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**Research Report**

# Brain activity explains message effectiveness: A mega-analysis of 16 neuroimaging studies

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## Abstract

Persuasive communication in marketing, political, and health domains influences sales, elections, and public health. We present a mega-analysis (a pooled analysis of raw data) of 16 functional MRI datasets (572 participants, 739 messages, and 21,688 experimental trials) assessing the neural correlates of the effectiveness of messages in individual message receivers and at scale (in large groups of message receivers who did not undergo neuroimaging). Existing theories suggest that decision-making is driven by expected rewards and perceived social relevance associated with the expected outcomes of a given choice. Consistent with these theories, we find that (i) brain activity implicated in reward and social processing is associated with message effectiveness in individuals and at scale across diverse domains (e.g. marketing and health campaigns); (ii) exploratory analysis further suggests language, emotion, and sensorimotor processes as pertinent to message effectiveness; and (iii) brain activity provides complementary information on message effectiveness at scale beyond self-reports provided by the same neuroimaging participants. This study offers novel insights into the neurocognitive mechanisms underlying effective messaging, highlights a path toward greater unity and efficiency in persuasion research, and suggests practical intervention targets for message design.

**Keywords:** message effectiveness, neuroforecasting, persuasion, reward, mentalizing

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## Significance Statement

Media messages influence people's preferences and behaviors across various domains, including marketing, politics, and health. What makes some messages more likely to influence the minds of their audiences? Pooling available data from 16 neuroimaging datasets collected from multiple geographical regions and topic domains, we find that messages eliciting greater activation in brain systems associated with reward and social relevance are more likely to influence both individuals and large groups. Brain activity provides additional insights into how messages resonate with broad audiences beyond what can be explained by participants' self-reports. This study enhances our understanding of persuasion, suggesting that certain basic mechanisms may be active across different messaging contexts and may inspire novel strategies targeting these mechanisms.

## Introduction

Diverse actors in marketing, politics, and health communication rely on messaging via mass and social media to influence sales, election results, public health outcomes, and more (1–3). Thus, practitioners and scientists across disciplines and topic domains are motivated to understand what makes messages persuasive, that is, effective in changing attitudes and behaviors. Yet, existing research on message effectiveness rarely examines the drivers of message effectiveness using a unified framework that applies the same concepts and measurements across a wide range of messages, contexts, and populations. This gap prevents the development of a cohesive theoretical understanding of message effects across different contexts. A mega-analysis (i.e. reanalysis of raw data from multiple studies (4)) can address this issue by revealing broader patterns of message effectiveness that individual studies may not be able to capture on their own.

Reanalyzing neuroimaging studies on message effects, in particular, can reveal basic neural and psychological mechanisms underlying persuasion. Decades of neuroscience and behavioral science research highlight diverse types of expected rewards and perceived social implications of choices as drivers of human decision-making (5–8). Here, we hypothesize that heightened activation of the brain's reward and social processing systems is a precursor of message effectiveness. Our central contribution is that we test this hypothesis through a mega-analysis of 16 functional MRI datasets, encompassing 21,688 experimental trials from 572 participants and 739 messages from various topic domains.

## Reward and social cognition as psychological pathways of persuasion

One major class of persuasion theories focuses on how anticipated rewards shape people's choices. For instance, Rational Choice Theory (9), often used to explain financial choices and market behaviors in economics, posits that individuals maximize the utility of their choices based on preferences and available information. Reasoned action models, such as the integrated behavior model (10) favored in communication science, enumerate specific factors such as existing attitudes, norms, and perceived behavioral control that are evaluated and integrated to influence intentions and behavior. Although there is little interaction between these approaches, both of them directly describe or imply an internal process of weighting various psychological inputs, integrating them into a unitary value (i.e. a weighted sum of anticipated benefits and costs, also called the common currency of choice (11)), which then drives changes in preferences and behaviors. Despite high-level similarities, individual models vary in their conceptualization and operationalization of both anticipated reward and potential inputs to reward computations, hindering efficient knowledge exchange between subfields.

Another major group of approaches to understanding message effectiveness focuses on social processes. For example, social cognitive theory posits that people's behavior is influenced by observing and understanding others' behaviors and related outcomes (12, 13). Theories of normative conduct (14) and social behavior (15) emphasize the role of norms, while communication scientists have also identified interpersonal communication (16) and narratives (17, 18) as means of persuasion via identification with others. These theoretical traditions collectively suggest that messages prompting people to think about others' thoughts, feelings, or behaviors are more likely to be effective, but vary in their focus on and operationalization of specific social processes.

## Persuasion in the brain

Over the last 2 decades, researchers in communication, social neuroscience, neuromarketing, and neuroeconomics have increasingly used neuroimaging techniques, primarily functional magnetic resonance imaging (fMRI), to capture real-time brain responses to messages (6, 19). Building on findings from economics, psychology, marketing, and communication science, neuroimaging studies have identified indicators of reward and social processing as potential neural correlates of message effectiveness.

Foundational studies in neuroeconomics on value-based decision-making and choice behavior have revealed a core set of brain regions involved in anticipating and receiving rewards, including the medial prefrontal cortex (mPFC), ventral tegmental area (VTA), and nucleus accumbens (NAcc) (20–22). This reward system weights inputs from multiple brain areas depending on the individual's contexts and goals (22) to inform diverse choices (11, 20). This neural architecture also responds to effective messaging across various domains including health communication, marketing, and fundraising campaigns (6, 7).

In parallel, research in social neuroscience has identified brain regions involved in the process by which people understand themselves and the minds of others, termed mentalizing (23). This involves a wide range of cortical midline structures including mPFC and posterior cingulate cortex (PCC), and lateral regions including temporoparietal junctions (TPJ) and temporal poles (TP) (24). Several studies have linked activity in subsets of these regions to the effectiveness of various types of messages, including newspaper articles, TV commercials, and written arguments (25–28).

Although these existing neuroimaging studies suggest that both the reward (7) and mentalizing systems (6, 8) likely process aspects relevant to message effectiveness, each was guided by different theoretical and empirical approaches and their reported findings are not readily comparable. This lack of consistency hinders the identification of overarching and context-sensitive mechanisms of persuasion. Here, we directly test whether brain activity implicated in reward and mentalizing is associated with message effectiveness on average across studies by reanalyzing existing data under a consistent neural operationalization. Specifically, we examine neural responses during exposure to a wide range of messages in predefined sets of brain regions—one set associated with personal rewards, and the other set with mentalizing—and examine their relationships with message effectiveness. This analysis may provide evidence for common intervention and assessment targets with the potential for cross-contextual utility.

Because reward and mentalizing share common neural substrates, particularly in the medial wall of the prefrontal cortex, we also examine constituent brain sub-regions within mentalizing and reward systems individually. Additionally, in an exploratory whole-brain analysis, we identify other neural correlates of message effectiveness beyond our initial hypotheses and interpret the underlying psychological mechanisms with the aid of a meta-analytic database pooling insights of the broader neuroscientific literature.

## Message effectiveness in individuals and at scale

Important persuasive effects take hold in individuals who change their minds or behaviors after seeing a given message, and at scale where mediated messages could shift the collective responses of large target groups. A unique set of neuroimaging studies examined both whether brain activity recorded in individuals can predict indicators of message effectiveness in these same individuals and also message effectiveness at scale (i.e. how larger, independent groups who did not undergo neuroimaging would respond to the same messages; e.g. 26, 34, 38, 53, an approach sometimes described as "neuroforecasting" (7)). Evidence from individual studies shows that neural and self-report responses to messages collected from the same individuals do not always align in predicting which messages are likely to be most effective at scale. Some researchers theorized that neuroimaging may better detect immediate and potentially nonconscious reactions that retrospective self-reporting might miss. This implies that certain neural indicators of message effectiveness may generalize better than others to large groups (5). We test this idea directly by comparing how brain activity relates to message effectiveness both in individuals and at scale across studies. We also explore whether neural and self-report responses to messages collected in the same individuals provide overlapping or complementary insights into message effectiveness at scale.

## Mega-analysis of 16 neuroimaging studies

To achieve these goals, we conducted a mega-analysis, that is a re-analysis of raw functional neuroimaging data from 16 studies that examined the neural correlates of message effectiveness in individuals and at scale (Table 1). Study participants varied in age, gender, country of residence, and cultural backgrounds. Message stimuli covered a range of contexts such as TV ads, health promotion campaigns, newspaper articles, and donation campaigns. Although each study was motivated by different theories and reported a diverse range of neural metrics, the underlying datasets share key similarities: (i) participants were exposed to messages while undergoing neuroimaging, (ii) after message exposure participants provided an evaluation of the message (measuring message effectiveness in individuals), and (iii) message effectiveness was also assessed per message by a larger, independent group of message recipients (measuring message effectiveness at scale).

We examine, at the brain level, why and how messages influence individual minds and the collective mind of larger groups. Specifically, we (i) test whether neural responses related to reward and mentalizing correlate with message effectiveness in individuals and at scale, (ii) leverage the statistical power of our pooled data to explore other neural correlates of message effectiveness, and (iii) assess the overlap between neural and self-report responses collected in individuals undergoing neuroimaging in explaining message effectiveness at scale.

# Results

## Brain activity linked to message effectiveness within individuals undergoing neuroimaging

Neural responses to messages in a priori meta-analytically defined reward and mentalizing regions (drawn from Neurosynth, a database of the extant neuroscientific literature, see Materials and methods) were both associated with the extent to which the same scanned individuals reported these messages to be effective (reward: estimate = 0.032, 95% CI [0.012, 0.052], marginal $R^2 = 0.00088$, conditional $R^2 = 0.18565$; mentalizing: estimate = 0.037, 95% CI [0.005, 0.068], marginal $R^2 = 0.00123$, conditional $R^2 = 0.18701$) (Figs. 1A and S4).

Within the constituent sub-regions of each Neurosynth mask, significant effects were found for NAcc and VTA for the reward system, and for TP, vmPFC, and cerebellar sub-regions of the mentalizing system (Fig. 1A, Table 2). Supplementary materials tabulate variances explained (Table S3), along with additional regions of interest (ROI) within reward, mentalizing, and other systems (Table S5). A whole-brain parcellation analysis confirmed the involvement of similar regions (e.g. reward-related regions like NAcc, vmPFC which is implicated in both reward and mentalizing, and regions related to mentalizing like PCC; Fig. 2A) and further highlighted the left inferior frontal gyrus, a region associated with language processing as well as negative associations with activity in somatosensory regions (Table S4).

To help interpret the psychological mechanisms implicated by the observed neural correlates of message effectiveness, we estimated a whole-brain voxel map of message effectiveness (i.e. how each voxel's activity corresponded to message effectiveness in individuals) and compared it to a collection of 100 meta-analytic maps from Neurosynth, which represent neural activity patterns associated with diverse topics studied in the extant neuroscientific literature. Consistent with the above observations, this analysis suggests the involvement of reward, social processing, and language (topics 33, 71, and 23, respectively, in the Neurosynth 100-topic space). Somatosensory processes (topic 82) were negatively associated with message effectiveness in individuals (Table S6).

## Brain activity in individuals linked to message effectiveness at scale

After averaging neural responses to the same message across individuals undergoing neuroimaging, both reward and mentalizing-related neural signals were positively associated with message effectiveness at scale (reward: estimate = 0.080, 95% CI [0.005–0.154], marginal $R^2 = 0.00633$, conditional $R^2 = 0.00749$; mentalizing: estimate = 0.132, 95% CI [0.038–0.225], marginal $R^2 = 0.01730$, conditional $R^2 = 0.03016$) (Figs. 1B and S4).

Among the sub-regions, significant effects were observed in the VTA of the reward system, and in the dmPFC, TP, and cerebellar sub-regions of the mentalizing system (Fig. 1B, Tables 2 and S3 for model estimates and variances explained, and Table S5 for additional ROIs). Whole-brain parcellation analysis further highlighted the role of mentalizing regions (e.g. bilateral TP and dmPFC), and also identified activity in the right fusiform face area as positively associated with message effectiveness at scale (Table S4).

**Table 1.** Details of the neuroimaging datasets.

| | Related publication | Study location | Message type | Message N | Participant N | Mean age | % female | Message effectiveness in individuals | Message effectiveness at scale | Structural image acquisition | Functional image acquisition |
|---|---|---|---|---|---|---|---|---|---|---|---|
| A | (29) | Philadelphia, US | Antismoking animated web banner ads | 23 | 46 | 31.9 | 42.9 | Quit intention | Click-through rate | Voxel size = 1.02 × 1.02 × 1.2 mm; matrix size = 256 × 256, 124 slices | Repetition time (TR) = 2 s; echo time (TE) = 30 ms; voxel size = 3.44 × 3.44 × 3.0 mm; slice gap = 0 mm; matrix size = 64 × 64, 43 slices |
| B | (30) | Philadelphia, US | Antismoking image ads | 40 | | | | Relevance to self | Click-through rate | | |
| C | (31) | Los Angeles, US | Antismoking video ads | 10 | 29 | 44.4 | 48.4 | Quit intention* | Campaign hotline call volume | Voxel size = 1.5 × 1.5 × 4.0 mm; matrix size = 128 × 128, 34 slices | TR = 2 s; TE = 30 ms; voxel size = 3.0 × 3.0 × 4.0 mm; slice gap = 1 mm; matrix size = 64 × 64, 34 slices |
| D | (32) | Philadelphia, US | Antidrinking image ads | 90 | 58 | 22.9 | 56.1 | Relevance to self | Perceived effectiveness | Voxel size = 0.94 × 0.94 × 1.0 mm; matrix size = 192 × 256, 160 slices | TR = 1 s; TE = 32 ms; voxel size = 2.5 × 2.5 × 2.5 mm; slice gap = 0 mm; matrix size = 84 × 84, 56 slices |
| E | (33) | Santa Barbara, US | Antimarijuana video ads | 32 | 27 | 20.3 | 100 | Perceived effectiveness* | Perceived effectiveness | Voxel size = 0.94 × 0.94 × 0.9 mm; matrix size = 256 × 256, 192 slices | TR = 2 s; TE = 30 ms; voxel size = 3.0 × 3.0 × 3.5 mm; slice gap = 0.5 mm; matrix size = 64 × 64, 33 slices |
| F | + | Philadelphia, US | Volunteer recruitment image ads | 30 | 38 | 21.5 | 61.5 | Perceived effectiveness | Click-through rate | Voxel size = 0.94 × 0.94 × 1.0 mm; matrix size = 192 × 256, 160 slices | TR = 1.5 s; TE = 25 ms; voxel size = 3.0 × 3.0 × 3.0 mm; slice gap = 0 mm; matrix size = 66 × 66, 54 slices |
| G | (34) | Stanford, US | YouTube documentary thumbnails | 64 | 39 | 25.3 | 62.5 | Watch intention | View counts | Voxel size = 0.9 × 0.9 × 0.9 mm; matrix size = 256 × 256, 186 slices | TR = 2 s; TE = 25 ms; voxel size = 2.9 × 2.9 × 2.9 mm; slice gap = 0 mm; matrix size = 80 × 80, 46 slices |
| H | | | YouTube documentary videos | 32 | | | | Perceived engagement | View counts | | |
| I | (35) | Stanford, US | Crowdfunding project image ads | 36 | 29 | 23.3 | 46.7 | Funding intention | Funding percentage | Voxel size = 0.9 × 0.9 × 0.9 mm; matrix size = 256 × 256, 186 slices | TR = 2 s; TE = 25 ms; voxel size = 2.9 × 2.9 × 2.9 mm; slice gap = 0 mm; matrix size = 80 × 80, 46 slices |
| J | | | Crowdfunding project image ads | 36 | 32 | 23.6 | 53.1 | Funding intention | Funding percentage | | |
| K | (36) | Stanford, US | Microlending image ads | 80 | 26 | 22.4 | 46.4 | Funding intention | Funding percentage | Voxel size = 0.9 × 0.9 × 0.9 mm; matrix size = 256 × 256, 186 slices | TR = 2 s; TE = 25 ms; voxel size = 2.9 × 2.9 × 2.9 mm; slice gap = 0 mm; matrix size = 80 × 80, 46 slices |
| L | (37) | Rotterdam, NL | Movie-trailers | 18 | 28 | 20.9 | 50.0 | Liking | Liking | Voxel size = 1.0 × 1.0 × 1.0 mm; matrix size = 256 × 256, 192 slices | TR = 2.07 s; TE = 9 ms; voxel size = 3.5 × 3.5 × 3.5 mm; slice gap = 0 mm; matrix size = 64 × 64, 34 slices |

(continued)

**Table 1.** Continued

| | Related publication | Study location | Message type | Message N | Participant N | Mean age | % female | Message effectiveness in individuals | Message effectiveness at scale | Structural image acquisition | Functional image acquisition |
|---|---|---|---|---|---|---|---|---|---|---|---|
| M | (25) | Rotterdam, NL | Consumer product TV ads | 35 | 58 | 36.4 | 56.9 | Liking | Liking | Wave 1 ($n = 40$): voxel size = 1.0 × 1.0 × 1.0 mm; matrix size = 256 × 256, 176 slices<br>Wave 2 ($n = 20$): voxel size = 1.0 × 1.0 × 1.0 mm; matrix size = 256 × 256, 192 slices | Wave 1 ($n = 40$): TR = 3 s; TE = 40 ms; voxel size = 3.0 × 3.0 × 3.6 mm; slice gap = 0.6 mm; matrix size = 80 × 80, 35 slices<br>Wave 2 ($n = 20$): TR = 2.14 s; TE = 25 ms; voxel size = 3.0 × 3.0 × 3.6 mm; slice gap = 0.6 mm; matrix size = 64 × 64, 43 slices |
| N | (38) | Philadelphia, US | Consumer product TV ads | 37 | 28 | 29.0 | 45.5 | Liking | Liking | Voxel size = 0.9 × 0.9 × 0.9 mm; matrix size = 264 × 259, 185 slices | TR = 2 s; TE = 30 ms; voxel size = 2.95 ×2.95 × 4.4 mm; slice gap = 0.4 mm; matrix size = 80 × 80, 34 slices |
| O | (26) | Philadelphia, US | News article abstracts | 80 | 40 | 20.6 | 70.7 | Read intention | Share counts | Voxel size = 0.94 × 0.94 × 1.0 mm; matrix size = 192 × 256, 160 slices | TR = 1.5 s; TE = 25 ms; voxel size = 3.0 × 3.0 × 3.0 mm; slice gap = 0 mm; matrix size = 66 × 66, 54 slices |
| P | (39) | Philadelphia, US/Amsterdam, NL | News article abstracts | 96 | 94 | 21.4 | 49.0 | Read intention | Share counts | US participants ($n = 46$): voxel size = 1.0 × 1.0 × 1.0 mm; matrix size = 192 × 256, 224 slices<br>Dutch participants ($n = 50$): voxel size = 0.945 × 0.945 × 1 mm; matrix size = 256 × 256, 220 slices | US participants ($n = 46$): TR = 0.55 s; TE = 30 ms; voxel size = 3.0 × 3.0 × 3.3 mm; slice gap = 0.3 mm; matrix size = 80 × 80, 36 slices<br>Dutch participants ($n = 50$): TR = 0.55 s; TE = 30 ms; voxel size = 3.0 × 3.0 × 3.3 mm; slice gap = 0.3 mm; matrix size = 80 × 80, 36 slices |

+, unpublished dataset (see Section S1.1 for details); *, measures of message effectiveness collected after neuroimaging (otherwise collected during neuroimaging); US, United States, NL, The Netherlands.

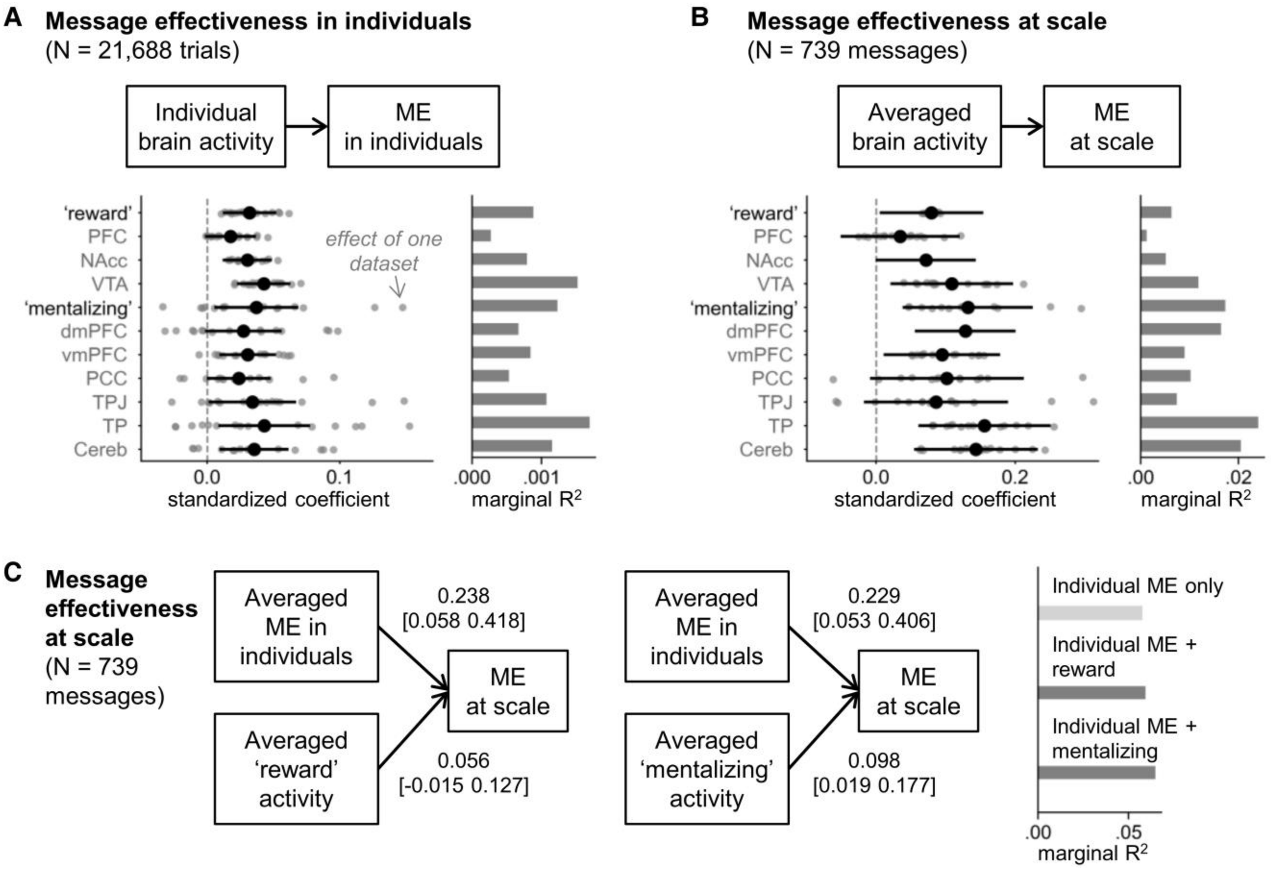

**Fig. 1.** Neurosynth ROIs analysis. A) Association between brain activity and self-report message effectiveness (ME) in individuals undergoing neuroimaging. B) Association between averaged brain activity of individuals undergoing neuroimaging and ME at scale (in large groups that did not undergo neuroimaging). C) Association between averaged brain activity of individuals undergoing neuroimaging and ME at scale, after taking into account averaged self-report ME from the same neuroimaging participants. PFC, prefrontal cortex; NAcc, nucleus accumbens; VTA, ventral tegmental area; dmPFC, dorsolateral prefrontal cortex; vmPFC, ventromedial prefrontal cortex; PCC, posterior cingulate cortex; TPJ, temporoparietal junction; TP, temporal pole; Cereb, cerebellum.

**Table 2.** Model estimates of Neurosynth ROIs and their sub-regions.

| | Message effectiveness in individuals (Fig. 1A) | | | Message effectiveness at scale (Fig. 1B) | | | Message effectiveness at scale with self-report as covariate (Fig. 1C) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Est | 95% CI | P | Est | 95% CI | P | Est | 95% CI | P |
| 'Reward' | 0.032 | 0.012, 0.052 | 0.009 | 0.080 | 0.005, 0.154 | 0.062 | 0.056 | −0.015, 0.127 | 0.155 |
| PFC | 0.018 | −0.002, 0.037 | 0.098 | 0.034 | −0.051, 0.120 | 0.445 | 0.025 | −0.061, 0.111 | 0.579 |
| NAcc | 0.030 | 0.011, 0.049 | 0.008 | 0.072 | −0.000, 0.144 | 0.052 | 0.053 | −0.015, 0.121 | 0.130 |
| VTA | 0.042 | 0.022, 0.063 | 0.002 | 0.109 | 0.021, 0.197 | 0.039 | 0.058 | −0.019, 0.135 | 0.152 |
| "Mentalizing" | 0.037 | 0.005, 0.068 | 0.041 | 0.132 | 0.038, 0.225 | 0.024 | 0.098 | 0.019, 0.177 | 0.025 |
| dmPFC | 0.027 | −0.002, 0.056 | 0.094 | 0.128 | 0.056, 0.201 | 0.009 | 0.088 | 0.016, 0.160 | 0.021 |
| vmPFC | 0.030 | 0.009, 0.052 | 0.016 | 0.095 | 0.011, 0.178 | 0.050 | 0.068 | −0.011, 0.146 | 0.116 |
| PCC | 0.024 | −0.000, 0.048 | 0.076 | 0.102 | −0.009, 0.212 | 0.101 | 0.081 | 0.001, 0.160 | 0.062 |
| TPJ | 0.034 | 0.001, 0.067 | 0.066 | 0.086 | −0.018, 0.190 | 0.136 | 0.059 | −0.027, 0.145 | 0.196 |
| TP | 0.043 | 0.008, 0.078 | 0.029 | 0.156 | 0.061, 0.251 | 0.010 | 0.112 | 0.032, 0.192 | 0.012 |
| Cereb | 0.035 | 0.009, 0.061 | 0.021 | 0.143 | 0.055, 0.232 | 0.009 | 0.113 | 0.043, 0.183 | 0.007 |

CI are estimated based on Wald statistics while *P* values are estimated using Satterthwaite's degrees of freedom method.

Neurosynth decoding of the whole-brain voxel map suggested message effectiveness at scale was positively associated with neural activity patterns related to social processing, emotion, and language (topics 71, 91, and 12), and negatively associated with pain and sensorimotor functions (topics 69 and 82; Table S6).

Leave-one-study-out cross-validation analyses showed that predictions of message effectiveness in individuals and at scale were robust to the exclusion of individual datasets (Section S4.3).

## Brain activity and self-report in individuals provide complementary information about message effectiveness at scale

The average self-report ratings of message effectiveness from individuals undergoing neuroimaging also tracked message effectiveness at scale (estimate = 0.244, 95% CI [0.063, 0.425], marginal $R^2 = 0.05708$, conditional $R^2 = 0.16403$). We thus examined the extent to which variance in message effectiveness at scale explained

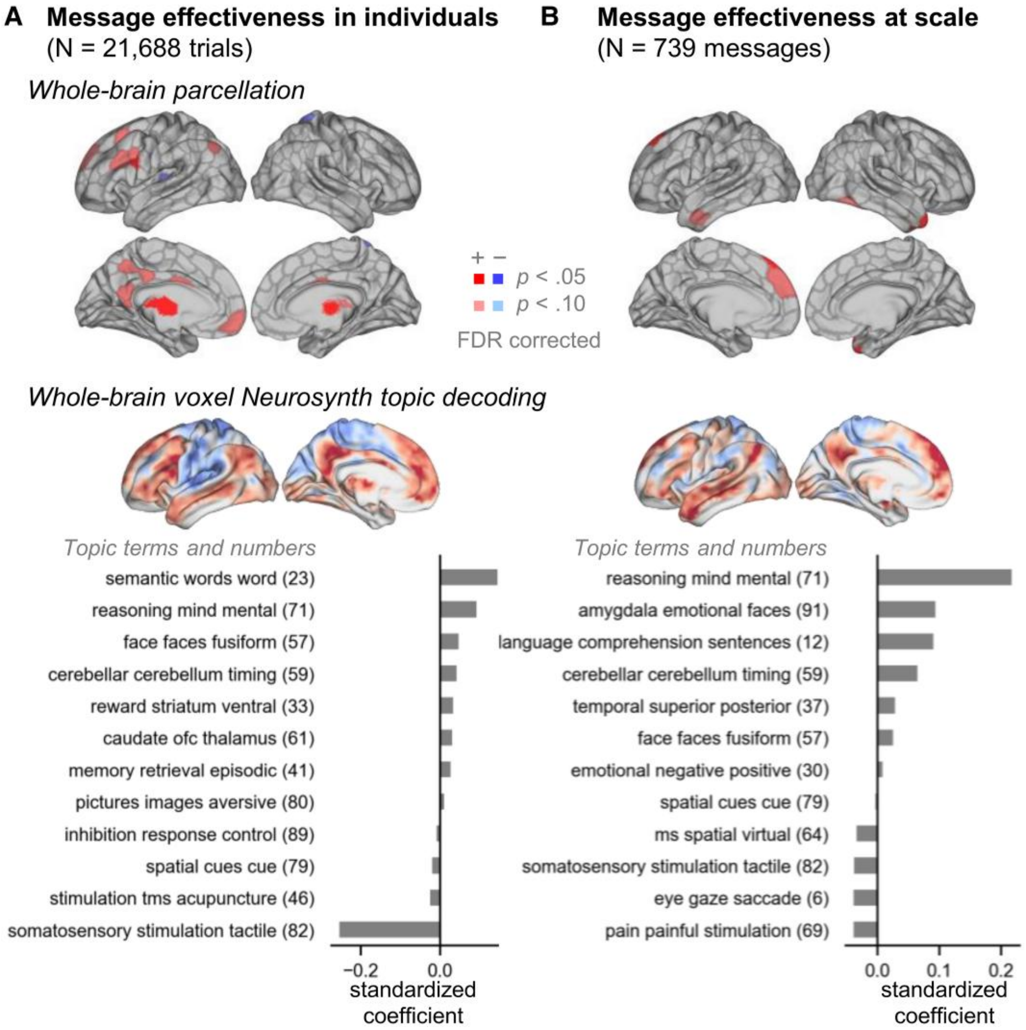

**Fig. 2.** Whole-brain parcellation analysis and Neurosynth decoding. A) Association between brain activity and self-report message effectiveness (ME) in individuals undergoing neuroimaging. B) Association between averaged brain activity of individuals undergoing neuroimaging and ME at scale (in large groups that did not undergo neuroimaging).

by individual self-reports and brain activity overlapped (Fig. 1C). Averaged mentalizing brain activity improved the explanatory power of a baseline model including only self-reports (mentalizing: estimate = 0.098, 95% CI [0.019, 0.177], marginal $R^2 = 0.06486$, conditional $R^2 = 0.17791$; reward: estimate = 0.056, 95% CI [−0.015, 0.127], marginal $R^2 = 0.05941$, conditional $R^2 = 0.16761$ (see Tables 2, S2, and S3 for model estimates and variances explained; Table S5 for additional ROI).

## Discussion

Using data from 16 neuroimaging studies across a wide range of topic domains, we found that neural responses to messages in brain regions associated with reward and social processing track the effectiveness of these messages, both in the same individuals who underwent neuroimaging and at scale (in larger, independent groups of message receivers). Further, self-reported perceptions of each message and corresponding neural responses measured in the same individuals (especially in regions related to social processing) provided complementary information about message effectiveness at scale, suggesting that neural responses can offer unique insights into how messages resonate with broad audiences. Although individual previous studies have made similar claims, each focused on a specific context or population. By pooling these studies in our mega-analysis approach, we identified neural mechanisms that generalize across different messaging contexts.

### Neural correlates of message effectiveness

First, we found that neural responses to messages in brain regions meta-analytically associated with reward were positively related to message effectiveness in both individuals undergoing neuroimaging and at scale. Specifically, message effectiveness in individuals was associated particularly strongly with activity in reward sub-regions such as NAcc and VTA. Messages that elicited stronger activity in the VTA, a key part of the dopaminergic reward system (40), were more successful at scale. These brain regions are consistently implicated in the anticipation and receipt of personal rewards (19) as well as social conformity (41). These findings highlight potential common substrates that are key components of disconnected, yet related, theories in economics (9) and communication science (10), which explain changes in preferences and behaviors via a process of weighing the values of different choice options.

Second, we found that activity in brain regions associated with mentalizing tracked message effectiveness in individuals and at scale, with particularly strong effects within the TP, the dorsomedial prefrontal cortex, and cerebellar regions. Although neuroimaging studies on message effectiveness have not historically emphasized the role of mentalizing (c.f. (42)), research on the neural bases of social influence consistently shows that mentalizing is involved when people update their preferences upon learning that they are misaligned with others (43–45). These findings are also consistent with prior theorizing that describes a variety of social mechanisms in persuasive processes observed within different fields such as psychology (46) and communication science (47), and highlight potential commonalities across this fragmented theoretical landscape.

Marginal $R^2$ values (Fig. 1A and B, Table S3) for models pooling all studies indicate that fixed effects of brain activity explained 0.03–0.17% ($M = 0.10\%$) of the variance in message effectiveness in individuals, and 0.12–2.41% ($M = 1.17\%$) of the variance in message effectiveness at scale. This highlights the difficulty in predicting individual message effectiveness at the trial level, while at the message level, effects on message effectiveness at scale roughly translate to an average Cohen's $d$ of 0.22, suggesting a small effect size. For comparison, a coordinate-based meta-analysis of 49 studies using a monetary incentive delay task yielded task effect sizes of $d = 0.28$–$0.44$ in various reward-related brain regions (48). In addition to this average effect size, our mega-analysis approach also allowed us to compare effect sizes across studies for the first time. While small on average, effect sizes ranged from small to medium between individual studies (e.g. Figs. 1 and S5). Leave-one-study-out validation analysis shows that message effectiveness predictions are not dependent on any one study's inclusion. These findings highlight the robustness of the predicted brain–behavior relationships, despite the diversity of tasks, measures, and stimuli in our database, while underscoring a need for further work that examines sources of heterogeneity.

Beyond hypothesized reward and mentalizing mechanisms, we explored the possibility that additional processes might be associated with message effectiveness. Whole-brain parcellation analysis and voxel-based Neurosynth decoding uncovered a positive association between activity in regions associated with language processing during message exposure and message effectiveness both in individuals and at scale. This interpretation is consistent with persuasion theories such as the Elaboration Likelihood Model (49) and Heuristic Systematic Model (50) suggesting that a deeper engagement with the message content is a sign of effective messaging. The negative association between activity in regions linked to sensorimotor processes and message effectiveness requires more in-depth investigation, as it could be related to task-related artifacts, such as the need for participants to respond with a button press after each message in most included studies. Additionally, both Neurosynth decoding and further supplementary analyses suggest that activity in regions associated with emotion was positively associated with message effectiveness, echoing research highlighting the importance of emotion in information processing (51) and message propagation (52).

We further found evidence of divergence between message effectiveness in individuals and at scale. Examining a priori ROIs for hypothesis testing, message effectiveness both in individuals and at scale was associated with brain activity in the VTA of the reward system and vmPFC, TP, and cerebellar sub-regions of the mentalizing system. Message effectiveness in individuals showed additional significant associations with activity in the reward sub-region NAcc and message effectiveness at scale was additionally associated with activity in the dmPFC mentalizing sub-region. The exploratory whole-brain parcellation analysis, which required more stringent correction for multiple comparisons, showed no overlap in regions associated with message effectiveness in individuals and at scale. Lastly, Neurosynth decoding and further supplementary analyses showed that brain regions implicated in emotion only showed associations with message effectiveness at scale. Extending prior theorizing that primarily focused on the reward system (36), these findings are in line with the idea that lower-level responses to messages, especially on an emotional or interpersonal level, may be more universal and thus more generalizable from individual brains to larger groups across message domains. We present this speculation cautiously given the exploratory nature of these analyses, and because different sub-regions have differing degrees of voxel coverage in our datasets (Table S1). Nevertheless, these preliminary findings enrich the ongoing discussion of the mechanisms that support neuroforecasting.

## Leveraging brain activity to understand and improve message effectiveness

Averaging across studies, brain activity in regions associated with mentalizing provided complementary information about message effectiveness at scale beyond what could be gathered from self-report responses to the messages of the same individuals who underwent neuroimaging. Large-scale message effectiveness depends on numerous factors that may not be fully captured through self-report measures sampled from smaller groups. Incorporating self-report measures relevant to social processing might improve the prediction of message effectiveness at scale. For example, in a recent study (53), self-reports of mentalizing after viewing TV ads ("to what extent did the ad make you think about the characters' feelings and intentions") improved the prediction of these ads' market success beyond simple evaluations of ad liking. Several prior studies also found that reward-related neural responses added complementary information about message effectiveness at scale beyond self-reports (e.g. 26, 31, 34–36). In this mega-analysis, the complementary effect of neural reward activity appeared to be somewhat sensitive to analytic choices. However, the interval estimates obtained with what we deemed to be the most rigorous analysis pipeline were not precise enough to confidently confirm the effect across experiments. Limitations of the existing data and the exploratory analysis approach do not allow us to systematically identify potential moderators of this effect such as choice domain, analytic and methodological choices (also see Limitations section), highlighting the need for more confirmatory work.

Further, designing interventions that engage key psychological processes during message exposure may lead to more effective message generation and dissemination. For example, tailoring health-promoting messages to increase personal relevance (54) and inducing a self-affirming mindset before message exposure (55) have been shown to engage reward-processing regions, increasing message acceptance and health-promoting behavior. Prompting individuals to consider how a message is relevant to people they know has also been linked to mentalizing activity in the brain and subsequent sharing of the message (56). Such intervention studies offer examples of effective communication design informed by neuroscience research but have generally been conducted within specific contexts. Greater interdisciplinary cross-talk may allow communicators of various domains to exchange knowledge and experiences and to efficiently focus on key psychological processes identified here.

## Limitations and future directions

Although these findings significantly advance the current understanding of message effectiveness, they also highlight fruitful

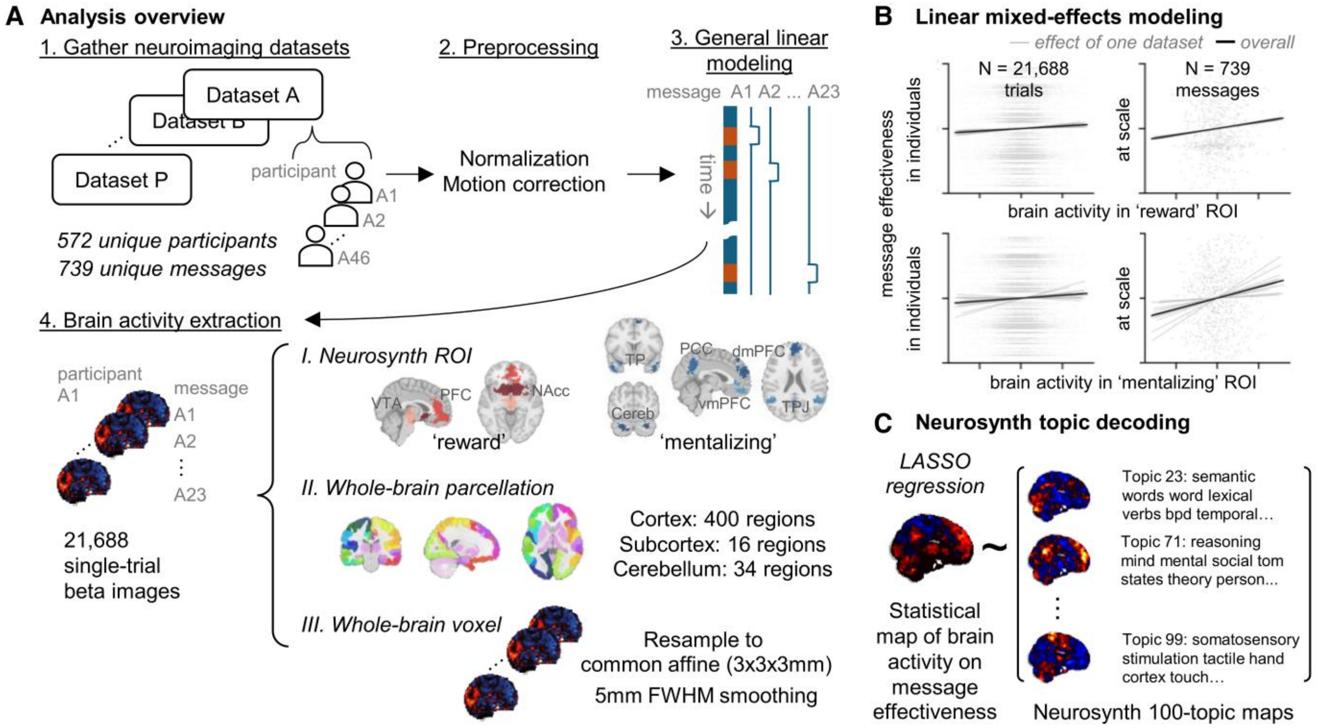

**Fig. 3.** A) Analysis overview. B) LMMs examining associations between normalized brain activity (x-axis) and normalized message effectiveness (ME; y-axis), both in individuals (left) and at scale (right). C) Neurosynth topic decoding overview. ROI, region of interest; PFC, prefrontal cortex; NAcc, nucleus accumbens; VTA, ventral tegmental area; dmPFC, dorsolateral prefrontal cortex; vmPFC, ventromedial prefrontal cortex; PCC, posterior cingulate cortex; TPJ, temporoparietal junction; TP, temporal pole; Cereb, cerebellum; FWHM, full width at half maximum.

directions for future work. First, despite key similarities, the datasets in our mega-analysis differed in several ways, including the types of messages shown (e.g. message modality and topic domain), operationalizations of message effectiveness in individuals and at scale (e.g. self-reported message liking vs. objective click-through rates), neuroimaging acquisition parameters which may impact signal coverage and quality (e.g. (57); see Table S1 for details), and task protocols. Because several of these factors are confounded in our database, we cannot confidently draw conclusions about the causes of heterogeneity of effects across datasets, such as the relatively large variance in the association of mentalizing with message effectiveness. Future interdisciplinary collaborations that standardize operational procedures such as task protocols and MRI acquisition parameters would enable researchers to more systematically test for moderators of key effects. In addition, the average effect sizes observed were somewhat sensitive to analytical choices such as specific ROIs (see, e.g. Table S5) and preprocessing pipelines, highlighting the need for continued efforts put into replication and pre-registered confirmatory work (e.g. (26, 39)) that can clarify when and why each of the hypothesized processes is most relevant.

Second, our current correlational findings and inferences about the psychological processes underlying observed brain activity (albeit supported by meta-analytic tools) should be seen as a first step in a chain of evidence that ultimately leads to confirmatory experiments to test our conclusions, for example by directly manipulating the psychological processes identified as likely precursors of message effectiveness.

Third, although this mega-analysis covers a wide range of domains and multiple geographic locations, it is still largely limited to participants in Western, Educated, Industrial, Rich Democracies (or "WEIRD" samples). Yet, culture influences norms and values that shape message effectiveness (58) and implementation of neural processing (59). Although early evidence suggests that neural indicators of message effectiveness are more cross-culturally stable than self-report measures (39), a domain-general theory of message effectiveness for diverse target audiences ultimately requires empirical evidence across equally diverse samples.

## Conclusion

By combining 16 neuroimaging datasets, we found that neural indicators of reward, mentalizing, emotion, and language processing were associated with message effectiveness in individuals and at scale. These insights highlight the potential of specific neural markers to serve as: (i) useful proximal indicators of message effectiveness that can be assessed across message types, domains, and disciplines, (ii) key components of cross-disciplinary theorizing and knowledge exchange on message effectiveness, and (iii) potential targets for intervention approaches geared towards evoking, for instance, reward or social processing in target audiences. Taken together, these findings advance our understanding of why some messages are effective while others are not, opening up new avenues for research on message effectiveness and effective communication strategies in fields such as health promotion, marketing, and public policy.

## Materials and methods

This mega-analysis utilized 16 fMRI datasets involving 572 participants and 739 diverse messages (totaling 21,688 trials) collected by the co-authors. All but one of these datasets have been reported elsewhere (Table 1). Section S1.1 reports details on the unpublished Dataset F. Like all other included studies, Dataset F is based on an ethically approved protocol (IRB protocol #818800) and full informed consent from all participants. In each study, participants were exposed to several messages while undergoing fMRI using 3T magnets. Self-report indicators of message effectiveness were collected from the study participants (either during neuroimaging or shortly thereafter). Indicators of message effectiveness at scale were obtained from larger, independent samples or populations, in the form of either self-reports or behavioral observations (e.g. click-through rate of web banners, donations).

The included studies represent diverse topic domains including health and crowdfunding campaigns, newspaper articles, web banners, television commercials, public service announcements, movie-trailers, and online videos (Table 1; Sections S1.2 and S1.3, and Figs. S1 and S2).

The analysis overview is illustrated in Fig 3A. In brief, for each dataset, we extracted trial-wise brain activity (from each participant during exposure to each message). Then, we modeled relationships between brain activity and message effectiveness (in individuals and at scale).

## Brain activity extraction

We preprocessed the raw neuroimaging data using the default fmriprep pipeline (60) (apart from seven datasets for which neuroimaging data were available in preprocessed form based on SPM pipelines), and estimated single-trial beta images (i.e. whole-brain responses to individual messages) per participant and message exposure using general linear models (GLMs). We used the least-squares-all approach, estimating all trials simultaneously in a single model using separate boxcar regressors (61). The duration of the boxcar regressors corresponds to the message exposure time, which varies across datasets and stimuli (from ∼4 s for static images to 60 s for TV advertisements). The results of these GLMs are brain images containing beta values that represent the average brain activity during the entire duration of exposure to each message for each participant. Details on preprocessing and GLM estimation can be found in Sections S2.1 and S2.2. From the beta images, we extracted brain activity using three methods: (i) predefined ROIs based on Neurosynth, (ii) whole-brain parcellation maps, and (ii) whole-brain voxels.

## Neurosynth ROIs

To examine our primary hypotheses related to reward and social processing, we relied on Neurosynth (version 7; (62)), an automatic meta-analysis of 14,371 neuroscientific articles, to identify the pertinent neural substrates. Specifically, we used the whole-brain statistical maps of voxels in which activity is associated with the terms "reward" and "mentalizing," respectively, thresholded at $P < 0.01$ corrected for false discovery rate (FDR). These maps are based on reports in extant neuroscientific studies containing these terms. To further explore the role of individual subregions within the two larger masks, we isolated major contiguous clusters per mask and organized them in distinct groups (Sections S2 and S3). From the "reward" mask, we identified VTA, NAcc, and PFC clusters; from the "mentalizing" mask, we identified vmPFC, dmPFC, PCC, bilateral TPJ, bilateral TP, and bilateral cerebellar clusters. Within the reward and mentalizing masks and each sub-region ROI, we averaged the voxel-wise beta values of the single-trial images to operationalize neural responses to messages. To facilitate the integration of our findings with the existing literature, we also tested ROIs that have been reported to be involved in reward and social processing in previous literature (Table S5).

## Whole-brain parcellation

In addition to Neurosynth ROIs, we conducted exploratory whole-brain analyses to identify potential additional neural correlates of message effectiveness. To this end, we parcellated the brain into 450 regions using published brain atlases: 400 cortical regions (63), 16 subcortical regions (64), and 34 cerebellar regions (65). Within each parcellated region, we averaged the voxel-wise beta values of the single-trial images as the brain activity measure.

## Whole-brain voxel

To enable a Neurosynth decoding analysis (details below), we further examined brain activity in individual voxels across the whole brain. After resampling the beta images from different datasets into a common 3 × 3 × 3 mm affine, a 5 mm full width at half maximum smoothing kernel was applied. Since each study and participant has slightly different brain coverage which affects this voxel-wise analysis more severely than the ROI analyses above, we retained only voxels where in every dataset, BOLD signal was recorded in at least half of that study's participants (52,059 voxels) for whole-brain voxel-wise Neurosynth decoding (see Section S2.4, Fig. S3).

## Explaining message effectiveness with brain activity

After each extraction method (Neurosynth ROIs, whole-brain parcellations and whole-brain voxels), linear mixed-effects models (LMM) were estimated with message effectiveness in individuals (Fig. 3B, left panels) and at scale (Fig. 3B, right panels) as the dependent variable (DV) and brain activity as independent variable (IV), with a nested random slopes-and-intercepts structure for each dataset and each participant (message effectiveness in individuals), or for each dataset (at scale). There were 21,688 observations for which both measures of message effectiveness in individuals and at scale were available (i.e. each participant's exposure to each message in each dataset). For message effectiveness at scale, we calculated the averaged brain activity for each message in each dataset, resulting in 739 observations (one per message). Both IV and DV were normalized within datasets before LMM estimation. Further cross-validation analyses are described in Section S4.3.

For Neurosynth ROIs and their sub-regions, we analyzed LMM coefficients to determine whether brain activity was associated with message effectiveness in individuals and at scale. Whole-brain parcellation LMMs allowed further identification of other neural substrates of message effectiveness, with statistical significance adjusted for FDR.

To help interpret the underlying psychological processes, the whole-brain statistical maps from the voxel-based LMMs were compared against the Neurosynth database. We used a published set of 100 whole-brain statistical maps associated with various topics extracted by latent Dirichlet allocation topic modeling from the abstracts of neuroscientific articles in the Neurosynth database (100-topic space) (66). These topics ranged from neuropathology (e.g. topic 10: schizophrenia, symptoms, risk, abnormalities, disorder…) to various psychological processes (topic 50: perceptual, perception, interaction, sensory, visual…; 71: reasoning, mind, mental, social, tom, states…). We used LASSO regressions to identify which of these 100 Neurosynth topic maps best explained the message effectiveness maps in individuals and at scale (Fig. 3C). The regularization parameter was determined by a 10-step search in [0.1, 1] using 5-fold cross-validation. For each regression, the message effectiveness maps and the Neurosynth topic maps were resampled to be a common affine, vectorized, and normalized. We also tested 50- and 400-topic spaces and found similar results (Table S6).

Finally, to examine whether brain activity provided additional explanatory power in predicting message effectiveness at scale beyond self-reports from neuroimaging participants, we estimated LMMs that included both averaged brain activity and averaged self-report message effectiveness of the same participants as IVs.

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## Supplementary Material

Supplementary material is available at *PNAS Nexus* online.

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## Data Availability

Data and analysis code are available at https://osf.io/bzypv/?view_only=f90505dea848435cbde6e7e8c7b91338.

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