Review article

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Multivariate decoding of fMRI data

Towards a content-based cognitive neuroscience

Introduction

Within the last two decades, functional magnetic resonance imaging has become one of the most widely used tools in human cognitive neuroscience (for an overview of fMRI see e.g., [1]). FMRI measures the neural activity in a 3-dimensional grid of roughly 1–3 mm resolution. Most cognitive neuroscience studies measure blood oxygen level dependent (BOLD) signals, which indirectly reflect processes in the underlying neural tissue [2]. One of the major features—but also challenges—of neuroimaging is that it yields very complex, high-dimensional data sets including up to several hundred thousand voxels. Traditionally, the data have been analyzed with a "mass univariate" general linear model approach [3] that assesses task-related modulation for each voxel separately. One limitation of this approach is that the high-dimensional fMRI data contain substantial information in the patterning and correlation between voxels. Such information is neglected by these more traditional mass univariate analyses.

In recent years, multivariate pattern analysis (MVPA) techniques (also referred to as multivariate decoding, ◘ **Fig. 1**) have been introduced to the field of fMRI [4, 5, 6] (for recent overviews over several multivariate techniques and their applications see e.g., [6, 7, 8, 9]). Multiple classification algorithms are put to use, spanning from k-nearest neighbor classifiers, Gaussian naïve Bayes classifiers, linear discriminant analysis, linear and non-linear support vector classification and regression to ridge regression (for discussion of different classifiers see e.g., [9]). These techniques use part of the data to train a classifier to predict which out of several specific cognitive states a subject is in (e.g., whether she/he was preparing to do a left or right hand movement). The classifier is then tested on a remaining, *independent* test data set, to see how accurately it can classify this data. This results in a measure of classification accuracy that can be used to tell how well the classifier can predict a cognitive state from human brain activity (◘ **Fig. 1**). Classifiers can be applied to whole brain data or can be used to make predictions from a subset of voxels such as a region of interest (ROI). An unbiased way to map over the entire brain the information contained in local patterns of brain activity is the so called searchlight technique [10, 11]: A small region is defined around every single voxel in the brain, and then classification is performed using the multivariate data within this small region. Finally, every voxel gets assigned the classification performance of its local surround which results in a map of decoding information across the entire brain.

This review contains a selective summary of cognitive neuroscience studies that use fMRI and MVPA that have been performed in the past few years by our research group. In a first part, several studies are presented for applications of classification techniques in cognitive neuroscience. These studies use MVPA techniques to address questions of *content* in brain activity, such as for example which specific visual stimulus a person was visually imagining. In the second part, a series of methodological developments are shown

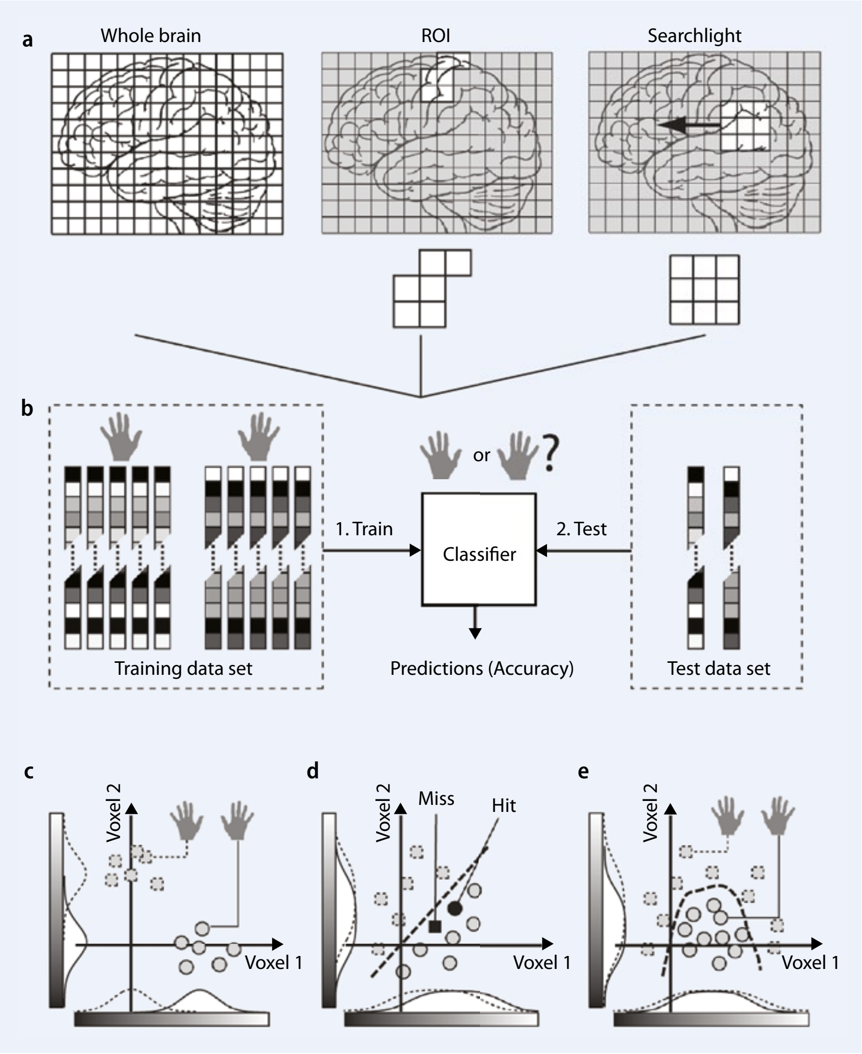

Fig. 1 ▲ Multivariate decoding of fMRI signals. fMRI measures brain activity in a three-dimensional grid of voxels. For simplicity only two dimensions are illustrated here. **a** Pattern (feature) vectors for multivariate analysis can be extracted from the whole brain, regions of interest (*ROI*) or using a searchlight. **b** Repeated measurements of two task conditions (e.g., left vs. right hand movement) are split into a training and test data set. A classifier is first trained (*1. Train*) on the training data. Then, the classifier is used to predict (*2. Test*) the label (task condition) of the independent test data pattern vectors. The different dimensions of the vector can be considered as axes of an N-dimensional coordinate system where N is the number of voxels. **c**, **d**, **e** Illustration of a classifier in a two-dimensional space (adapted from [5]). The marginal distributions are plotted on the corresponding axes. **c** In the easiest case, it is possible to separate the repeated measurements of both stimulus classes (*circles* and *squares*) on either of the two axes. The marginal distributions do not overlap. **d** In this case, the marginal distributions are largely overlapping precluding classification based on the activity of one voxel alone. However, by taking into account the activity in both voxels it is possible to fully separate the multivariate responses to both stimuli using a linear decision boundary. After learning the decision boundary on a training data set, a new measurement can be made that can be used to test the ability of the classifier to correctly predict the label of an independent measurement. If the multivariate response falls on the correct side of the decision boundary this will result in a *hit* ("correct"), if it falls on the wrong side this will result in a *miss* ("error"). **e** In some cases, a linear decision boundary is not sufficient, and a non-linear decision boundary is required

that go beyond simple classification and extend current methods. In particular, we will illustrate how multivariate decoding can be used to study information flow between regions and even between brains, how 3D-searchlight decoding methods can be constrained to the cortical surface (2D) to more accurately capture the cortical anatomy, and how classifiers can be used for medical diagnostics. The studies summarized in this review have all been conducted within the same research laboratory and thus do not have the aim to provide an extensive overview over MVPA approaches in fMRI. Rather they constitute a biased selection of topics in which MVPA have been shown to provide important insights into cognitive neuroscience questions, often giving answers that could not have been obtained with standard techniques.

Decoding cognitive content from multivariate fMRI data

Visual imagery and perception share substrates in the brain

One important application of classifiers is to study the coding of perceptual content in visual brain regions. Whereas traditional fMRI approaches have focused on overall activity in visual brain regions and on retinotopy, multivariate pattern analysis allows us to study how specific visual stimuli are encoded in detailed activity patterns of the visual brain. In one study [12], we investigated the cortical encoding of object categories in object-selective cortical regions. Importantly, we also assessed to which degree the codes for specific objects are similar for imagined visual stimuli ("imagery") as opposed to physically presented images ("veridical perception"). The ability to conjure up images of the world in the "mind's eye" is a hallmark of human cognition and allows for the potentially infinite flexibility in thinking [13]. The experience of imagery is similar to the experience of veridical seeing: It can be described by the content, i.e. "what" one sees, and the location, i.e. "where" one sees it in the visual field. This suggests that imagery and perception might share common substrates in the brain. We tested this hypothesis in an fMRI experiment [12]. For this, we first identified regions of the visual brain that respond preferentially, but not exclusively to the perception of specific categories: scenes, body parts, and faces. These are called category-selective regions. Then, subjects either saw images of the aforementioned categories presented either left or right of fixation, or they were cued auditorily to visually imagine a picture in the same locations (Fig . 2a, b). We then extracted the activation patterns evoked during imagery and veridical perception in order to test whether patterns were similar for specific contents and locations using multi-voxel pattern classification (Fig. 2c). Indeed, imagery and perception shared a common substrate for the preferred category in all category selective regions. Interestingly, in most category-selective regions we were also able to decode the non-preferred categories, suggesting that information is not strictly localized within individual processing modules, but instead is broadly distributed across visual areas. Next, we investigated whether imagery and perception share a common substrate of location in the visual/imaginary field by training a classifier on imagery and testing it on veridical perception (Fig. 2d). Imagery classifiers could be used to predict veridical perception in medial, but not lateral category-selective regions, suggesting that imagery and perception share a common substrate only in the medial visual brain.

Perceptual learning in prefrontal cortex

An important question for the encoding of visual contents in the brain is whether the representations exhibit stability across time, even though human perception exhibits substantial plasticity and learning. For decades the dominant view in visual perceptual learning was that behavioral improvements during perceptual learning are accompanied by changes in early visual representations. Thus, one might expect that the neural code for visual contents changes across learning as well. However, this view was mainly based on psychophysical data [14] and received only inconsistent support form neural recording studies (for an overview see [15]). In contrast, more recent work suggests that perceptual performance improvements might rather be related to changes in higher decision-making areas beyond sensory cortex [16]. Similarly, reward-related learning in general is accompanied by activity changes in decision-making areas such as the anterior cingulate cortex (ACC). In principle, areas that update and represent action values in reward-based tasks could also integrate sensory information in the context of perceptual decision making. In a study [15], we used a model-based neuroimaging approach in combination with multivariate decoding to test the idea that visual perceptual learning can be accounted for by reinforcement learning involving changes in higher decision-making areas. We trained 20 subjects on an orientation-discrimination task with explicit performance feedback over the course of four days (Fig. 3a, b). Behavioral improvements in perceptual choices (Fig. 3c) were well explained by a reinforcement learning model for perceptual decision making (Fig. 3d). Learning in this model is accompanied by an enhanced read-out of sensory information, thereby establishing noise-robust representations of decision variables that form the basis for perceptual choices (Fig. 3e). To identify activity patterns that encode information about stimulus orientation (x) and model-derived decision variables (DV), we used information mapping techniques (searchlight decoding in combination with multivariate support vector regression models). We found sensory evidence (orientation) encoded in early visual cortex (Fig. 3f, left) by idiosyncratic activity patterns (Fig. 3f, middle). However, these representations did not change with training (Fig. 3f, right). Only activity patterns in the ACC tracked learning-related changes in the model-derived decision variables. Importantly, distributed activity patterns in the ACC contained significantly more information about the model-derived decision values (that changed with learning) than the mere stimulus orientation (Fig. 3g). These results provide strong evidence for perceptual learning related changes in higher cortical regions and show that perceptual learning can be accounted for by a reinforcement process. This means that perceptual and reward-based learning are likely to be based on a common neurobiological mechanism. Furthermore, our results show that the neural code for visual contents does not change across perceptual learning in adults, thus the representations exhibit temporal stability.

Abstract

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Multivariate decoding of fMRI data. Towards a content-based cognitive neuroscience

Abstract

The advent of functional magnetic resonance imaging (fMRI) of brain function 20 years ago has provided a new methodology for non-invasive measurement of brain function that is now widely used in cognitive neuroscience. Traditionally, fMRI data has been analyzed looking for overall activity changes in brain regions in response to a stimulus or a cognitive task. Now, recent developments have introduced more elaborate, content-based analysis techniques. When multivariate decoding is applied to the detailed patterning of regionally-specific fMRI signals, it can be used to assess the amount of information these encode about specific task-variables. Here we provide an overview of several developments, spanning from applications in cognitive neuroscience (perception, attention, reward, decision making, emotional communication) to methodology (information flow, surface-based searchlight decoding) and medical diagnostics.

Keywords

Functional neuroimaging · Multivariate decoding · Information flow · Perceptual learning · Decision making

Bottom-up saliency in natural scenes

When an object is different than its surround it is said to visually “pop out”. Such salient stimuli automatically capture our attention, an effect that is believed to be driven by sensory stimulus features in a “bottom-up” fashion. This could be a fast moving object that pops out from other, stationary objects, or a colorful object surrounded by gray ones. Computational models [17] typically assume that the saliency is represented as a map that encodes how salient the visual input at each position in the visual field is. After such a graded saliency map is calculated, a winner-take-all (WTA) mechanism can then be used to select the most salient (i.e. “in-

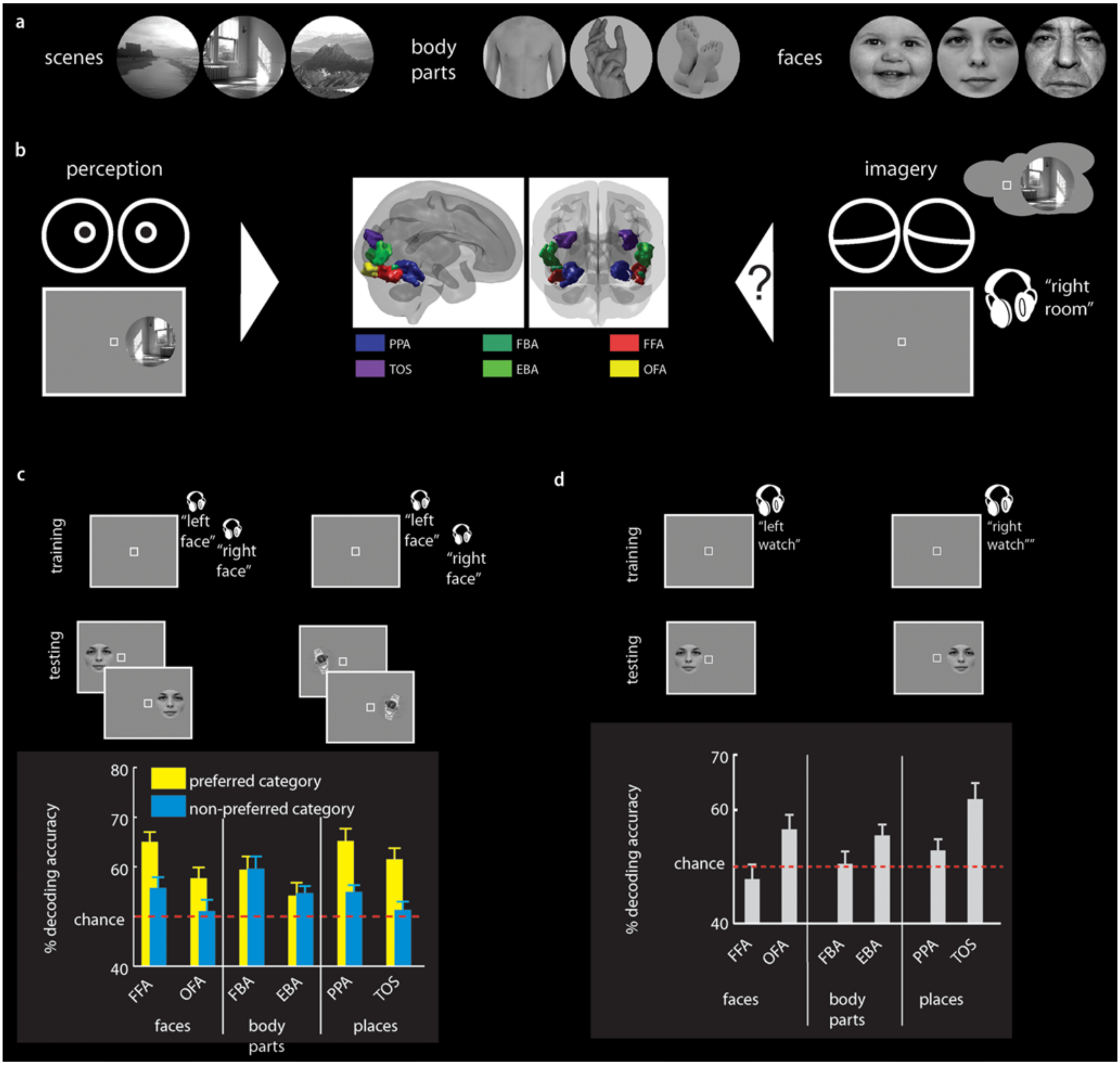

Fig. 2 ▲ Investigating shared substrates of imagery and perception in the human brain with fMRI. **a** Participants veridically perceived or imagined specific exemplars of scenes, body parts or faces. **b** Perception of the aforementioned categories preferentially activates focal regions in the visual brain: the parahippocampal place area (*PPA*) and transverse occipital sulcus (*TOS*) for scenes, the fusiform body area (*FBA*) and extrastriate body area (*EBA*) for body parts, and the fusiform face area (*FFA*) and occipital face area (*OFA*) for faces. Our experimental question was whether imagery of the same categories would activate these regions in a manner similar as perception for both content ("what is seen") and location ("where in the visual field something is seen"). For this, subjects either saw or imagined the images shown in **a**. **c** A support vector machine was trained to distinguish between brain activation patterns evoked during imagery of different categories, and tested on brain patterns evoked during perception. All category selective regions contained above-chance information about their preferred category, and most also about their non-preferred categories. **d** A support vector machine was trained to distinguish between locations during imagery and tested the classifier on locations of veridically perceived images. The results indicate that imagery and perception share a common substrate in medial, but not lateral category-selective regions. Figure adapted from [12]

teresting") position to which covert or overt attention is subsequently guided. In one study [18], we were interested in whether graded saliency and WTA-thresholded saliency representations could be separately identified in the human brain. Subjects viewed 100 different black and white photographs in a rapid event-related fMRI paradigm. Because we were interested in the bottom-up properties of the stimuli and not the ensuing attention shifts themselves we ensured that subjects' attention was diverted away from the pictures using a demanding fixation task at the center of the screen. For each of the

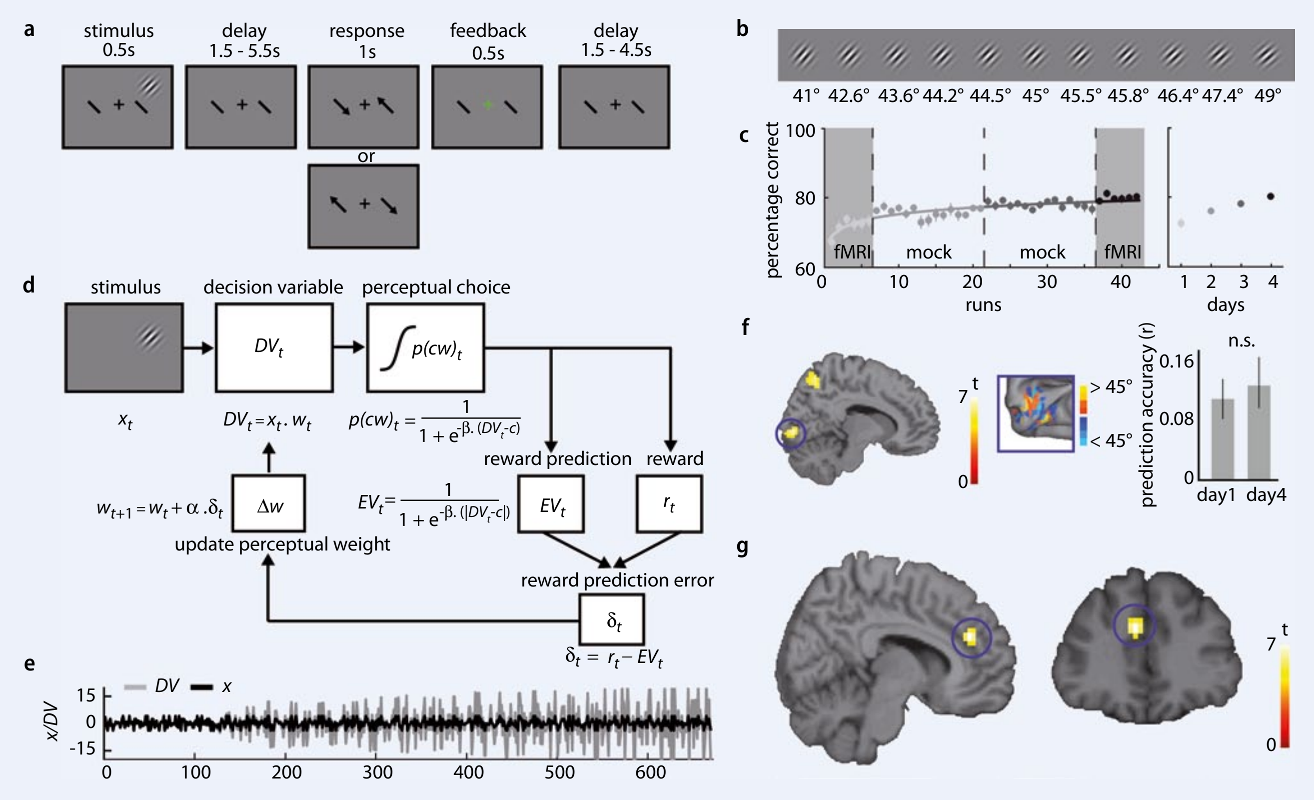

Fig. 3 ▲ Perceptual learning in the prefrontal cortex (PFC). **a** Orientation discrimination task. **b** Subjects had to indicate whether a presented orientation is tilted clockwise or counter-clockwise from 45°. **c** Performance improved over the four training days. **d** A reinforcement learning model for perceptual decision making was designed to account for subjects' behavioral improvements. **e** Model derived subjective evidence (*DV*, *gray line*) increased over training, whereas stimulus orientation (*x*, *black line*) remained in the same range. **f** Objective stimulus orientation was encoded in the left lower visual cortex (*left*), by distributed patterns of activity (*middle*). However, information about stimulus orientation did not change across learning. **g** A region in the medial PFC contained significantly more information about the model-derived subjective evidence than the objective stimulus orientation. Figure adapted from [15]

100 images we calculated the spatial saliency map using the SaliencyToolbox for Matlab [19]. We then averaged the saliency values individually for each of the four quadrants, excluding the center to which attention was directed. This gave us *graded saliency* values individually for the four quadrants of each image (◘ **Fig. 4c**). According to a computational model [17], the graded saliency would then be thresholded by a WTA process, marking the quadrant with the highest saliency value as the most salient position (*WTA saliency*). Using a parametric univariate analysis for the fMRI data the graded saliency representation was found to be encoded in visual cortex and posterior intraparietal sulcus (pIPS). A subsequent multivariate pattern classification additionally revealed that WTA-thresholded saliency was encoded in distinct regions in anterior intraparietal s ulcus (aIPS) and the frontal eye fields (FEF) (◘ **Fig. 4g**). In conclusion, bottom-up attentional signals from the unattended surround appear to be processed automatically and reach higher visual areas such as aIPS and FEF. These latter areas could then be involved in initiating potential shifts of attention.

Non-topographic representations of visual spatial attention in prefrontal cortex

Attention is not just directed by salient, attention-grabbing features in our environment. Instead, humans have the ability to *voluntarily* direct their attention to spatially defined targets in the visual field. Several cortical regions are known to spatially represent the visual field in topographic maps and could thus be candidates for top-down attentional control signals. Importantly, these topographic representations become less pronounced when moving from early visual areas toward extra-occipital areas. We employed multivariate pattern analysis to identify cortical representations of the currently attended position in the visual field. Importantly, using a decoding approach we did not have to rely on the assumption that attention would be encoded in a spatial map. Instead, we would be able to identify even spatially anisotropic distributions of cells that code for specific attended subregions of the visual field. In an fMRI study [20], participants shifted their visuospatial attention toward cued targets (◘ **Fig. 5a**). By applying a searchlight-technique on the cortical surface ([10], ◘ **Fig. 5b**, ◘ **Fig. 13**) we identified topographically organized representations in the occipital and posterior parietal cortices which are in line with previous "attention-o-topic" mapping studies. Impor-

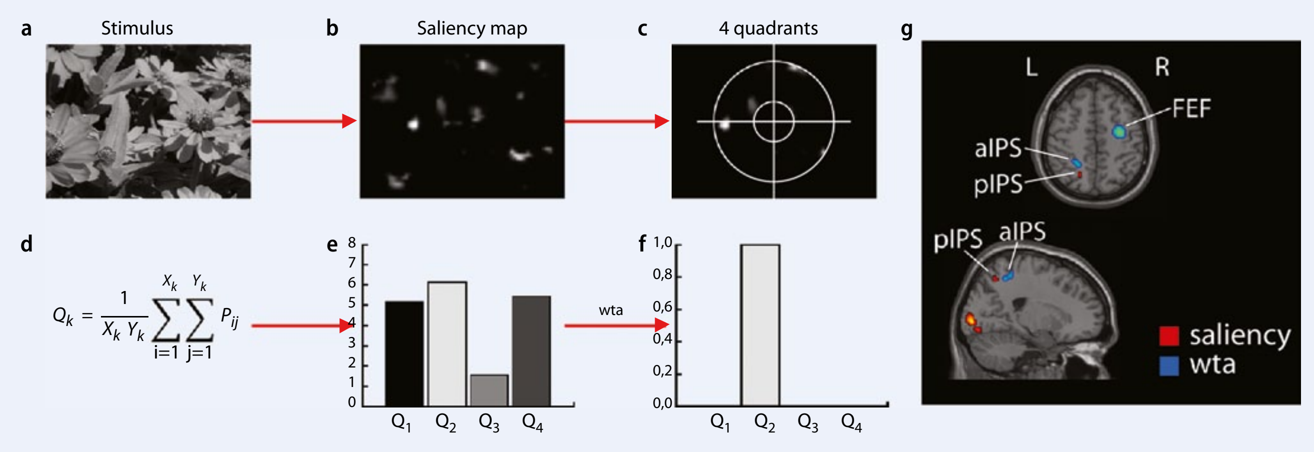

Fig. 4 ▲ Bottom-up saliency in natural scenes. **a–f** Methods: **a** 100 different photographs of natural scenes were presented. **b** For each photograph the corresponding saliency map was calculated. **c** Saliency values in 4 quadrants were used for all further analysis. The center was excluded because subjects attended to this position for the fixation task. **d** For each quadrant the average saliency was calculated. **e** One parameter defined graded saliency for each quadrant. **f** Graded saliency was thresholded by a winner-take-all (*WTA*) process which marked only the most salient quadrant. **g** Results: Graded saliency correlated with activation in visual cortex and posterior IPS (*red*). The most salient quadrant (*WTA saliency*) could be decoded from local spatial activation patterns in anterior IPS and FEF (*blue*) (results are thresholded at $p < 0.05$, FWE corrected). *aIPS* anterior intraparietal sulcus, *pIPS* posterior intraparietal sulcus, *FEF* frontal eye fields. Figure adapted from [18]

tantly, additional information on the current position of visuospatial attention was also found in non-topographically organized areas in the human prefrontal cortex, including the right middle frontal gyrus and the right ventrolateral prefrontal cortex (▣ **Fig. 5c**). This shows that beyond topographically organized areas, information on visuospatial attention is represented in spatial but non-topographic neuronal activity patterns in the human frontal cortex.

Decoding perceptual decisions and perceptual guessing

In bright daylight, we can normally identify objects in our environment effortlessly. There is sufficient sensory information for us to make perceptual judgments. However, under difficult viewing conditions (darkness, fog) information is reduced such that stimuli can be difficult to see. We might even have the impression to be purely guessing. This raises two important questions: (1) What happens to neural object representations under low visibility? Are the sensory representations of objects disrupted, or are other processes responsible for our inability to see stimuli under difficult viewing conditions (e.g., say signals in prefrontal cortex, see above)? (2) Which signals are used to determine our choices, and how do these signals differ under high and low visibility? For example, even under low visibility our choices might still be based on a read-out of noisy sensory signals. Alternatively, a dedicated guessing system could determine the choices under low visibility, involving a different brain network. We addressed this question by using a multivariate pattern searchlight classification and tested which brain regions were predictive for stimuli and choice outcomes under different visibility conditions [21]. In this fMRI study, participants made perceptual choices for images from three categories: pianos, chairs and non-object noise images (▣ **Fig. 6b**). On each trial participants were presented with brief, repeated mask–target–mask sequences, which either did not strongly affect image visibility (high visibility condition) or rendered the images close to invisible (low visibility condition) (▣ **Fig. 6a**). A classifier was then trained on activation patterns from all brain regions for each visibility condition separately to predict stimuli and choice outcomes from activation patterns from independent data. First, we found that *object-related* information in object-sensitive brain region lateral occipital complex (LOC) was absent for invisible stimuli. Second, we were interested in decoding the choices from brain activity. Patterns of brain signals from LOC predicted choices only under high visibility (green regions, ▣ **Fig. 6c**). This most likely reflected the successful use of visual information for decision making. Choices under low visibility, when participants reported to be guessing, however, could not be predicted from sensory regions. Instead, a region in medial posterior parietal cortex, mainly located in the precuneus, became predictive for choices under low visibility (red regions, ▣ **Fig. 6c**). Taken together, our study revealed a double-dissociation of predictive regions for perceptual decisions under high and low visibility. Interestingly, the medial posterior parietal region, which was predictive for perceptual guessing, highly overlapped with a region that we recently found to be involved in free decision making [22] (see next section) and that has been discussed to be involved in a variety of self-related higher cognitive functions [23]. We concluded that this region might be related to a mechanism for ‘internal’ decision making, when external input falls short on providing sufficient information to overcome a decision conflict.

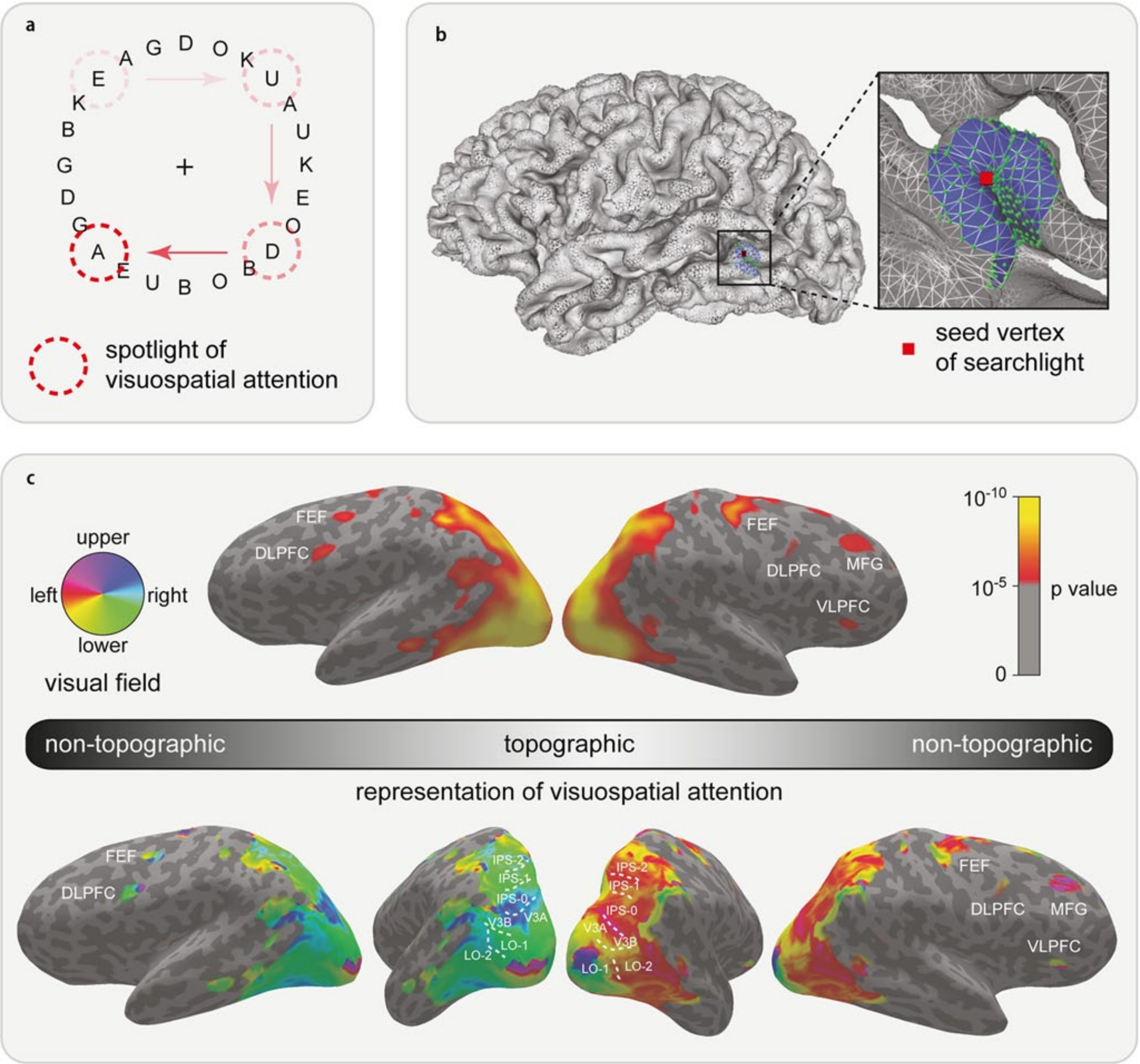

Fig. 5 ▲ Spatial but non-topographic representation of visual attention in human frontal cortex. **a** Participants covertly shifted visual attention toward cued locations in the visual field. **b** fMRI-BOLD activity patterns of localized "searchlights" on the cortical surface were screened for the content of information on the current location of visuospatial attention. **c** A widespread network of cortical areas contains information on the current location of visual attention. The representation is globally changing from a topographic encoding in occipitoparietal to a non-topographic encoding in prefrontal areas. Figure adapted from [20] and [10]

Decoding free decisions from human brain activity

Decision making does not always involve making judgements about sensory stimuli. As human beings, we are constantly making conscious decisions between different choices, sensory and non-sensory. For example, we take for granted that our voluntary actions are the result of conscious decisions for specific intentions. However, this subjective impression is increasingly challenged by recent findings suggesting that our free decisions to act may not be totally governed by the conscious mind, but may be initiated by unconscious mental processes before conscious decisions are made. Using fMRI and multivariate analysis we showed that specific motor decisions could be decoded from unconscious brain activity even up to a few seconds before subjects were consciously aware of their decisions [22]. Subjects freely and spontaneously decided to make either a left or right button press and subsequently reported via a letter-stream clock the time when they first made the conscious motor decision (◘ **Fig. 7a**). MVPA techniques revealed that, a few seconds *before*

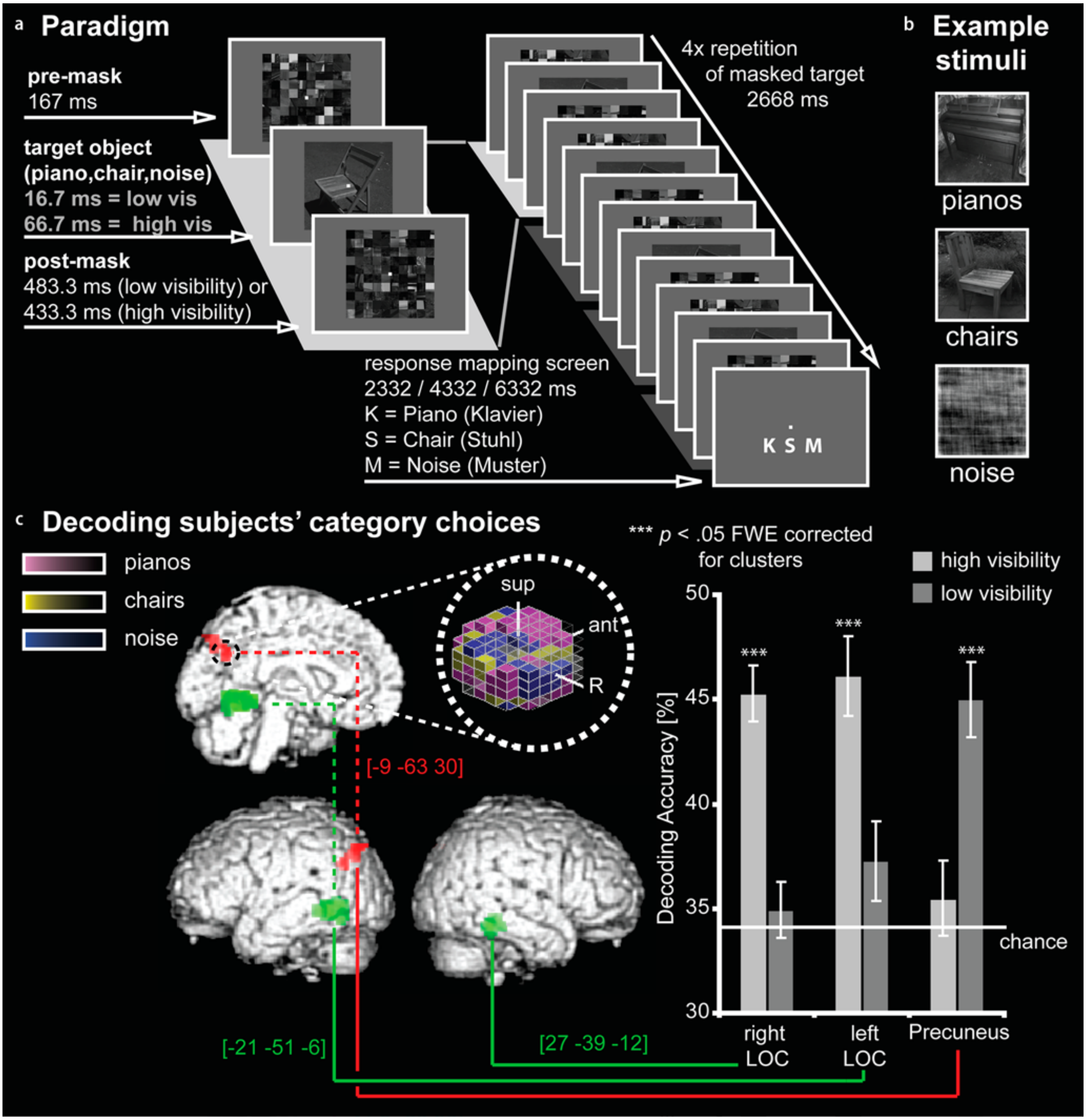

Fig. 6 ▲ Experimental paradigm and results from perceptual decision experiment. **a** In the scanner, brief, flashed mask–image–mask sequences were presented to 14 participants, rendering target images either visible or close to invisible. The associations between response buttons (operated with fingers of the right hand) and categories were pseudo-randomized on a trial-by-trial basis in order to de-correlate category choices and motor responses. **b** Images from three categories (pianos, chairs, noise; one example image is displayed) were presented in the scanner, half in each visibility condition. **c** Whole-brain searchlight decoding results for category choices. Choices under high visibility could only be decoded from bilateral LOC (*green*). Perceptual guesses under low visibility could only be decoded from precuneus (*red*). Chance level was 33% for three categories. For better visualization, results are displayed with $p < 0.0001$ uncorrected. Example of one individual spatial activation pattern is shown with voxels responding preferentially to one category being color-coded and scaled for illustration. Figure adapted from [21]

the decision was consciously made, high-level control regions including lateral and medial frontopolar cortex, and precuneus/posterior cingulate, already began to encode the content of the upcoming decision in their local spatial patterns of activity, despite showing no overall increase in fMRI signal (◘ **Fig. 7b**). Once the decision reached conscious awareness, re-

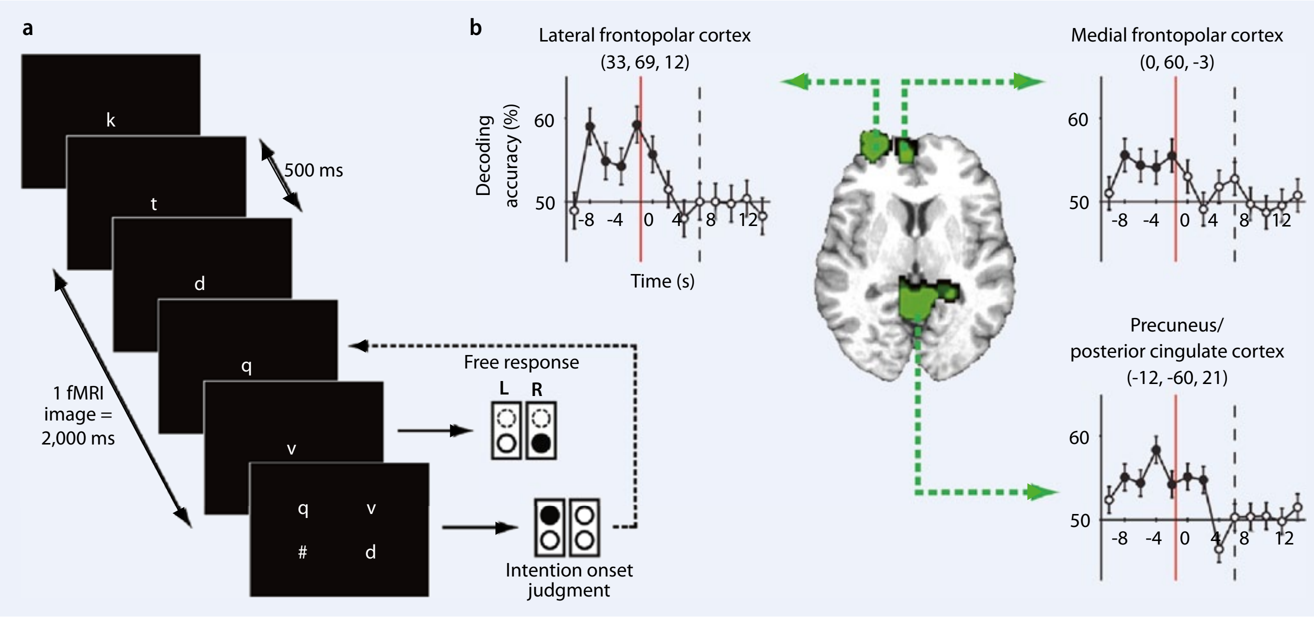

Fig. 7 ▲ Decoding motor intentions before they reach conscious awareness. **a** Measuring the onset time of conscious motor intentions. Subjects spontaneously decided to press either the left or right button (freely chosen) with their corresponding index finger while viewing a random letter string updated every 500 ms. Subsequently, they selected from a response-mapping screen the letter presented when they first made the conscious decision, thus revealing the onset time of the conscious motor intention. **b** Brain areas where the specific outcome of the motor decision could be decoded before reaching conscious awareness. The accuracy with which the subject's free choice to press the left or right button could be decoded at separate time points from the spatial patterns of brain activity in each region are depicted in the graphs (*solid line* left axis; *filled symbols* significant at $p < 0.05$; *open symbols* not significant; *error bars*, s.e.m.; chance level is 50%). In each graph, the earliest time at which the subjects became aware of their choices is indicated by the *vertical red line*, while the *dashed vertical line* shows the onset of the next trial. Figure adapted from [22]

gions that were involved in executing the voluntary motor action including the pre-SMA, SMA and bilateral primary motor cortices began to encode the content of the motor decision. In contrast, the timing of the decision could be decoded from the pre-SMA and SMA a few seconds before reaching awareness, but not from the frontopolar and precuneus/posterior cingulate regions. Thus, there appears to be a double dissociation in the very early stages of motor intention formation, between brain regions shaping the specific decision outcome and those determining the timing of the decision. In the light of these and other related findings, the causal relationship between conscious will and brain processes might need to be re-examined.

The compositionality of rule representation in prefrontal cortex

In most of our actions, we are not free to choose between different options. Instead, the tasks we perform require us to follow specific rules for successful behavior. Rules are widely used in everyday life to organize actions and thoughts in accordance with our internal goals. One of the questions we were interested in was how specific rules are encoded in brain activity. At the simplest level, single rules can be used to link individual sensory stimuli (e.g., seeing a green pedestrian light) to their appropriate responses (cross the road). However, most complex tasks require the combination of multiple rules, to form compound rule sets (walk on green, stop on red). It is known that frontal and parietal cortices are involved in rule representation. However, a fundamental issue still needs to be clarified: Is the neural representation of compound rules *compositional*, i.e. built on the neural representation of their constituent rules (◘ **Fig. 8a**)? In one experiment [24], we asked subjects to remember and apply either single or compound rules (◘ **Fig. 8b, c**). Multivariate searchlight decoding was applied to fMRI data collected in the phase between cue presentation and target onset (◘ **Fig. 8b**). We found that information on the visual features of the cues was encoded in the occipital and lateral parietal cortices, while information on the active compound rules was stored in lateral parietal and ventro-lateral prefrontal cortex (◘ **Fig. 8d**). Furthermore, in ventrolateral prefrontal cortex, it was possible to decode the compound rules by training classifiers only on the single rules they were composed of. These findings suggest that the lateral parietal cortex is involved in translating the cues into their meaning. Only the latter information is then made available to the infero-lateral frontal cortex, which maintains it during the delay. Furthermore, and most importantly, these findings show for the first time that the code used to temporarily store rule information in the lateral prefrontal cortex is compositional. Compositionality of the code helps explain the flexibility of human behaviour, because it allows us to build together more and more complex behaviour patterns from simple constituent building blocks.

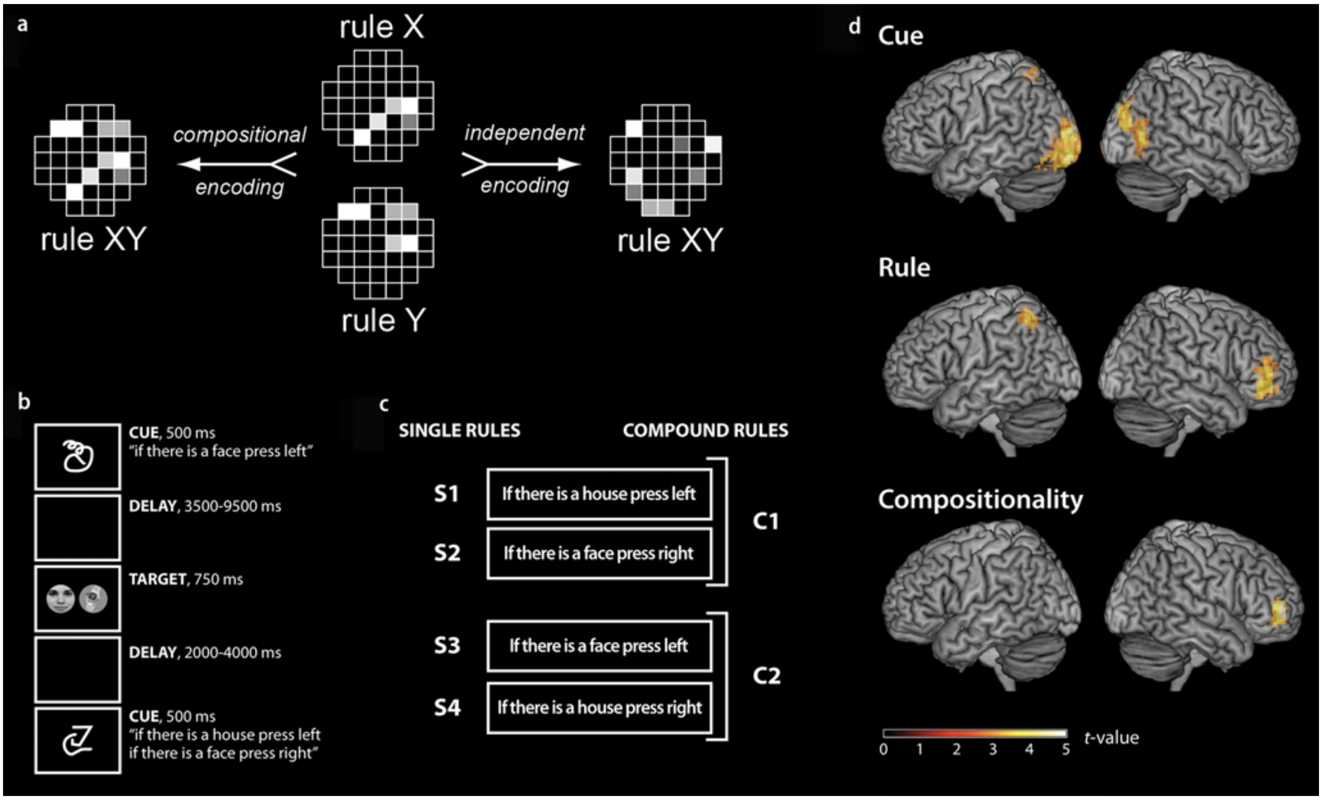

Fig. 8 ▲ Compositionality of rule representation. **a** Alternative ways of coding complex rules. *Middle* Examples of activity patterns coding for two single rules: Rule X and Rule Y. Two alternative coding possibilities for the compound rule formed by Rule X and Rule Y are illustrated. The first possibility (*left*) is to use a compositional code so that the pattern coding for the Rule XY would be the combination of the patterns for Rule X and Rule Y alone. An alternative possibility (*right*) is to use an independent code so that the pattern for Rule XY would be unrelated to the patterns for Rule X and Rule Y. **b** Timeline of a single trial of the experimental paradigm. At the beginning of each trial, the cue informed the subjects which rule had to be followed. After a delay, the target image was presented. Subjects had to apply the active rules to the target stimuli and derive the correct response as fast as possible. **c** Rules used in the experiment. Four single rules (*left side*, *S1–S4*) and two compound rules (*C1–C2*) were used. Compound rules are formed by two single rules, e.g., C1 = S1 + S2. **d** Regions where it was possible to decode from local patterns of activation which cue was presented (*top*) and which compound rule was active in a specific trial (*middle*). *Bottom* Compositionality analysis: Regions in which it was possible to decode which compound rule was active by only relying on information extracted from the local patterns of activation associated with single rules. Figure adapted from [24]

Decoding reward value

Objects in our environment are not just defined by their physical stimulus characteristics, but also by the reward we expect to obtain from them. Previous electrophysiological work in non-human primates has suggested that reward value is encoded by different populations of positive and negative value-coding neurons in the orbitofrontal cortex (OFC) (see e.g., [25]). A neural coding of reward value should fulfill two criteria. First, the neural representation should *generalize* across different sensory cues predicting the same reward. That is, a given reward value should be represented by the same neural code when predicted by different sensory stimuli. Second, according to reinforcement learning theory [26], value should be represented by the same neural code independently of whether a certain reward value is *expected* or actually *received*. To examine whether the neural response patterns in the human OFC fulfill these criteria, we designed an experiment in which different sensory cues predicted different amounts of reward (◘ **Fig. 9a,** [27]). Subjects were trained to associate the sensory cues and the rewards prior to fMRI acquisition. Using cues defined by two feature dimensions (color, rotation direction) allowed us to dissociate reward representations from representations of the individual sensory feature dimensions. For each subject, only specific conjunctions of color and rotation were predictive of a certain reward value, whereas the individual sensory features were not correlated with the reward value (◘ **Fig. 9b**). We then decoded high vs. low value cues independent of the sensory features of the cues, by training and testing a linear support vector classifier (SVC) on sensory cues with the same expected value but orthogonal sensory properties. This analysis revealed a network of regions including the medial OFC where activity patterns that encode high vs. low expected values are independent of the sensory features.

Furthermore, by training and testing the classifier on data from the anticipation and reward receipt phase, respectively, we identified a region in the medial OFC where neural coding of reward value is independent of whether the reward is anticipated or actually received

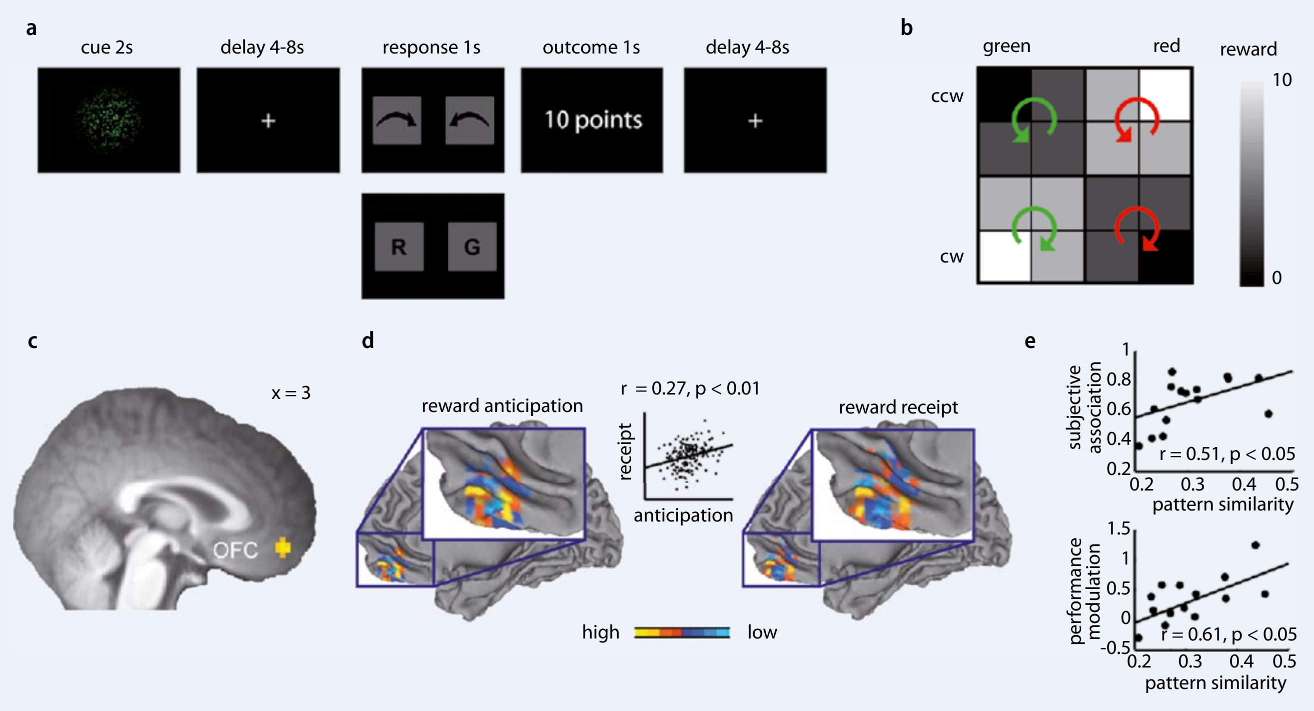

Fig. 9 ▲ Neural coding of expected reward value. **a** Simple reward providing decision-making task. **b** XOR association between sensory cues (color, rotation direction) and reward magnitude. **c** In the medial OFC neural coding of reward value is independent of whether the reward is anticipated or actually received. **d** Example of idiosyncratic value-coding response patterns during anticipation (*left*) and reward receipt (*right*). Activity in *yellow areas* increases with increasing value (positive value-coding) and activity in *blue areas* decreases with increasing value (negative value-coding). Both patterns are significantly correlated across space within-subject (*middle*). **e** The similarity of the value-coding response patterns during expectation and receipt is significantly related to explicit (*top* subjective association) as well as implicit measures of reward learning (*bottom* performance modulation). Figure adapted from [27]

(▣ **Fig. 9c**). Inspection of the support vector weights suggested that highly idiosyncratic and detailed patterns of increasing and decreasing activity are associated with increasing reward value. This patterning is in line with a population coding model of expected value where positive and negative value-coding neurons are randomly distributed in the OFC, as suggested by single-unit recordings in monkeys [25]. The patterns coding for value during anticipation and receipt of reward were similar within each subject, suggesting an idiosyncratic neural code for value (▣ **Fig. 9d**). Moreover, across subjects, the degree of this similarity was correlated with explicit and implicit measures of how well subjects had learned the association between the sensory cues and the reward value (▣ **Fig. 9e**). This suggests that reward learning involves the emergence of neural response patterns during anticipation that code specific reward outcomes. In a follow-up experiment, we directly tested this idea and showed that patterns during reward anticipation and reward receipt become similar during the acquisition of reward predictions [28].

Neural encoding of future consumer choices for attended and unattended products

An important question is how the rewarding nature of objects guides our behavioral choices, as when we act upon preferences to different consumer objects. When subjects actively evaluate products and explicitly deliberate about purchasing, neural activation has previously been shown to reflect immediately *following* purchase decisions [29]. In one study [30], we aimed to demonstrate that brain responses predict subsequent purchase decisions even when attention is diverted from products and when consumer choices are currently not under consideration. To address these issues, two independent groups of subjects were presented with pictures of real cars while their brain activation was measured using fMRI. Subjects in the '*high attention*' group were instructed to actively evaluate each car on a four-point scale and to report their judgments after the picture of the car was removed (▣ **Fig. 10a**). Subjects in the '*low attention*' group, on the other hand, were engaged in a demanding visual fixation task that was unrelated to the images of cars simultaneously presented in the background (Fig. 10*b*). Thus, products were either task-relevant and closely attended to (high attention condition) or task-irrelevant and presented outside the focus of attention (low attention condition). After scanning, subjects of both groups had to state their willingness to buy each of these cars or not (▣ **Fig. 10c**). Notably, during scanning, subjects in *both* experimental groups were not aware that they were going to be asked to make purchase decisions later on. A searchlight decoding approach was then applied to investigate whether activation patterns obtained during product exposure predicted these individual consumer choices. We

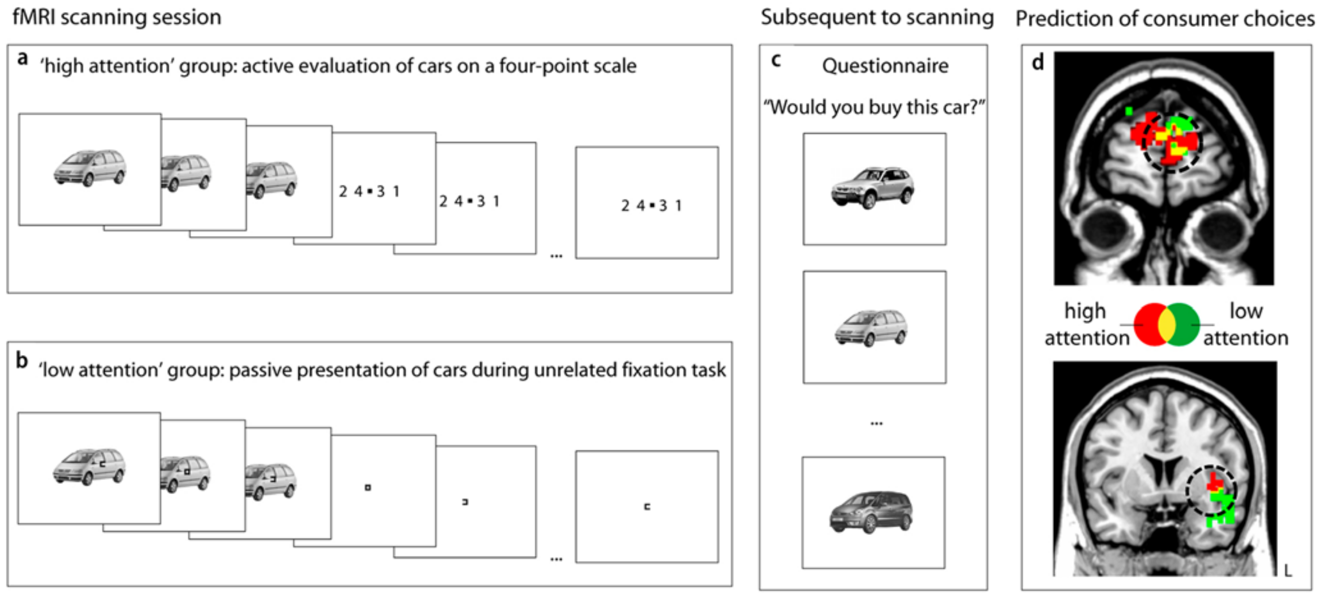

Fig. 10 ▲ Decoding of subsequent consumer choices from spatial activation patterns in the brain. Using fMRI, we measured brain responses for two independent groups of subjects that were presented with single pictures of cars. **a** Subjects in the 'high attention' group evaluated each car and reported their judgment via a button press. Thus, subjects in this group closely attended to products. **b** Subjects in the 'low attention' group performed a visual attention task (i.e., button presses to the left- or right-side opening of a fixation square) that was unrelated to the pictures of cars and diverted attention from these products. **c** Outside the scanner, subjects were again presented with the images of these cars and were asked to report their willingness to purchase this particular car. Till then, subjects of both groups were not informed that consumer choices would be required. **d** Multivariate pattern classification was applied to identify brain regions that predict these consumer choices. We found that activation patterns in the mPFC (*top*) and the insula (*bottom*) contained information on individuals' purchase decisions subsequent to scanning ($p < 0.05$, FWE corrected). Importantly, this was found to hold true for both experimental groups (*red* 'high attention' group; *green* 'low attention' group; *yellow* overlap of predictive regions across groups; *L* left hemisphere). Figure adapted from [30]

found that activation patterns in the medial prefrontal cortex (mPFC) and the insula reliable predicted subsequent consumer choices in the 'high attention' and the 'low attention' group (▣ **Fig. 10d**). Moreover, the predictive information (i.e. decoding accuracy) in these brain regions was comparable for conditions of high and low attention processing. These findings indicate that the brain automatically processes consumer products when purchase decisions are currently not under consideration and allows for neural predictions of economic decisions. Strikingly, our results indicate that such a prediction of consumer choices based on functional brain responses does not depend on attentional processing of consumer items.

Multivariate analyses of information flow and advances in decoding

As outlined in the previous sections, multivariate decoding provides a highly useful tool to study the encoding of highly specific sensory and cognitive representations. In the following section we will present work that allowed us to advance the methodological aspects of this research field.

Cortico-cortical receptive fields between topographically organized brain regions

The processing of information in the brain relies on the interaction between different cortical regions. Although fMRI measurements provide us with the spatial resolution to look at the fine-grained structure within cortical regions (e.g., the topographic organization of visual areas), to date, interactions between different brain regions in humans have mostly been studied by considering the *average* regional activity and thereby neglecting the fine-grained structure of brain activity. Standard functional connectivity measures can be extended substantially by investigating how precisely the activity of individual voxels in one region depends on the pattern of activity in a different region. We used a multivariate support vector regression (▣ **Fig. 11a**) to predict activity of voxels in visual area V3 from the activity in area V1 [31]. This approach results in two interesting measures: First, the prediction accuracies allow us to assess the amount of information that one brain area provides about activity in a remote part of the brain. Second, the distribution of the weights is a measure of the spatial pattern within that brain region (V1) that best predicts activity in the other (V3). In the visual cortex, this is equivalent to studying *cortico-cortical receptive fields* (CCRF), i.e. estimating which parts of one visual area contribute most to the activity of individual voxels in a different area. As expected, the average CCRF between V1 and V3 was clearly in line with the underlying visuotopic anatomical connectivity [32] when subjects were viewing a visual stimulation (▣ **Fig. 11b**, left). Interestingly, even

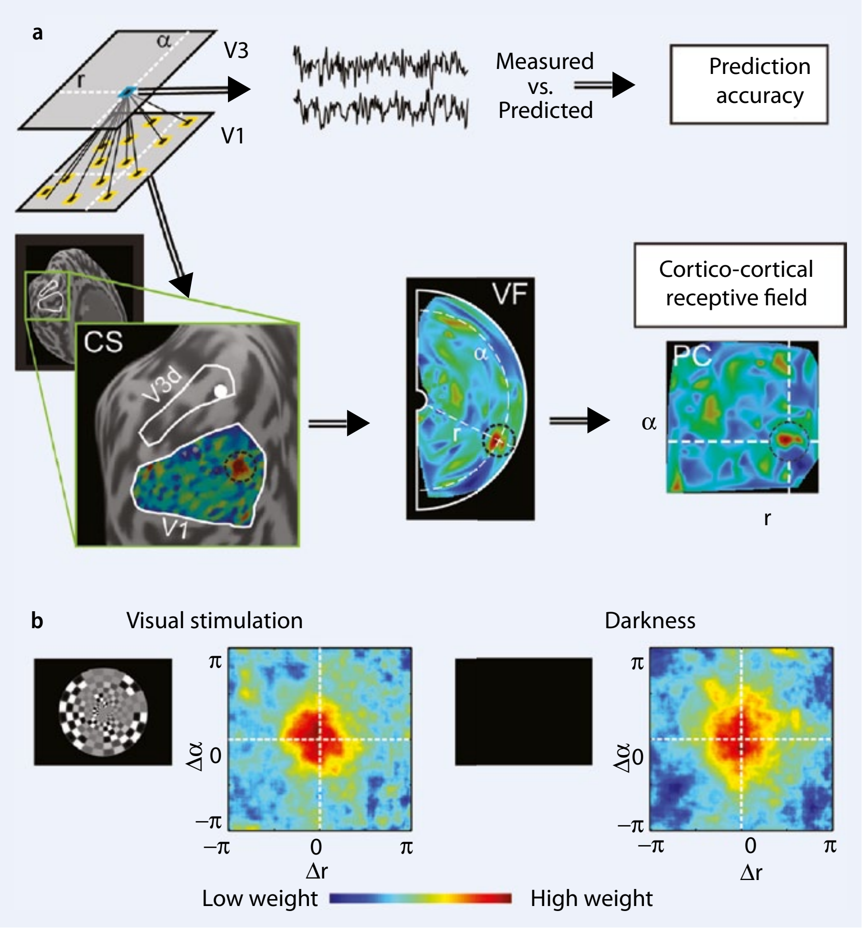

Fig. 11 ▲ Measuring cortico-cortical receptive fields (CCRF) with fMRI. **a** A support vector regression was used to predict the activity of a voxel in V3 (*blue*) from the pattern of activity of all voxels (*yellow*) in V1. The predicted and measured activity in V3 can be compared to obtain a measure of prediction accuracy. The distribution of the weights of the multivariate regression defines a CCRF. The CCRF can be illustrated on the cortical surface (*CS*) as well as in the visual field (*VF*), or it can be depicted in polar coordinates (*PC*). **b** The CCRF for all voxels in V3 was averaged to obtain the average topographic connectivity structure between V1 and V3. The connectivity structure under visual stimulation (*left* average of 4 subjects) and in complete darkness (*right* average of 8 subjects) is shown in relative polar coordinates Δr and Δα between V1 and V3. *Black panels* illustrate the visual stimulation. Figure adapted from [31]

in complete darkness, when subjects were blindfolded and had their eyes closed, the functional connectivity between the visual areas V1 and V3 was clearly retinotopic (▣ **Fig. 11b**, right). This finding suggests that spontaneous fluctuations are precisely orchestrated between remote brain regions despite the fact that most anatomical connections within cortex are local. The use of multivariate decoding techniques to study connectivity patterns and information flow between remote brain regions opens an interesting new window to look at interactions in large scale brain measurements obtained with fMRI.

Flow of affective information between communicating brains

Information-based imaging does not only allow for tracking the stream of information flow *within* individual brains, it also permits to image the flow of information *between* brains of individuals. Such between-brain flow of information occurs continuously whenever two individuals interact. One mechanism that has been proposed to play an important role in this transmission of information between individuals is common coding and resonance. The idea is that when one individual perceives another one's communicative signals (facial expression, gesture or movement, but also speech) this will activate an internal mirror representation of the underlying neural activity in the perceiver's brain, which will allow the perceiver to understand the sender's inner state, to anticipate the sender's behavior and to react appropriately. In other words, first-hand experience and perceiving someone else's experience is thought to activate similar neural networks, creating a 'shared space' between senders and perceivers of information. We used information-based imaging to investigate how such 'shared spaces' might emerge between senders and perceivers engaged in facial communication of affect ([33], ▣ **Fig. 12a**). In a first step, we used a simple univariate decoder to identify brain regions that carry *similar emotion-specific information* in both the sender's and the perceiver's brain. The decoder was trained to identify the sender's affective state based on the level of activity in a given voxel in the sender's brain. We then tested whether the same decoder could identify the communicated affective state from the level of activity in the same voxel in the perceiver's brain. This revealed a distributed 'shared network' for affect in the sender's and perceiver's brain including temporal, parietal, insular and frontal brain regions (▣ **Fig. 12b**). Next, we used a time-resolved multivariate decoder to investigate the temporal dynamics of information transmission from the sender's to the perceiver's brain. The decoder was trained on the sender's brain activity in the shared network at a given time point and then tested on the perceiver's brain activity at all other time points of a trial. Inspection of these time courses indicated that information from the sender's brain was dynamically reflected in the perceiver's brain, with a significant delay in the perceiver's brain. Interestingly, the delay between information in the sender's and the perceiver's brain decreased over time, possibly indicating some 'tuning in' of the perceiver with the sender (Fig. 12c). Our data support current theories of intersubjectivity by showing that emotion-specific information is encoded in a very similar way in the brains of senders and perceivers engaged in facial communication of affect. Furthermore, they show that in-

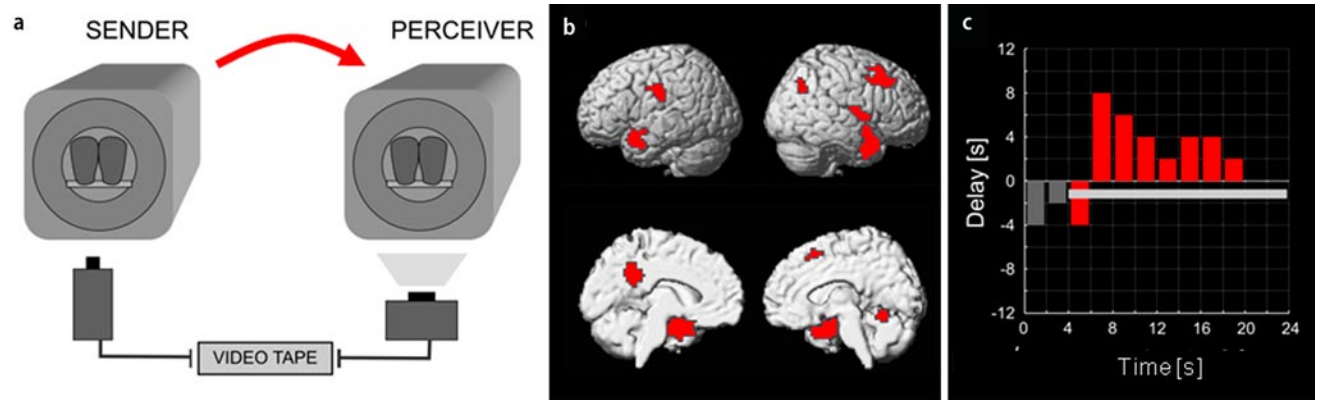

Fig. 12 ▲ Information flow between communicating brains. **a** Experimental design. Communication partners (romantic couples) were told that they would be scanned simultaneously and that one of them (the perceiver) would see the other (the sender) throughout scanning via a video camera. The sender (the female partner) was asked to submerge herself into a specific emotional situation and to facially express her emotional feelings. The perceiver (the male partner) was uninformed about the sender's task and asked to try to feel with the sender. In fact, the sender's facial expression was videotaped during scanning and shown to the perceiver when he was scanned immediately after scanning of the sender had been completed. **b** Brain regions that carry similar emotion-specific information in the sender's and the perceiver's brain. Voxels in which a decoder solely trained on the sender's brain activity could successfully (significantly better than chance) predict the communicated affect from the perceiver's brain activity are highlighted ($p < 0.01$, corrected at cluster level). **c** Decrease of the temporal delay between information in the sender's and in the perceiver's brain during an emotional period. 0s indicates the beginning of a 20s-emotional period. Figure adapted from [33]

formation within this network is successively transferred from the sender's brain to the perceiver's brain (with a substantial delay in the perceiver's brain), eventually leading to what has been called a 'shared space' of affect [34].

Cortical surface-based searchlight decoding

Specific information about cognitive processes can be assessed by analyzing the local voxel patterns of fMRI signals with multivariate pattern classification. In order to localize these patterns and therefore map the information distributed in the brain, three-dimensional (3D) searchlight methods are commonly used, in which spherical sub-volumes of the fMRI measurements are extracted and their distributed information analyzed consequently [11]. To further improve the pattern localization, we proposed a cortical surface-based alternative to the 3D-searchlight technique [10], see also [35]. Surface-based searchlights are constructed according to distance along the cortical sheet—the intrinsic metric of cortical geometry—instead of Euclidean distance as in 3D-searchlights (◘ **Fig. 13a, b**). Using a paradigm in which the category of visually presented objects is decoded, we com-

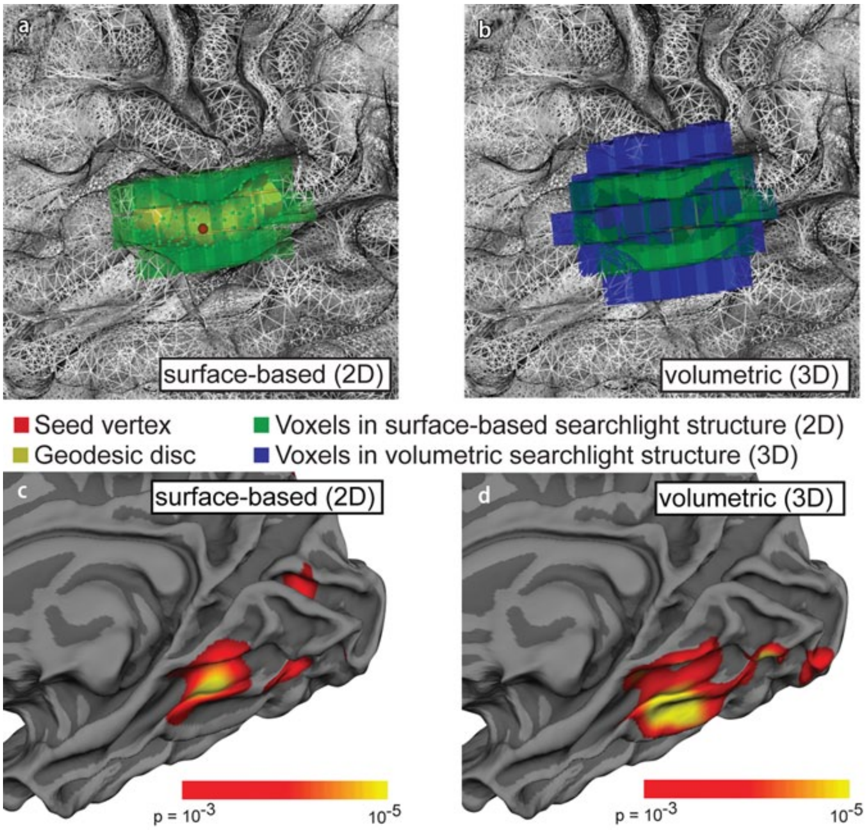

Fig. 13 ▲ Comparison of surface-based searchlight and 3D-searchlight. **a** Voxels (*green cubes*) in functional image space that are included in the surface-based searchlight. **b** Voxels (*blue cubes*) included in the volumetric searchlight (3D) at the same location. **c**, **d** Distributions of *p*-values from a group statistic comparing the decoding accuracy against chance level are shown on the averaged white matter surface. While the results obtained with the volumetric method **d** clearly spread through the fusiform gyrus, the surface-based method **c** locates the effects only within the collateral sulcus. Figure adapted from [10]

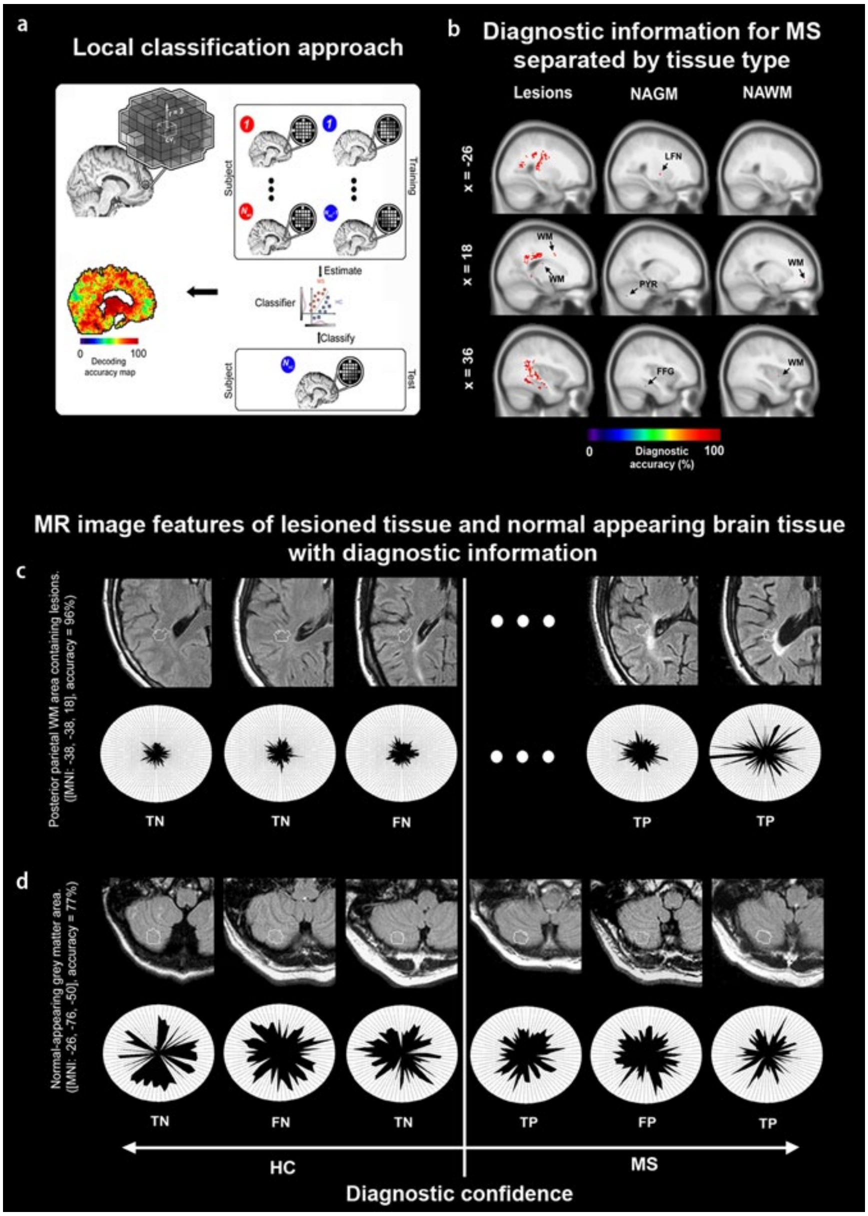

Fig. 14 ▲ Diagnostic information for MS in areas with lesions and normal-appearing brain areas. **a** Local classification approach: Local spherical patterns were extracted from individual MR images (*top left*) and used for classification between multiple sclerosis (*MS*) patients and healthy controls (*top right*). The result is a map, which indicates the decoding accuracy for each position in the brain (*bottom*). **b** Diagnostic information for MS separated by tissue type: Regions containing diagnostic information are depicted separately for lesion matter, normal-appearing grey matter (*NAGM*) and normal-appearing white matter (*NAWM*). *FFG* fusiform gyrus, *LFN* lentiform nucleus, *PYR* pyramis, *WM* white matter. **c, d** MR image features of lesioned tissue and normal-appearing brain tissue with diagnostic information: Examples of individual intensity patterns are shown for healthy controls (*HC*) and MS patients in native space, separately for lesioned tissue (**c**) and NAGM (**d**). The border of the pattern is marked by white contour lines and the polar plots below represent the distribution of intensity values within this pattern. Whereas for lesioned tissue the classifier actually uses lesion information, it is hard to see any difference by naked eye for NAGM. Therefore, the classifier uses information, which is kind of invisible to the human eye. Figure adapted from [36]

pared this method to the standard 3D-searchlight technique on decoding sensitivity and spatial specificity. Group analyses of decoding accuracies produced by both methods showed similar distribution of informative regions (▪ **Fig. 13c, d**). The surface-based method however achieved a higher spatial specificity with comparable peak values of significance. Our findings also show that a surface centered in the middle of the gray matter contains more information compared to the white-gray boundary or the pial surface. Furthermore, by extracting patterns that are local in cortical coordinates, the surface-based method avoids the accumulation of noise sources that lie outside of the gray matter and samples information from voxels that represent 'true' cortical neighbors.

Diagnostic information for multiple sclerosis in normal-appearing brain areas

Finally, pattern recognition algorithms can also be used for clinical diagnostics in disease classification from MRI signals. In a recent study [36], we used pattern-recognition techniques to investigate diagnostic information for multiple sclerosis (MS; relapsing-remitting type) contained in standard MR images. Specifically, we analyzed information contained in patterns extracted from lesioned, but also from normal-appearing grey and white matter (NAGM/NAWM) areas (▪ **Fig. 14**). Following the current diagnostic guidelines for MS [37], NAGM and NAWM measured by conventional MR do not contain diagnostic information. An experienced neurologist conducted a lesion mapping based on MR images acquired from 41 MS patients and 26 healthy controls with a turbo inversion recovery magnitude (TIRM) sequence. TIRM images were spatially normalized and segmented into three areas of homogenous tissue (lesions, NAGM and NAWM) based on the lesion mapping and templates from a brain tissue atlas. For each tissue-specific area, multiple local classification analyses were conducted based on voxel intensity patterns extracted from small spherical subregions of these larger areas to classify subjects into groups (MS patient vs. healthy control). The diagnostic accuracy obtained for each spherical subarea is considered as a measure of regional diagnostic information (▪ **Fig. 14**). For the analysis based on lesioned tissue, a posterior parietal WM area contained maximal diagnostic information (96% accuracy, $p<10^{-13}$). Among NAGM areas, a cerebellar region was maximally informative (84% accuracy, $p<10^{-7}$). Finally, a posterior brain region was maximally informative among

NAWM areas (91% accuracy, $p < 10^{-10}$). We found regions with diagnostic information for MS in lesioned, NAGM, and NAWM areas. Identification of information in NAGM and NAWM counteracts the common notion that standard MR techniques are too insensitive to capture disease-related tissue variations in normal-appearing areas of MS patients.

Conclusion

As our technical abilities to measure brain activity and brain structure increase, the analysis methods have to advance with them to make use of the multi-dimensional nature of the data. Here, we have presented several studies that have used MVPA and fMRI to study mental states in humans. While multivariate data analysis has substantially extended the scope of neuroimaging, there are still many open questions on how particular aspects of information are represented in the underlying neural circuits from which fMRI can only provide a very indirect measure. How is the distributed representation of objects, imagination, learning, perceptual choices, free choices or rules related to the topology of the underlying neural circuitry? It will be one of the challenges to narrow down the gap between the informative patterning measured in fMRI signals and the function and topology of neural structures whose activity gives rise to the fMRI signal. Overall, MVPA techniques applied to fMRI data have opened a new content-selective perspective for looking at human brain activity.

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