

Functional Neuroimaging of Belief, Disbelief, and Uncertainty

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Objective: The difference between believing and disbelieving a proposition is one of the most potent regulators of human behavior and emotion. When one accepts a statement as true, it becomes the basis for further thought and action; rejected as false, it remains a string of words. The purpose of this study was to differentiate belief, disbelief, and uncertainty at the level of the brain.

Methods: We used functional magnetic resonance imaging (fMRI) to study the brains of 14 adults while they judged written statements to be “true” (belief), “false” (disbelief), or “undecidable” (uncertainty). To characterize belief, disbelief, and uncertainty in a content-independent manner, we included statements from a wide range of categories: autobiographical, mathematical, geographical, religious, ethical, semantic, and factual.

Results: The states of belief, disbelief, and uncertainty differentially activated distinct regions of the prefrontal and parietal cortices, as well as the basal ganglia.

Interpretation: Belief and disbelief differ from uncertainty in that both provide information that can subsequently inform behavior and emotion. The mechanism underlying this difference appears to involve the anterior cingulate cortex and the caudate. Although many areas of higher cognition are likely involved in assessing the truth-value of linguistic propositions, the final acceptance of a statement as “true” or its rejection as “false” appears to rely on more primitive, hedonic processing in the medial prefrontal cortex and the anterior insula. Truth may be beauty, and beauty truth, in more than a metaphorical sense, and false propositions may actually disgust us.

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The capacity of the human brain to believe or disbelieve ostensible statements of fact (eg, “You left your wallet on the bar.” “That white powder is anthrax.”) is clearly part of its machinery for the initiation and control of complex behavior. Although references to “belief” states have appeared occasionally in the neuroscientific literature,¹ no one has characterized belief itself at the level of the brain.

Actions that require the influence of goals and logical inferences appear to be the product of “top-down” control of the neural pathways that connect ascending sensory processes with descending motor outputs. The prefrontal cortex (PFC) is considered to be the locus of such control. The ability of higher-order representations to guide behavior requires that the architecture of the PFC be multimodal, broadly integrative (of both exteroceptive and interoceptive states), and highly plastic.² The PFC may use its higher-order representations in the selection and guidance of behavior by biasing (and thereby resolving) the competition between lower-

level inputs.³ Neuromodulatory pathways also project from the brainstem to the PFC, offering a mechanism by which reward signals can strengthen the connections that underwrite successful, complex behaviors.² The signature of PFC damage is haphazard, inappropriate, and impulsive behavior, together with the inability to acquire new behavioral rules; the component actions of complex behavior are generally spared, but their purposeful integration invariably suffers.⁴ The human capacity for behavioral and emotional self-regulation continues to develop throughout adolescence, until the PFC becomes myelinated fully.⁵

Although there is substantial evidence of functional segregation within the PFC, the connectivity of this region suggests that functional networks have their nodes distributed widely, and thus may be difficult to resolve with current techniques of neuroimaging.⁶ Like other higher cognitive processes, belief and disbelief likely emerge from the activity of neural circuits that participate in a wide variety of cognitive and behavioral

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tasks. We would not expect, therefore, to find regions of the PFC dedicated exclusively to belief and disbelief. Nevertheless, it is reasonable to expect that these cognitive conditions are sufficiently distinct that they might be differentiated using functional magnetic resonance imaging (fMRI).

Subjects and Methods

Subjects

Fourteen adults (18–45 years old; 7 men, 7 women) gave written consent to participate in this study. All were right-handed native speakers of English. Subjects had no history of neurological or psychiatric disorders and were not taking any prescribed medication at the time of scanning. This study was approved by the Institutional Review Board at University of California Los Angeles (UCLA).

Experimental Design

While in the scanner, subjects were presented with a series of short statements through a video-goggle display worn over their eyes. After reading each statement, they were asked to evaluate its truth content with the press of a button, indicating “true” (belief), “false” (disbelief), and “undecidable” (uncertainty). The presentation of stimuli was self-paced. Each participant received 3 functional scans of 7 minutes (approximately 100 trials) in length. Because we were attempting to understand belief, disbelief, and uncertainty in a content-independent manner, subjects were presented with statements from many different categories: mathematical, geographical, autobiographical, religious, ethical, semantic, and factual. All statements were designed to be clearly true, false, or undecidable. For example:

Mathematical:

$(2 + 6) + 8 = 16$
62 can be evenly divided by 9.
 $1.2^{57} = 32608.5153$

Geographical:

California is larger than Rhode Island.
Wisconsin is on the West Coast of the United States.
Senegal borders Guinea.

Semantic:

“Gigantic” means “huge.”
“Devious” means “friendly.”
“Akrasia” means “weakness of will.”

Factual:

Most people have 10 fingers and 10 toes.
Eagles are common pets.
The Dow Jones Industrial Average rose 1.2% last Tuesday.

Autobiographical:

You have two sisters.
You were born in New York.
You had eggs for breakfast on December 8, 1999.

Ethical:

It is bad to take pleasure at another's suffering.
Children should have no rights until they can vote.
It is better to lie to a child than to an adult.

Religious:

A Personal God exists, just as the Bible describes.
There is probably no actual Creator God.
Jesus spoke 2,467 words in the New Testament.

An effort was made to balance each scan with respect to category content and response valence (“true,” “false,” or “undecidable”). Given the unpredictable nature of certain subject responses, however, strict balancing could not be achieved. The truth-value of some stimuli (especially in autobiographical, ethical, and religious categories) necessarily varied across subjects. It is unlikely, however, that this variation introduced a confound, because these individual statements could be judged “true,” “false,” or “undecidable” in any case; for example, the statement “You have brown hair” would be true for some subjects and false for others, but its truth-value could be easily assessed regardless. After scanning, subjects reviewed their recorded responses to all statements to ensure that they reflected their actual beliefs. Erroneous responses, or those statements that, on debriefing, could not be clearly evaluated by subjects were excluded from subsequent data analysis.

Scanning

All scanning was performed on a Siemens Allegra 3T scanner (Siemens, Milwaukee, WI). Each subject received three functional scans of approximately 7 minutes in length. Functional images were acquired in the anterior commissure–posterior commissure orientation using T2*-weighted echo planar scans (TR = 2500 milliseconds; TE = 50 milliseconds; flip angle = 90 degrees; field of view = 200×200 mm, slice thickness = 4 mm; number of slices = 21; interslice gap = 1 mm; bandwidth = 3,256 Hz/pixel). Anatomic images were acquired using a magnetization-prepared rapid gradient-echo sequence (TR = 2300 milliseconds; TE = 2.1 milliseconds; inversion time = 1,100 milliseconds; flip angle = 8 degrees; field of view = 256×256 mm; slice thickness = 1 mm; number of slices = 160; interslice gap = 0.5 mm; bandwidth = 320 Hz/pixel).

Analysis

All functional data were analyzed using FSL (FMRIB Image Analysis Group, Oxford University, Oxford, United Kingdom; <http://www.fmrib.ox.ac.uk/fsl>).^{7,8} We performed standard preprocessing (ie, slice timing correction, motion correction, brain extraction, spatial smoothing [using a 5 mm kernel], high-pass filtering, and prewhitening) before contrast modeling.

Stimuli were presented in inhomogeneous blocks to increase the probability of signal detection. For example, statements expected to be judged “true” were grouped together in blocks of five to seven, with occasional “false” and “undecidable” statements interleaved to ensure that the subjects remained on task. The same grouping applied to false and undecidable trials as well. For the purposes of data analysis, a

trial began the moment a statement appeared and ended with the subject's response.

Responses were then analyzed in an event-related manner. Individual judgments of "true" (belief), "false" (disbelief), and "undecidable" (uncertainty) were binned together across all stimulus categories. Our maps of blood oxygen level dependent (BOLD) signal changes were the result of pairwise contrasts between each of the three task conditions.

Results

Reaction time data were acquired on all subjects (mean reaction time for belief trials = 3.26 seconds; disbelief trials = 3.70 seconds; uncertainty trials = 3.66 seconds). The mean differences in reaction time, although small, were significant (t test for belief vs disbelief and belief vs uncertainty [$p(\text{belief} < \text{disbelief}) < 5 \times 10^{-11}$; $p(\text{belief} < \text{uncertainty}) < 5 \times 10^{-9}$]). The reaction times of disbelief and uncertainty trials did not differ significantly ($p[\text{uncertainty} < \text{disbelief}] < 0.2$).

Belief

Contrasting belief and disbelief (belief – disbelief), across all stimulus categories, yielded a discrete region of magnetic resonance imaging signal increase in the ventromedial prefrontal cortex (VMPFC) (Fig 1A), specifically in rostral regions of the *gyrus rectus* and the *orbitomedial gyrus*, predominantly in the left hemisphere. A similar pattern of signal changes was detected within certain of our category-specific contrasts (see Figs 1B, C).

Disbelief

The contrast between disbelief and belief (disbelief – belief) showed increased BOLD signal in the *left inferior frontal gyrus*, the *anterior insula* (bilateral) the *dorsal anterior cingulate*, (extending to the *superior frontal gyrus*) and in the *superior parietal lobule* (Fig 2).

Uncertainty

When compared with both belief and disbelief, judgments of uncertainty were associated with a positive signal change in the *anterior cingulate cortex* (ACC) (Fig 3) and decreased signal in the *caudate* (Fig 4).

Discussion

Several psychological studies^{9–11} appear to support Spinoza's conjecture¹² that the mere comprehension of a statement entails the tacit acceptance of its being true, whereas disbelief requires a subsequent process of rejection. Understanding a proposition may be analogous to perceiving an object in physical space: We seem to accept appearances as reality until they prove otherwise. Our behavioral data support this hypothesis, in so far as subjects judged statements to be "true" more quickly than they judged them to be "false" or "undecidable".

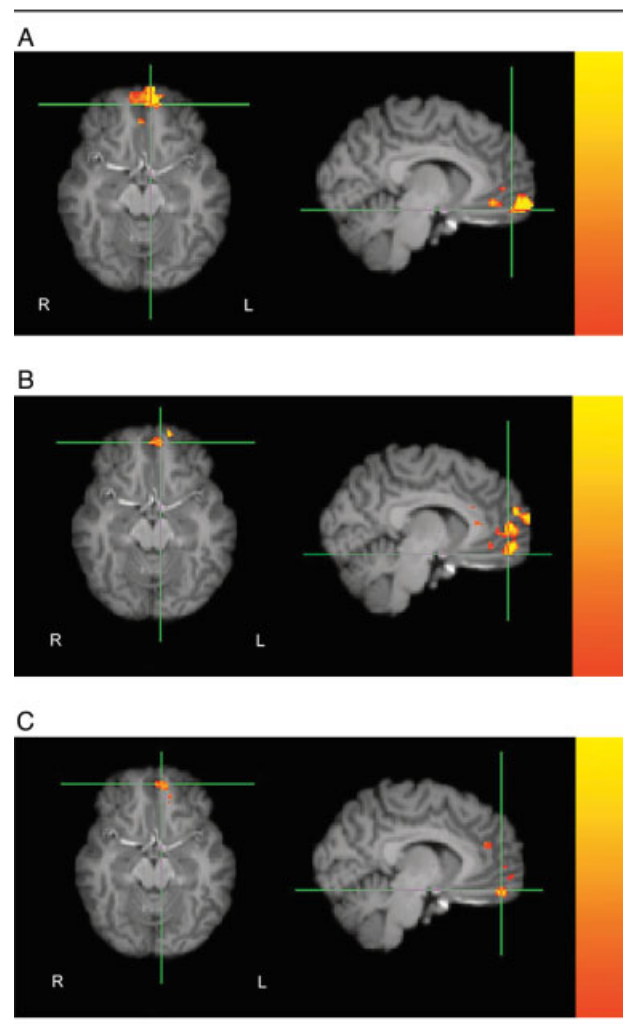


Fig 1. Belief – disbelief. (A) Those ventromedial prefrontal cortex (VMPFC) regions showing positive blood oxygen level dependent (BOLD) signal for judgments of truth (belief) – judgments of falsity (disbelief) across seven stimulus categories: autobiographical, ethical, factual, geographical, mathematical, religious, and semantic (maximum Z-score = 3.56). (B) The same subtraction for mathematical judgments alone (maximum Z-score = 3.52). (C) The subtraction for ethical judgments alone (maximum Z-score = 3.00). Most category-specific contrasts failed to achieve statistical significance in our study. Color bar ranges from $2.0 < Z \leq 3.0$ unless otherwise indicated.

Experimental Limitations

fMRI studies in general have several limitations. Perhaps first and most important are those of statistical power and sensitivity. We chose to analyze our data at extremely conservative thresholds to exclude the possibility of type I (false-positive) detection errors, reducing our susceptibility to the problem of multiple comparisons. This necessarily increases our type II error (false-negative rate). Thus, we may have failed to detect activity in additional brain regions involved in the formation of belief states. Furthermore, in whole-brain

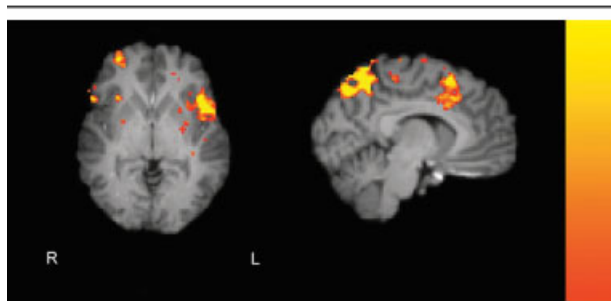


Fig 2. Disbelief – belief. Axial image shows increased blood oxygen level dependent (BOLD) signal in the inferior frontal gyrus (primarily the left), the right middle frontal gyrus, and the anterior insula (bilateral) when judgments of falsity (disbelief) are compared with judgments of truth (belief) across all stimulus categories. Sagittal image shows increased signal in the superior parietal lobule, the cingulate cortex, and superior frontal gyrus within the same contrast (maximum Z-score = 3.8).

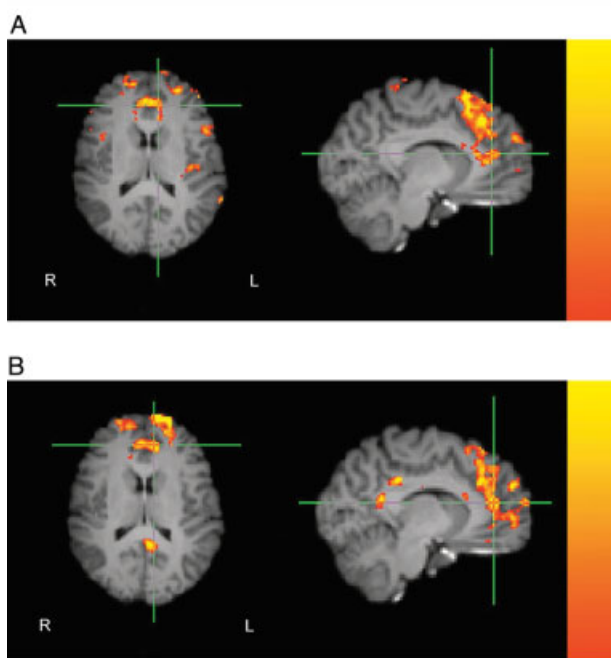


Fig 3. Uncertainty. The above figure shows increased signal in the anterior cingulate and superior frontal gyrus during those trials in which subjects were unable to judge the truth or falsity of a given statement. (A) Uncertainty – belief (maximum Z-score = 3.98). (B) Uncertainty – disbelief (maximum Z-score = 4.16). This subtraction also yielded increased signal in the posterior cingulate.

studies such as these, the analyses implicitly assume uniform detection sensitivity throughout the brain, though it is well known that several brain regions, including the orbitofrontal and rectal gyri, show reduced magnetic resonance signal in the low-bandwidth fast imaging scans used for fMRI because of the relatively

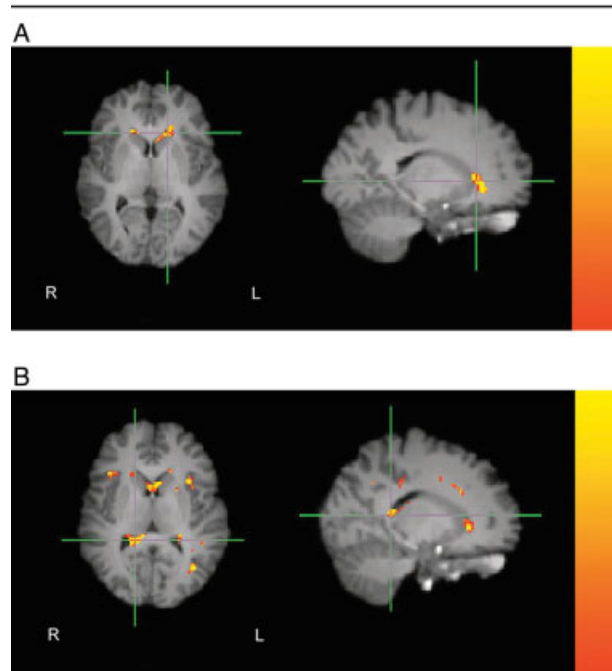


Fig 4. Belief and disbelief – uncertainty. (A) Increased blood oxygen level dependent (BOLD) signal in the head of the caudate, primarily in the left hemisphere, in all belief trials – all uncertainty trials (maximum Z-score = 3.46). (B) Increased signal in the head and tail of the caudate, primarily in the right hemisphere, in all disbelief trials – all uncertainty trials (maximum Z-score = 4.08). There is increased signal in the anterior insula, bilaterally. Color bar ranges from $2.5 < Z \leq 3.0$.

inhomogeneous magnetic field created there. Thus, false-negative rate may be further increased in these brain areas.

Field inhomogeneity also tends to increase the magnitude of motion artifacts. When motion is correlated to the stimuli, this can produce false-positive activations. The interleaved event-related design for our study greatly reduced the possibility of such false-positive activation, however. We note also that we did not observe or control for eye movements, and we cannot exclude the possibility that some of the brain activity we see is related to eye movements, though there is little reason to expect a strong correlation of such movements, or their cortical control, with the stimulus timing.

We operationalized the states of belief, disbelief, and uncertainty by having subjects rate statements as “true,” “false,” and “undecidable.” Notably, this method would be insensitive to any differences that may exist between types of belief, disbelief, and uncertainty. Is not knowing whether *Your mother was slightly taller than her grandmother* the same as not knowing whether *You have seen an even number of cars in the last week*? Our experimental design would not allow us to

resolve questions of this sort. The goal of this study was to determine whether belief, disbelief, and uncertainty could be distinguished as general states of cognitive acceptance, rejection, or indecision, independent of propositional content.

This is, to our knowledge, the first attempt to study belief at the level of the brain. Consequently, there was little basis to generate a hypothesis about the specific neural correlates of belief before scanning, apart from anticipating regions of interest in the PFC. Post hoc analyses are a flaw of many neuroimaging studies, and we acknowledge the importance of distinguishing between activations predicted by hypothesis and those that arise without a prior prediction.

Belief

The VMPFC receives strong reciprocal connections from the limbic system, the basal ganglia, and the association cortex of the parietal lobe. This region of the frontal lobes appears to be instrumental in linking factual knowledge with relevant emotional associations,⁴ in modulating behavior in response to changing reward contingencies,¹³ and in goal-based action selection.¹⁴ The VMPFC is also activated by reasoning tasks that incorporate high emotional salience.^{15,16} Individuals with VMPFC lesions test normally on a variety of executive function tasks, but often do not integrate appropriate emotional responses into their reasoning about the world. They also fail to habituate normally to unpleasant somatosensory stimuli.¹⁷ The circuitry in this region that links decision making to emotions appears to be rather specific because VMPFC lesions do not disrupt fear conditioning, or the normal modulation of memory by emotionally salient stimuli.⁴ Although reasoning appropriately about the likely consequences of their actions, these individuals appear unable to feel the difference between good and bad choices.

In our study, the only significant positive signal differences for the contrast of belief – disbelief were found in the VMPFC. Our analysis suggests that this signal change was due to a greater decrease in signal during disbelief trials than during belief trials when compared with the implicit baseline. This region often shows reduced signal during extended cognitive tasks.¹⁸ The VMPFC also has been implicated in ongoing reality monitoring, and lesions here can lead to spontaneous confabulation.¹⁹ Whatever its cause at the level of the brain, confabulation appears to be a condition in which belief processing has run amok because of a failure to subject emergent memories and associations to ongoing truth-testing.

The involvement of the VMPFC in belief processing suggests an anatomic link between the purely cognitive aspects of belief and emotion/reward. Even judging the truth and falsity of emotionally neutral propositions ac-

tivated brain regions that are strongly connected to the limbic system. It is not clear from these data whether emotional engagement enters directly into the assessment of propositional validity or whether it is a secondary consequence of the cognitive process, but the fact that ethical belief showed a similar pattern of activation to mathematical belief suggests that the physiological difference between belief and disbelief can be independent of a proposition's content and affective associations (see Figs 1B, C).

Disbelief

We found a similar pattern of activation in the frontal lobes for the contrast disbelief – belief as has been found for negative – positive responses in the Sternberg working memory task (in which subjects are asked to judge whether a newly presented stimulus matches, or fails to match, a remembered one).²⁰ Judgments of propositional falsity (vs truth) in our study and negative responses (vs positive) in the Sternberg task appear to be similar in cognitive terms, and it seems natural that they should share some of the same neural correlates. (It is also notable that negative responses in the Sternberg task take longer than positive ones, regardless of stimulus set size.) In our task, however, the rejection condition (disbelief) also showed increased signal in medial regions of superior parietal lobule, bilaterally (see Fig 2). This is an area that has strong connectivity with the medial PFC, though its recruitment in the present task is not readily explained based on prior studies. This contrast also showed signal in the dorsal portion of the ACC, a region that is activated when subjects judge the self-relevance of words.²¹ It does not appear surprising that judgments of self-relevance – non-self-relevance and judgments of truth – falsity would invoke similar regions of processing because both tasks require that propositions (at least tacitly) be judged for their validity.

When compared with both belief and uncertainty, disbelief was associated in our study with bilateral activation of the anterior insula (see Figs 2, 4B), a primary region for the sensation of taste.^{22,23} The anterior insula has been regularly linked to pain perception²⁴ and even to the perception of pain in others.²⁵ This region, together with left frontal operculum (also active in the contrast disbelief – belief), appears to mediate negatively valenced feelings such as disgust.²⁶ Studies of olfaction have shown that the left frontal operculum is engaged when subjects are required to make active judgments about the unpleasantness of odors.²⁷ Thus, regions that have been regularly implicated in the hedonic appraisal of stimuli, often negative, appeared in our study to respond preferentially when subjects rejected written statements as “false.” Our results appear to make sense of the emotional tone of disbelief, plac-

ing it on a continuum with other modes of stimulus appraisal and rejection.

Uncertainty

In phenomenological terms, uncertainty is a state in which a given representation of the world cannot be adopted as a guide to subsequent behavior, cognition, or emotional processing. If a person does not know what he or she believes to be true (eg, “Is the hotel north of Main Street or south of Main Street?” “Was he talking to me or to the man behind me?”), then the link between thought and subsequent affect and motor action cannot be established. Uncertainty can be distinguished readily from belief and disbelief in this regard, because in the latter states, the mind has settled on a specific, actionable representation of the world. The results of our study suggest two mechanisms that may account for this difference.

The contrasts uncertainty — belief and uncertainty — disbelief yielded positive signal in the ACC. This region of the medial PFC has been widely implicated in error detection²⁸ and response conflict,^{29,30} and regularly responds to increases in cognitive load and interference.³¹ It has also been shown to play a role in the perception of pain.³² With respect to its cytoarchitecture, the ACC has been subdivided into dorsal and ventral sections. The ventral ACC is phylogenically older, projects primarily to limbic structures, and is more often associated with emotional processing. The dorsal ACC has few connections to the limbic system and is more often implicated in cognitive functions.³³ In our study, although there was considerable overlap in the contrasts uncertainty — belief and uncertainty — disbelief, they yielded a BOLD signal difference primarily in dorsal (cognitive) and ventral (emotional) regions of the ACC, respectively. This leads us to conclude that these regions of the ACC differentially contribute to judgments of truth and falsity.

Response conflict and uncertainty might share many features in common. Surely a conflict between judging a statement to be “true” (belief) and judging it to be “false” (disbelief) could lead to a judgment of “undecidable” in a forced choice task of the sort used in our study. It is unlikely, however, that all forms of uncertainty will be reducible to prepotent “true” and “false” responses in competition. Just as the answer to the question “What is the third planet from the sun?” is unlikely to be the product of response competition between the answers “Venus” and “Mars,” it appears certain that some statements can be judged undecidable more or less directly (eg, “There are an even number of birds in Michigan at this moment.”). Nevertheless, given the fact that our study relied on a forced choice paradigm, it could be expected to elicit some degree of response conflict, especially during undecided trials.

Differences in reaction time are generally interpreted

as differences in cognitive load. The fact that the reaction time data for disbelief and uncertainty trials were statistically indistinguishable, although these trials yielded different patterns of neural activation in our paired contrasts, makes it unlikely that cognitive load differences account for the signal changes we detected in this experiment.

Our results also suggest a role for the basal ganglia in mediating the cognitive and behavioral differences between decision and indecision because both belief and disbelief showed increased signal in the caudate when compared with uncertainty (see Fig 4). It has long been believed that one of the functions of the basal ganglia is to provide a route by which cortical association areas can influence motor action. Projections to the striatum from association cortex predominantly run through the caudate, whereas inputs from sensorimotor cortex are largely mediated by the putamen.³⁴ Projections from the orbital and medial PFC appear to primarily target the medial edge of the caudate.³⁵ The caudate has displayed context-specific, anticipatory, and reward-related activity in a variety of animal studies³⁶ and has been implicated in cognitive planning in humans.³⁷ It has also been shown to respond to feedback in both reasoning and guessing tasks when compared with the same tasks without feedback.³⁸ In cognitive terms, one of the principal features of feedback is that it systematically removes uncertainty. The fact that both belief and disbelief showed highly localized signal changes in the caudate, when compared with uncertainty, appears to implicate basal ganglia circuits in the acceptance or rejection of propositions about the world.

The human brain is a prolific generator of beliefs. Indeed, personhood is largely the result of the capacity of a brain to evaluate new statements of propositional truth in light of countless others that it already accepts. By recourse to intuitions of truth and falsity, logical necessity and contradiction, human beings are able to knit together private visions of the world that largely cohere. The results of our study suggest that belief, disbelief, and uncertainty are mediated primarily by regions in the medial PFC, the anterior insula, the superior parietal lobule, and the caudate. The acceptance and rejection of propositional truth-claims appear to be governed, in part, by the same regions that judge the pleasantness of tastes and odors.

These results suggest that the differences among belief, disbelief, and uncertainty may one day be distinguished reliably, in real time, by techniques of neuroimaging. This would have obvious implications for the detection of deception, for the control of the placebo effect during the process of drug design, and for the study of any higher-cognitive phenomenon in which the differences among belief, disbelief, and uncertainty might be a relevant variable.

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