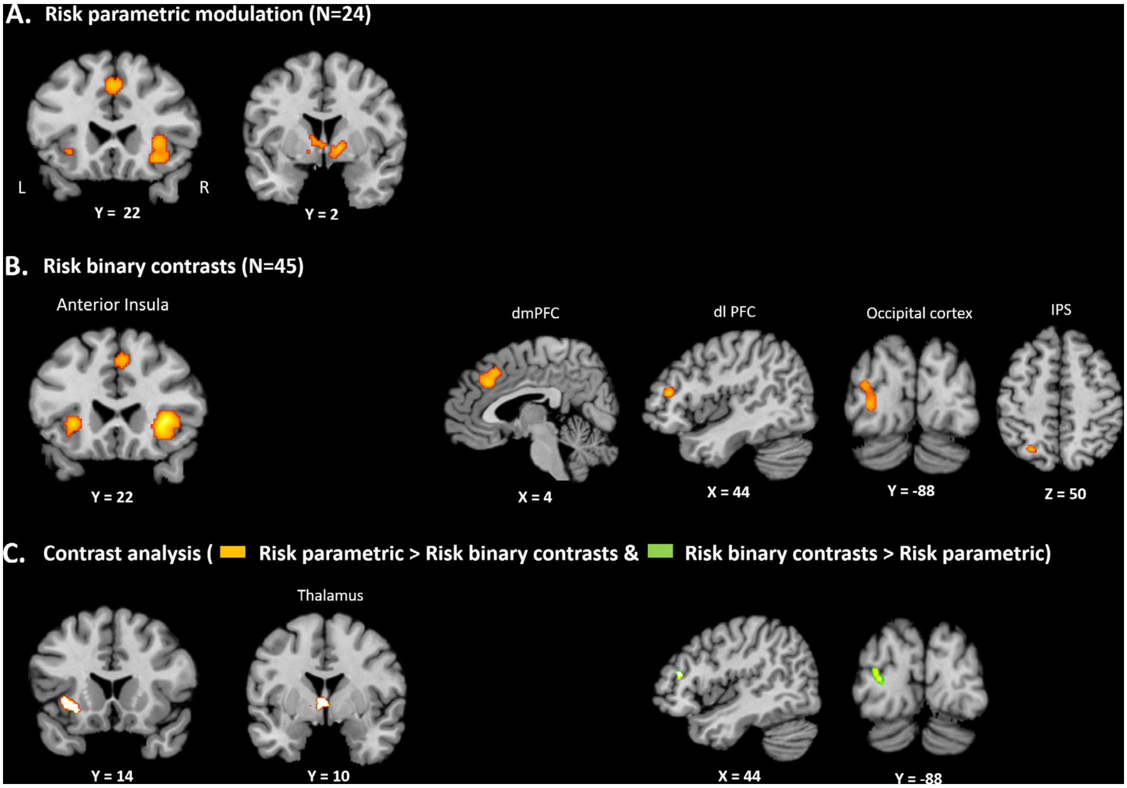

Fig. 3. Significant clusters of activation from Sub-ALE analysis on risk-processing and their contrasts. Consistent maximum for: (A) risk parametric modulation; (B) risk binary contrasts; (C) the contrasts of risk parametric modulation and risk binary contrasts. Brain regions showing higher activation of risk parametric modulation are illustrated in red, whereas regions showing higher activation of risk binary contrasts are illustrated in green. L, left. R, right. N: the number of related contrasts. dlPFC, dorsal lateral Prefrontal Cortex. IPS, Intraparietal Sulcus.

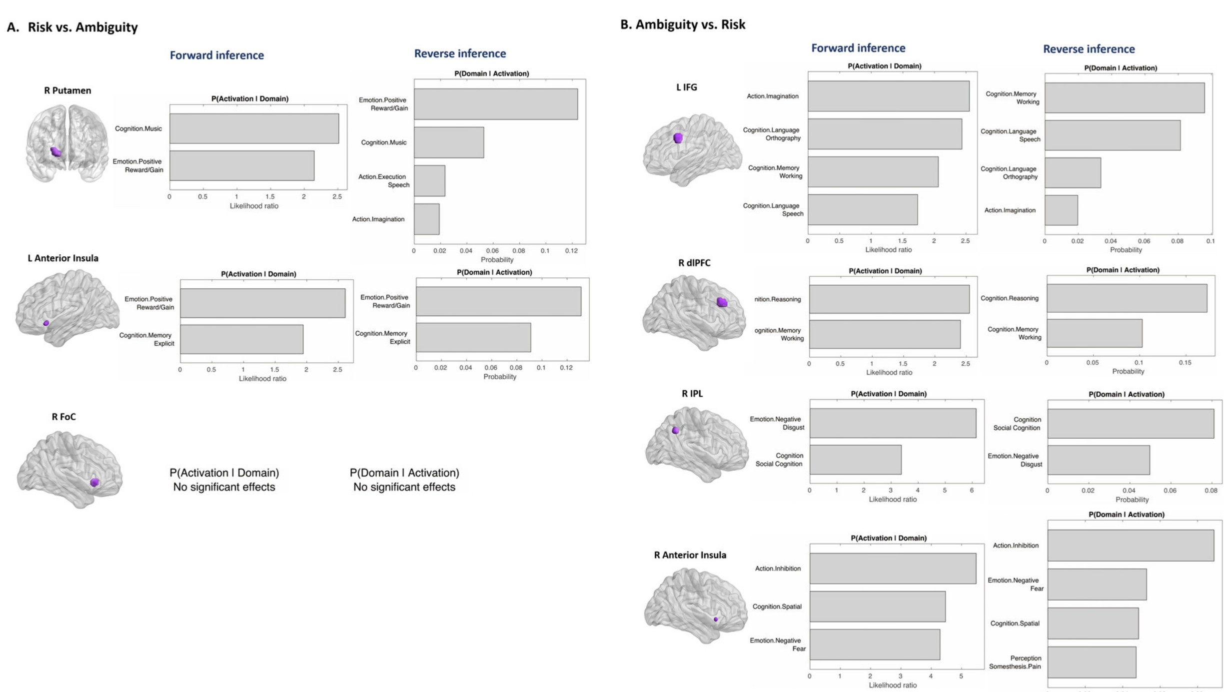

Fig. 4. Quantitative functional decoding on each cluster from the contrast analyses for risk vs. ambiguity (A) and ambiguity vs. risk (B). L, left. R, right. FoC, frontal operculum cortex (extension of Insula). dlPFC, dorsal lateral Prefrontal Cortex. IPL, inferior parietal lobule.

Table 8
Average contribution of each experimental for significant clusters on risk binary contrasts.

Cluster name	Study	N	Task	Contrast	No. of foci	Average contribution (%)
Anterior Insula (R)	Gorka et al. (2016)	37(10)	Slot-machine Task	Risky > Safe	6	22.63
	Helfinstein et al. (2014)	108 (N.A)	Balloon analogue Risk Taking Task	Risky > Safe	7	24.57
	Huettel (2006)	12(6)	Different Probability Reinforcement Task	Risk > Certainty & Ambiguity	15	4.15
	Lawrence et al. (2008)	15(15)	Iowa Gambling Task	Risky > Safe	10	0.63
	Rigoli et al. (2019)	23(10)	Two-choice Risk Task	Risky > Safe	7	17.84
	Sun et al. (2017)	18(9)	Iowa Gambling Task	Risky > Safe	15	3.61
	Wright et al. (2013)	24(6)	Wheel of fortune Task	Risky > Safe	18	6.83
	Xue et al. (2010)	14(7)	Modified Cups Task	Risky > Safe	8	2.03
	Zhang et al. (2019)	25(11)	Modified Cups Task	Risky > Safe	10	17.72
dmPFC (R)	Abidi et al. (2018)	14(7)	Probability Discounting Task	High > Low Risk	5	0.43
	Blankenstein et al. (2017)	50(25)	Wheel of Fortune Task	Risk > Ambiguity	17	4.83
	Brevers et al. (2016)	15(6)	Iowa Gambling Task	Risk > Ambiguity	5	0.7
	Cohen et al. (2005)	16(9)	Two-choice Gambling Task	High > Low Risk	5	0.37
	Dong et al. (2015)	22(N.A.)	Two-options Risky Task	High > Low Risk	2	4.36
	Gorka et al. (2016)	37(10)	Slot-machine Task	Risky > Safe	6	6.48
	Guo et al. (2013)	15(N.A)	Poker Cards Task	Risky > Safe	18	4.16
	Helfinstein et al. (2014)	108 (N.A)	Balloon analogue Risk Taking Task	Risky > Safe	7	5.79
	Huettel (2006)	12(6)	Different Probability Reinforcement Task	Risk > Certainty & Ambiguity	15	5.46
	Labudda et al. (2008)	16(8)	Game of Dice Task	High > Low risk	6	0.15
	Lawrence et al. (2008)	15(15)	Iowa Gambling Task	Risky > Safe	10	5.52
	Minati et al. (2012)	22(12)	Gambling Task	Risk > Ambiguity	5	0.16
	Mohr et al. (2010b)	19(8)	Risk Perception and Investment Decision Task	Risky > Safe	2	3.4
	Paulus et al. (2003b)	17(11)	Risky-Gains Task	Risky > Safe	5	5.88
	Rigoli et al. (2019)	23(10)	Two-choice Risk Task	Risky > Safe	7	5.43
	Roy et al. (2011)	23(8)	Wheel of Fortune Task	Risky > Safe	51	12
	Stern et al. (2014)	17(8)	Incentive Card Task	High > Low Risk	4	3.14
	Sun et al. (2017)	18(9)	Iowa Gambling Task	Risky > Safe	15	4.2
	van Leijenhorst et al. (2006)	26(9)	The probability risk cake Task	High > Low Risk	16	7.18
	Weber and Huettel (2008)	23(12)	Preference elicitation task	Risky > Safe	16	7.54
	Wright et al. (2013)	24(6)	Wheel of Fortune Task	Risky > Safe	18	7.65
	Zhang et al. (2019)	25(11)	Modified Cups Task	Risky > Safe	10	5.14
IPS (L)	Blankenstein et al. (2017)	50(25)	Wheel of Fortune Task	Risk > Ambiguity	17	1.98
	Ernst et al. (2004)	17(N.A)	Wheel of Fortune Task	Risk > Ambiguity	19	9.7
	Guo et al. (2013)	15(N.A.)	Poker Cards Task	Risky > Safe	18	0.13
	Lawrence et al. (2008)	15(15)	Iowa Gambling Task	Risky > Safe	10	11.73
	Matthews et al. (2004)	12(7)	Lane Risk Task	Risky > Safe	4	13.79
	Rigoli et al. (2019)	23(10)	Two-choice Risk Task	Risky > Safe	7	5.97
	Roy et al. (2011)	23(8)	Wheel of Fortune Task	Risky > Safe	51	17.13
	van Leijenhorst et al. (2006)	26(9)	The probability risk cake Task	High > Low Risk	16	9.59
	Weber and Huettel (2008)	23(12)	Preference elicitation task	Risky > Safe	16	1.68
	Wright et al. (2013)	24(6)	Wheel of fortune task	Risky > Safe	18	13.57
	Zhang et al. (2019)	25(11)	Modified Cups Task	Risky > Safe	10	14.67
Occipital Cortex (L)	Brevers et al. (2015)	10(8)	Card-Deck Paradigm	Risky > Safe	6	10.99
	Christopoulos et al. (2009)	13(8)	Two-choice Gambling Task	High >Low Risk	1	8.3
	Ernst et al. (2004)	17(N.A)	Wheel of Fortune Task	Risk > Ambiguity	19	13.99
	Gorka et al. (2016)	37(10)	Slot-machine Task	Risky > Safe	6	7.73
	Guo et al. (2013)	15(N.A)	Poker Cards Task	Risky > Safe	18	6.76
	Helfinstein et al. (2014)	108 (N.A)	Balloon analogue Risk Taking Task	Risky > Safe	7	8.55
	Labudda et al. (2008)	16(8)	Game of Dice Task	High > Low risk	6	7.22
	Minati et al. (2012)	22(12)	Gambling Task	Risk > Ambiguity	5	3.15
	Roy et al. (2011)	23(8)	Wheel of Fortune Task	Risky > Safe	51	7.67
	Smith et al. (2009)	25(13)	Wheel of Fortune Task	Risky > Safe	2	8.25
	Stern et al. (2014)	17(8)	Incentive Card Task	High > Low Risk	4	0.23
	Weber and Huettel (2008)	23(12)	Preference elicitation task	Risky > Safe	16	8.55
	Wright et al. (2013)	24(6)	Wheel of fortune task	Risky > Safe	18	8.03
	Zhang et al. (2019)	25(11)	Modified cups task	Risky > Safe	10	0.29
Anterior Insula (L)	Blankenstein et al. (2017)	50(25)	Wheel of Fortune Task	Risk > Ambiguity	17	12.1
	Ernst et al. (2004)	17(N.A)	Wheel of Fortune Task	Risk > Ambiguity	19	5.77
	Huettel (2006)	12(6)	Different Probability Reinforcement Task	Risk > Certainty & Ambiguity	15	20.06
	Minati et al. (2012)	22(12)	Gambling Task	Risk > Ambiguity	5	13.37
	Paulus et al. (2003b)	17(11)	Risky-Gains Task	Risky > Safe	5	11.12
	van Leijenhorst et al. (2006)	26(9)	The probability risk cake Task	High > Low Risk	16	9.59
	Vorobyev et al. (2015)	34(34)	Stoplight Game	Risky > Safe	24	10.31
	Weber and Huettel (2008)	23(12)	Preference elicitation task	Risky > Safe	16	7.48
	Wright et al. (2013)	24(6)	Wheel of fortune task	Risky > Safe	18	3.38
	Zhang et al. (2019)	25(11)	Modified Cups Task	Risky > Safe	10	6.56

Table 9
Average contribution of each experimental for significant clusters on Gain gambles in risk-processing.

Cluster name	Study	N	Task	Contrast	No. of foci	Average contribution (%)
Anterior Insula (R)	Engelmann and Tamir (2009)	10(7)	Wheel of Fortune Task	Risky Parametric	17	1.19
	Guo et al. (2013)	15(N.A)	Poker Cards Task	Risky > Safe	18	7.21
	Huettel et al. (2005)	12(9)	Probabilistic guessing	Risky Parametric	10	7.18
	Huettel (2006)	12(6)	Different Probability Reinforcement Task	Risk > Certainty & Ambiguity	15	6.82
	Kohno et al. (2015)	60(33)	Balloon Analogue Risk Taking Task	Risky Parametric	8	17.9
	Lawrence et al. (2008)	15(15)	Iowa Gambling Task	Risky > Safe	10	6.34
	Nagel et al. (2017)	18(N.A)	Strategy lottery choices	Risky Parametric	4	7.28
	Pan et al. (2019)	35(17)	Balloon analogue Risk Taking Task	Risky Parametric	9	0.67
	Rao et al. (2008)	14(8)	Balloon analogue Risk Taking Task	Risky Parametric	15	0.18
	Schonberg et al. (2012)	16(6)	Balloon analogue Risk Taking Task	Risky Parametric	5	5.83
	Sun et al. (2017)	18(9)	Iowa Gambling Task	Risky > Safe	15	8.16
	Symmonds et al. (2010)	16(N.A)	Single-shot Lottery Task	Risky Parametric	13	14.01
	van Leijenhorst et al. (2006)	26(9)	The probability risk cake Task	High > Low Risk	16	8.51
	Weber and Huettel (2008)	23(12)	Preference elicitation Task	Risky > Safe	16	8.69
dmPFC (R)	Hsu et al. (2009)	21(10)	Ellsberg Paradox Task	Risk > Ambiguity	12	15.88
	Huettel et al. (2005)	12(9)	Probabilistic guessing	Risky Parametric	10	1.59
	Huettel (2006)	12(6)	Different Probability Reinforcement Task	Risk > Certainty & Ambiguity	15	10.04
	Lawrence et al. (2008)	15(15)	Iowa Gambling Task	Risky > Safe	10	15.01
	Nagel et al. (2017)	18(N.A)	Strategy lottery choices	Risky Parametric	4	16.79
	Rao et al. (2008)	14(8)	Balloon analogue Risk Taking Task	Risky Parametric	15	15.91
	Rao et al. (2018)	222 (114)	Balloon analogue Risk Taking Task	Risky Parametric	16	0.13
	Schonberg et al. (2012)	16(6)	Balloon analogue Risk Taking Task	Risky Parametric	5	18.64
	Sun et al. (2017)	18(9)	Iowa Gambling Task	Risky > Safe	15	0.77
	Symmonds et al. (2010)	16(N.A)	Single-shot lottery Task	Risky Parametric	13	4.96
	Yazdi et al. (2019)	20(20)	Cambridge Gambling Task	Risky Parametric	7	0.23
Anterior Insula (L)	Christopoulos et al. (2009)	13(8)	Two-choice Gambling Task	High >Low Risk	1	4.75
	Congdon et al. (2013)	23(10)	Angling Risk Task	Risky Parametric	3	10.78
	Ernst et al. (2004)	17(N.A)	Wheel of Fortune Task	Risk > Ambiguity	19	22.64
	Guo et al. (2013)	15(N.A)	Poker Cards Task	Risky > Safe	18	2.66
	Huettel (2006)	12(6)	Different Probability Reinforcement Task	Risk > Certainty & Ambiguity	15	11.73
	Kohno et al. (2015)	60(33)	Balloon Analogue Risk-Taking Task	Risky Parametric	8	2.27
	Nagel et al. (2017)	18(N.A)	Strategy lottery choices	Risky Parametric	4	12.05
	Pan et al. (2019)	35(17)	Balloon analogue Risk Taking Task	Risky Parametric	9	0.18
	Rao et al. (2008)	14(8)	Balloon analogue Risk Taking Task	Risky Parametric	15	0.82
	Rao et al. (2018)	222 (114)	Balloon analogue Risk Taking Task	Risky Parametric	16	8.31
	Smith et al. (2009)	25(13)	Wheel of Fortune Task	Risky > Safe	2	12.44
	Weber and Huettel (2008)	23(12)	Preference elicitation task	Risky > Safe	16	11.3

IPL, both forward and reverse inference indicated an association with negative emotion (disgust) and social cognition. For the right anterior insula, there was an association with action (inhibition), spatial cognition, negative emotion (fear) and perception (pain).

3.6. Both task-based and task-free functional connectivity for clustered ROIs

Functional connectivity of the brain's task state (MACM) and of the brain's resting state (RSFC) for risk-processing exhibited similarities in the dorsomedial prefrontal cortex, inferior parietal cortex and ventral striatum, recapitulating default mode network (DMN). While in ambiguity, the significant clusters featured strong connectivity with the anterior insula, dlPFC and IPL, recapitulating multiple demand network (MDN), and are consistent across MACM and RSFC analyses (Fig. 5).

4. Discussion

Our meta-analyses results revealed that both risky and ambiguous decision-making activated the right anterior insula. Subsequent analyses specified that risky decision-making was more likely to engage the ventral striatum, dmPFC and left anterior insula, i.e. regions linked with reward processing and affective functions (Eickhoff et al., 2016). Meanwhile, making decisions in ambiguous tasks was more likely to activate the right anterior insula, dlPFC and IPL, i.e. regions linked to reasoning and negative emotions (Bode et al., 2013; Lamichhane and Dhamala, 2015). Both task-based and task-free functional connectivity

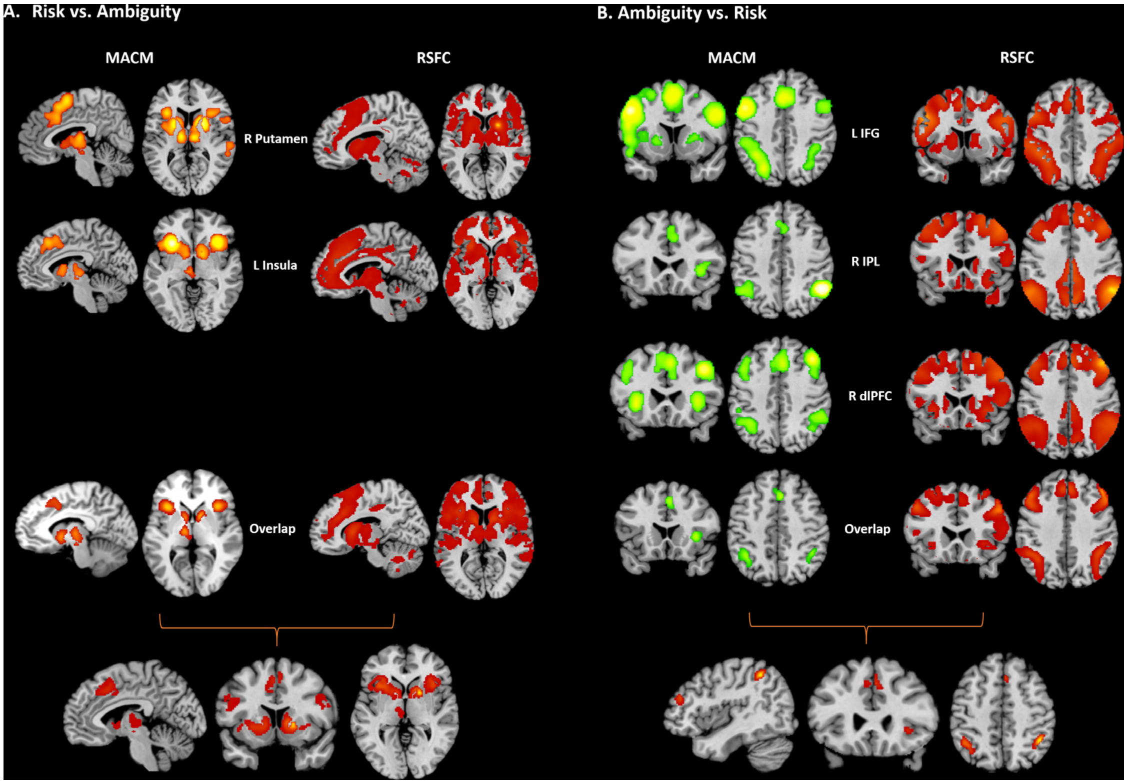

Fig. 5. Results for the task-based meta-analytic connectivity modelling (MACM) and task-free (resting state) functional connectivity (RSFC) analyses on the regions involved in the contrast analysis of risk vs. ambiguity (A) and ambiguity vs. risk (B). L, left. R, right. FoC, frontal operculum cortex (extension of Insula). dlPFC, dorsal lateral Prefrontal Cortex. IPL, inferior parietal lobule.

results further suggested that decision-making under risk involves regions implicated in processing reward, whereas processing of ambiguity additionally recruits brain regions associated with uncertainty and cognitive control.

In accord with recent research (Poudel et al., 2020), our findings revealed that both risk-processing and ambiguity-processing engaged the right anterior insula. Importantly, compared with risk binary contrasts, risk parametric modulation contrasts showed convergence in the left anterior insula and left thalamus, suggesting that these two regions may be specifically involved in encoding the degree of risk in a linear way rather than just risk-processing in general. Risk binary contrasts, when compared with risk parametric modulation, revealed convergence in the inferior frontal gyrus, indicating that the inferior frontal gyrus is sensitive to the presence of high risk. However, it is worth noting that studies using parametric modulation analysis may measure risk as a continuous variable and hence design tasks differently. Future studies may further investigate whether the processing of risk and the parametric encoding of risk levels are subserved by distinct brain regions. Notably, both LOEO and resampling analyses suggested that findings in our primary analyses were robust against potential outliers, an observation supported by the balanced contribution across all experiments for each cluster.

4.1. Common neural activity of both risk-processing and ambiguity-processing

Our findings confirmed that both processing of risk and ambiguity consistently activated the right anterior insula. The anterior insula has been found to encode risk prediction as well as risk prediction error (Preuschoff et al., 2008). The anterior insula may receive signals from other regions such as the ventral striatum (Cauda et al., 2012) and then integrate the inputs to characterise stimuli as reward or loss (Critchley and Harrison, 2013; Pizzagalli et al., 2009; Yu et al., 2020). The anterior insula has been reported to be involved in various functions, such as error awareness, physical and social pain processing and salience detection (Uddin, 2015). Our functional decoding analysis also revealed the broad functions that the anterior insula may be subserving. Accumulating evidence suggests a key role of the anterior insula in the integration of current and predictive feeling states, which may relate to somatic markers of risk-taking (Baek et al., 2017; Singer et al., 2009). The anterior insula is also closely connected with other reward and cognitive control-related brain regions, such as striatum and dmPFC. The right anterior insula may be involved in signalling the uncertainty of decisions to other brain regions and serving as a central hub to mobilize the brain decision-making networks to deal with the challenge of resolving such uncertainty. The lateralized activation of the right anterior insula in risk/ambiguity processing raises perplexing questions about the functional significance of insula. The left anterior insula has been shown to be also activated by positive and affiliative emotions (Craig and Craig, 2009). It has been posited that the left anterior insula is associated predominantly with parasympathetic activity, whereas the right anterior insula is more associated with sympathetic activity and negative emotions (Strigo and Craig, 2016). The lateralization observed in our study may suggest that risk/ambiguity engages enhanced arousal and vigilance as well as negative anticipative emotions. Such increase level of alertness and aversive feelings may better prepare individuals for the incoming challenges and negative consequences that are inherit in situations involving risk and ambiguity. As both risk and ambiguity decisions are probably more salient and entail potential errors and negative consequences, the anterior insula registers saliency and negative anticipation associated with uncertainty (Yu and Zhou, 2009). Based on our meta-analysis findings, it is difficult to assign precise functional roles to the right anterior insula in risk/ambiguity processing. Our findings confirmed the predominant role of right anterior insula in processing both risk and ambiguity. Interestingly, compared to risk, processing of ambiguity is more likely to engage the right anterior insula, which may indicate a higher level of uncertainty in ambiguous conditions (Motzkin et al., 2014).

Surprisingly, we failed to find convergence in brain regions that are believed to be heavily engaged in reward presentation and value-based decision-making, such as the vmPFC and ventral striatum (Hiser and Koenigs, 2018; McNamee et al., 2013) which are often co-activated during reward-related tasks. Through interactions with the ventral striatum, the vmPFC seems to encode decision values and integrate contextual information to support goal-directed decision making in a wide variety of contexts, including reinforcement learning (Rushworth et al., 2011), social cognition (Mobbs et al., 2009), and social decision making (Zhang and Gläscher, 2020). Additionally, vmPFC and ventral striatum may also play a necessary role in uncertain as well as certain decision-making in humans. For example, the vmPFC has been linked to inconsistent choices in preference judgement (Kurtz-David et al., 2019). Subjects with vmPFC damage demonstrated inconsistence in their preference judgement, suggesting that vmPFC is engaged in value-based decision making even in the absence of uncertainty (Kurtz-David et al., 2019). It is possible that these value-computation components that are common to the decision-making were cancelled out in the contrasts, e.g., risk>safe and ambiguity>certain. Future studies are needed to specifically examine the precise role of vmPFC and ventral striatum in risk/ambiguity processing.

4.2. Distinct neural profile for risk-processing

Our results revealed that the processing of risk is implemented in regions associated with reward and conflict detection, including the ventral striatum and the dmPFC. The ventral striatum has a predominant role in reward evaluation and reward expectation (Hsu et al., 2005). Activation of the ventral striatum has been associated with the prospect of higher monetary rewards (Breiter et al., 2001; Knutson et al., 2001; Schultz, 2002), with pleasurable primary rewards delivered unexpectedly (Berns et al., 2001), and also risk-taking traits. For instance, the ventral striatal response has been linked to sensation-seeking scores (Bjork et al., 2008), risk-taking propensity (Galvan et al., 2007), and psychopathic personality traits (Buckholtz et al., 2010). Consistent with several previous findings (Bolla et al., 2003; Critchley et al., 2001; Fukui et al., 2005; Hsu et al., 2005; Tanabe et al., 2007; Xue et al., 2008), we found that risk-processing specifically activated the dmPFC. Our MACM and RSFC results indicate that risks activated insula, striatum, and dmPFC. According to the somatic markers hypothesis, the dmPFC is a structure that triggers somatic states from secondary inducers (e.g., the uncertainty of choice; Bechara and Damasio, 2005). The dmPFC may receive information from the anterior insula to signal the riskiness of situations (Yu and Zhou, 2009). Thus, the activation of dmPFC may help one to register the conflict and uncertainty resulting from risky decisions. After all, this region is well known for conflict detection (Carter et al., 1998; Venkatraman and Huettel, 2012; Venkatraman et al., 2009).

Our sub-analyses revealed important modulating effects of the type of contrast/reward. For instance, the observation of distinct involvement of brain regions in encoding risk levels linearly and in detecting high versus low risk extends our knowledge of perceiving different levels of risk. Compared with the risks involving gains alone, neural responses of games that involved both gains and losses engaged stronger in left anterior insula, which provides some insight into risk perception regarding sensitivity to rewards. Interestingly, previous studies have shown that descriptive and experienced risk exert different influences on age-related effects on decision making (Defoe et al., 2015; Mata et al., 2011). We did not find a robust difference in convergence for the two types of risk after balancing the number of papers in the two datasets using resampling. Interestingly, when compared with ambiguity, descriptive risks and experienced risks did generate slightly different results. However, no significant difference was found after resampling, suggesting that different contrast patterns were mainly driven by the unbalanced sample size. This finding suggests that it is important to take sample size into account when running contrast analysis with unbalanced samples. Nevertheless, the distinction between descriptive and experienced risk is an intriguing topic for future empirical neuroimaging research.

4.3. Distinct neural profile for ambiguity-processing

Compared with decision-making under risk, the right dlPFC and IPL were found to be active in the processing of ambiguity. During decision making, dlPFC activity may reflect the trade-off between risk and rewards (Gowin et al., 2013), and the calculation of the subjective utility of the option (Camus et al., 2009; Christopoulos et al., 2009; Fiore and Gu, 2019; Holper et al., 2014; Huettel, 2006; Trepel et al., 2005). Additionally, dlPFC has been implicated in executive functioning, specifically cognitive control (Bari and Robbins, 2013; Mohr et al., 2010; Yuan and Raz, 2014), which regulates goal-orientated and flexible behaviours (Schonberg et al., 2012). Both structural and functional alterations of the dlPFC have been found in patients with internet gaming disorder (Ko et al., 2015; Liu et al., 2014; Yuan et al., 2017), substance addiction (Bolla et al., 2005; Qi et al., 2015), and behavioural addiction (Crockford et al., 2005). Activations in the lateral prefrontal cortex in response to expected utility were predicted by ambiguity preference (Huettel et al., 2006; Taya, 2012). However, the intervention of dlPFC using transcranial direct current stimulation (tDCS) were not able to produce consistent effects on risk-taking behaviours. Enhancing activity of dlPFC led to decreased risk-taking behaviours in the BART, while disrupting dlPFC activity was also associated with reduced risk preference (Fecteau et al., 2007; Wen et al., 2019). A large-scale study with 117 samples failed to find any significant effect of tDCS on dlPFC on risk-taking in the BART (Russo et al., 2017). Meanwhile, our meta-analysis suggests that dlPFC does play a crucial role in resolving ambiguity.

The IPL has previously been reported to encode decision-making involving ambiguous outcomes (Huettel, 2006; Paulus et al., 2003a; Roy et al., 2011). These two parietal regions may engage in computing and coding probability (Dehaene et al., 1999; Platt and Glimcher, 1999; Verney et al., 2003; Volz et al., 2003). As the likelihood of reward is unknown in ambiguous situations, participants may actively seek probability information. Surprisingly, our study did not find any concordance between regions that researchers claimed to encode ambiguity, such as amygdala and OFC (Hsu et al., 2005; Wang et al., 2017; Yang et al., 2017). The roles of these regions in the processing of ambiguity remain to be further examined.

4.4. Brain networks in risk and ambiguity

Functional decoding analysis results provide information about the functional characterization of brain regions. Our functional decoding findings indicate that putamen is associated with reward, dlPFC is associated with reasoning and working memory, while the right anterior insula is linked with inhibition, spatial cognition, fear and pain. It is worth noting that data-driven functional decoding is based on automated text-mining and may reveal additional possible relevant functions of the identified regions. These functions are not exclusive and may also not be relevant functions of these regions in this particular meta-analysis.

Both MACA and RSFC further showed overlapping and distinct brain networks involved in risk and ambiguity. Specifically, seed-based analysis (ROI seeds: right putamen and left anterior insula) revealed a coactivation pattern with dlPFC, IFG and ventral striatum for risk-associated regions. This pattern suggested that risk-processing related regions were connected to brain networks commonly involved in reward and salience processing (Andrews-Hanna et al., 2010). Such connectivity pattern has previously been shown to be related to risk-seeking performance and might be a potential neural marker for addctive behaviours (Andrews-Hanna et al., 2014; Deza Araujo et al., 2018; Zhang and Volkow, 2019). For ambiguity processing, the left IFG, right IPL, right dlPFC ROI seeds exhibited a coactivation pattern with the right anterior insula, dlPFC

Table 10
Average contribution of each experimental for significant clusters on Mix gambles in risk-processing.

Cluster name	Study	N	Task	Contrast	No. of foci	Average contribution (%)
Anterior Insula (R)	Gorka et al. (2016)	37(10)	Slot-machine Task	Risky > Safe	6	20.59
	Helfinstein et al. (2014)	108 (N.A)	Balloon analogue Risk Taking Task	Risky > Safe	7	22.23
	Preuschoff et al. (2006)	19(10)	Card gambling guessing	Risky Parametric	9	10.17
	Rigoli et al. (2019)	23(10)	Two-choice Risk Task	Risky > Safe	7	16.26
	Wright et al. (2013)	24(6)	Wheel of fortune Task	Risky > Safe	18	12.31
	Xue et al. (2010)	14(7)	Modified Cups Task	Risky > Safe	8	1.57
	Zhang et al. (2019)	25(11)	Modified Cups Task	Risky > Safe	10	16.87
Anterior Insula (L)	Gorka et al. (2016)	37(10)	Slot-machine Task	Risky > Safe	6	11.55
	Helfinstein et al. (2014)	108 (N.A)	Balloon analogue Risk Taking Task	Risky > Safe	7	13.23
	Mohr et al. (2010b)	19(8)	Risk Perception and Investment Decision Task	Risky > Safe	2	7.05
	Paulus et al. (2003b)	17(11)	Risky-Gains Task	Risky > Safe	5	11.67
	Preuschoff et al. (2006)	19(10)	Card gambling guessing	Risky Parametric	9	4.48
	Rigoli et al. (2019)	23(10)	Two-choice Risk Task	Risky > Safe	7	11.88
	Roy et al. (2011)	23(8)	Wheel of Fortune Task	Risky > Safe	51	17.09
	Stern et al. (2014)	17(8)	Incentive Card Task	High > Low Risk	4	0.93
	Wright et al. (2013)	24(6)	Wheel of fortune Task	Risky > Safe	18	13.3
	Zhang et al. (2019)	25(11)	Modified Cups Task	Risky > Safe	10	8.8
DmPFC (R)	Behrens et al. (2007)	18(9)	Probability-Tracking Task	Risky Parametric	1	1.48
	Brevers et al. (2016)	15(6)	Iowa Gambling Task	Risk > Ambiguity	5	16.75
	Gorka et al. (2016)	37(10)	Slot-machine Task	Risky > Safe	6	2.99
	Helfinstein et al. (2014)	108 (N.A)	Balloon analogue Risk Taking Task	Risky > Safe	7	16.79
	Kuhnen and Knutson (2005)	19(9)	The behavioural Investment Allocation Strategy Task	Risky Parametric	2	18.91
	Labudda et al. (2008)	16(8)	Game of Dice Task	High > Low risk	6	6.94
	Minati et al. (2012)	22(12)	Gambling Task	Risk > Ambiguity	5	0.27
	Roy et al. (2011)	23(8)	Wheel of Fortune Task	Risky > Safe	51	17.94
	Wright et al. (2013)	24(6)	Wheel of fortune Task	Risky > Safe	18	17.7
	Xue et al. (2010)	14(7)	Modified Cups Task	Risky > Safe	8	0.11

and IPL, suggesting that ambiguity-processing related regions interact with brain networks implicated in cognitive control and loss aversion (Leech et al., 2012). These findings further illustrate that brain networks linked to risk and ambiguity are overlapping but also distinct.

4.5. Comparison with previous studies

Unlike the previous meta-analysis, we only included data from healthy adults, removing the potential confounding effects of mental disorders on brain activity (Krain et al., 2006). Krain et al.'s study also used a loose threshold (FDR thresholded at $p < 0.05$, with a cluster extent threshold of 8 voxels), which may lead to false positive activity results. Another study (Mohr et al., 2010) only focused on risk in general and lumped all uncertainty related studies together, leaving the key difference between risk and ambiguity unknown.

The average contribution of studies that we reported for each resulting cluster, provide a confirmation that our results were not biased by the most dominant experiment (all MDE < 30%). Our study used a stringent threshold and performed LOEO and resampling analysis to validate our primary analysis. Such validation analysis is critical as ALE analysis is sensitive to outliers in the dataset, and whether two datasets are balanced also influences ALE contrast. In addition to identifying concordance in risk and ambiguity, we further examine the brain networks linked with key regions in risk and ambiguity using brain connectivity analysis and functional decoding. For instance, our functional decoding results show that risk-processing tends to engage positive emotions and gain/reward, whereas decisions under ambiguity tend to involve reasoning, inhibitory control and negative emotions. However, functional decoding results should be interpreted with caution due to the possibility of the reverse inference from neuroimaging data. Importantly, subsequent investigations of potential moderators further illustrate that the type of reward or contrast (linear regression versus binary contrast) also modulates brain activity patterns associated with risk.

4.6. Limitations and future directions

Several limitations related to the current meta-analyses should be discussed. First, similar to other meta-analysis studies, our meta-analysis included a variety of tasks. Heterogeneity in experimental designs, uncertainty manipulation, and statistical inference procedures inevitably would influence the results. We dealt with this issue by conducting a sub-analysis on studies that are more homogeneous. The pooled analysis of published results on risk/ambiguity did reveal brain regions that are robustly and consistently involved in decision making under risk/ambiguity. The inclusion of different types of contrasts, e.g., risk vs. no risk and risk vs. ambiguity may also potentially influence the conjunction and contrast analysis. Some experimental designs are tailored to examine the risk vs. ambiguity and ambiguity vs. risk contrasts. In this case, these studies have already controlled for the shared components. Although including these two types of contrasts in our meta-analysis may reduce the power to detect regions that are involved in both risk and ambiguity, our main findings still hold after removing these contrasts. Second, for tasks that require learning the reward probabilities, such as IGT and BART, the risk is not explicitly known as outcome probability, and risk-related contrasts are probably influenced by ambiguity. To participants, the early stage of experiments tends to reflect ambiguity processing, where they had not yet learnt enough information to estimate the outcome probability. In contrast, the late phase tends to reflect risk decisions after participants learned the outcome probability. In many studies, the neural analysis did not separate early and late phases. We believe the ambiguity levels between two risk conditions are comparable and the effects of ambiguity will be cancelled out in the high risk>low risk contrast. Nevertheless, strictly speaking, the neural results of these studies may still somehow be influenced by ambiguity. Future empirical research should systematically manipulate risk and ambiguity in learning tasks. Third, coordinate-based meta-analyses of neuroimaging data uses only the spatial coordinates and sample sizes from published studies. The image-based approach using full statistic images may be adopted in future studies to account for both within- and between-study variance if relevant summary images are available (Poldrack and Gorgolewski, 2017). Fourth, the limited number of studies included in this meta-analysis did not allow us to synthesise and compare neural signals associated with different stages of risk-processing, e.g., anticipation vs. decision-making stages. Nevertheless, we showed that lumping together studies in both stages and focusing only on the decision-making stage generated similar results, suggesting that our findings are not biased by the stage of decision-making. Future research should take distributed and interrelated representations of risk valuation into account. Fifth, MACM analyses that assess occurrences of activation across experiments, represent correlations of activation between brain regions rather than changes of BOLD signal in voxels over time-series (Eickhoff et al., 2011). Given that functional decoding provides statistical inference on the type of tasks that evoke activations in the same region (Henson, 2006), revealing the indirect association, results from functional decoding should therefore not be over-interpreted. Lastly, our meta-analyses only included studies on healthy participants. Abnormal risk-taking behaviours are characteristics of many psychiatric disorders (Balogh et al., 2013; Strawbridge et al., 2018). It would be interesting to further examine the neural correlates of risk-processing in patients with psychiatric disorders, such as addiction, depression and psychosis.

Conclusion

In conclusion, understanding the neural bases of processing risk and ambiguity is important because decision-making under uncertainty is a fundamental activity in daily life. The current results indicate that processing of risk and ambiguity engage overlapping yet distinct brain regions. Our findings suggest that processing of risk is more strongly associated with reward-related regions, whereas processing of ambiguity is more strongly associated with executive control and calculation. These results may improve our understanding of altered decision-making under uncertainty in psychiatric disorders by disentangling the neural correlates of processing risk and ambiguity (Buckholtz et al., 2017; Fujino et al., 2017). These stereotaxic maps may guide future neuroimaging research on ambiguity aversion and risk-taking.

Credit Statement

Shuyi Wu.: Data curation, Methodology, Writing- Original draft preparation. Sai Sun: Writing- Reviewing and Editing. Julia A. Camilleri: Methodology. Simon B. Eickhoff: Supervision, Software, Writing-Reviewing and Editing, Validation.: Rongjun Yu: Conception, Writing-Reviewing and Editing, Supervision.

Data and code availability statement

The data and/or code used in the study are available upon direct request.

Declaration of Competing Interest

None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2021.118109.

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