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Biological Psychiatry

Conditioned Hallucinations and Prior Overweighting Are State-Sensitive Markers of Hallucination Susceptibility

Eren Kafadar, Victoria L. Fisher, Brittany Quagan, Allison Hammer, Hale Jaeger, Catalina Mourgues, Rigi Thomas, Linda Chen, Ayyub Imtiaz, Ely Sibarium, Alyson M. Negreira, Elif Sarisik, Vasishta Polisetty, David Benrimoh, Andrew D. Sheldon, Chris Lim, Christoph Mathys, and Albert R. Powers

ABSTRACT

BACKGROUND: Recent advances in computational psychiatry have identified latent cognitive and perceptual states that predispose to psychotic symptoms. Behavioral data fit to Bayesian models have demonstrated an overreliance on priors (i.e., prior overweighting) during perception in select samples of individuals with hallucinations, corresponding to increased precision of prior expectations over incoming sensory evidence. However, the clinical utility of this observation depends on the extent to which it reflects static symptom risk or current symptom state.

METHODS: To determine whether task performance and estimated prior weighting relate to specific elements of symptom expression, a large, heterogeneous, and deeply phenotyped sample of hallucinators (n = 249) and nonhallucinators (n = 209) performed the conditioned hallucination (CH) task.

RESULTS: We found that CH rates predicted stable measures of hallucination status (i.e., peak frequency). However, CH rates were more sensitive to hallucination state (i.e., recent frequency), significantly correlating with recent hallucination severity and driven by heightened reliance on past experiences (priors). To further test the sensitivity of CH rate and prior weighting to symptom severity, a subset of participants with hallucinations (n = 40) performed a repeated-measures version of the CH task. Changes in both CH frequency and prior weighting varied with changes in auditory hallucination frequency on follow-up.

CONCLUSIONS: These results indicate that CH rate and prior overweighting are state markers of hallucination status, potentially useful in tracking disease development and treatment response.

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Progress in medicine requires an understanding of how abnormalities in the underlying mechanisms driving disease states lead to observable signs and symptoms. In endocrinology, heightened thyroid-stimulating hormone levels reflect disrupted thyroid functionality and are associated with the likelihood of symptom expression (1). While thyroid-stimulating hormone is not a directly observable sign or symptom, tracking this biomarker is essential to monitoring a patient's disease state.

As with hypothyroidism, identifying underlying pathways and monitoring markers of disease states is important for psychiatric disorders. In psychiatry, disorders are thought to arise because of abnormalities in information processing. Similar to serum thyroid-stimulating hormone levels, these abnormalities may not be directly observed but may be causally related to symptom expression. One promising route toward identifying biomarkers of information processing abnormalities that drive psychiatric symptom expression comes from computational psychiatry (2–4). Computational psychiatry provides mathematical frameworks for understanding the typical functioning of perceptual and cognitive systems and how specific disturbances may lead to psychiatric symptoms (3,4).

One such computational framework, predictive processing theory, has proven useful in identifying the mechanisms by which psychotic symptoms and brain states arise from aberrations in learning and inference (5–7). This approach has demonstrated promise as a tool for understanding hallucinations. Within predictive processing theory, perception is formally described as the process of inferring the cause of one's sensations by taking into account an internal model of (or expectations about) one's surroundings (priors) along with the available sensory evidence, weighted by their relative precisions (8–10). Here, precision can be understood as the participant's certainty or confidence placed in the sources of this information. Given this formulation of perception, hallucinations—percepts in the absence of a corresponding stimulus—may arise owing to overweighted priors relative to the weight afforded to incoming sensory evidence (7,11).

Empirical support for this idea has mounted over recent years (12). Several behavioral tasks sensitive to relative prior

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weighting (13–16) have demonstrated a relationship to hallucination propensity across clinical and nonclinical populations (14,17) as well as neurologic and psychiatric disorders (15). Critically, an overweighting of perceptual priors does not appear to be present in individuals with psychosis spectrum disorders without hallucinations (17), suggesting specificity of this abnormality to hallucinations and not psychotic illness writ large.

Although this combination of evidence supports the idea that overweighing perceptual priors is linked to a susceptibility toward hallucinations, no data currently exist to discern what the exact relationship between prior overweighting and hallucination susceptibility might be. For example, does a tendency to overweight priors represent a static risk factor that is stable over time, or does this tendency reflect changes in hallucination intensity that vary with current clinical state and treatments? These distinctions could reveal crucial information about the pathophysiological pathways leading directly to symptom expression and whether biomarkers based on this observation could be useful to track susceptibility toward hallucinations or response to treatment.

Here, we present data from a large, heterogeneous, extensively phenotypically characterized group of individuals with unusual perceptual experiences, including those with auditory hallucinations (AHs) (AH^+; $n = 249$) and without AHs (AH^-; $n = 209$). Participants completed the conditioned hallucination (CH) task, which has previously been shown to be sensitive to prior overweighting and propensity toward AHs (17,18). We replicate the findings that the CH task and estimated relative prior weighting are sensitive to hallucination propensity. We then extend these findings to demonstrate a strong relationship between prior weighting and the severity of hallucinatory experiences. Finally, we show that changes in prior weighting are sensitive to changes in recent hallucination frequency.

METHODS AND MATERIALS

Participants and Data Collection

Participants aged 18 to 65 completed a battery of demographic measures, clinical scales, and behavioral tasks as part of the online Yale Control Over Perceptual Experiences Project (https://www.spirit.research.yale.edu). The study was coordinated through Yale's instantiation of Research Electronic Data Capture (REDCap@Yale). REDCap is a Health Insurance Portability and Accountability Act–secure web-based software platform designed for data capture in research studies (19,20).

Recruitment was accomplished via advertising through specific partners (https://www.spirit.research.yale.edu/partners) who work with individuals with unusual perceptual experiences and unusual beliefs, both with and without a need for care, as well as broader posting via Amazon Mechanical Turk and social media platforms. All procedures were approved by the Yale University Institutional Review Board/Human Interest Committee. Participants provided informed consent and received monetary compensation for their participation, contingent on adequate completion of all study procedures. A screening survey excluded those who reported cognitive, neurologic, or seizure disorders or endorsed being under the influence of recreational drugs or alcohol at participation.

Phenomenological and Clinical Battery

Participants were screened for the presence of AHs via online self-report using the screening portion of the Chicago Hallucination Assessment Tool (CHAT) (21). This tool also provided an estimate of the frequency and recency of hallucinations across modalities. AH^+ participants also completed the Launay-Slade Hallucination Scale-Revised (LSHS-R) (22,23), Peters et al. Delusion Inventory (24), and the 9-item version of Raven's Progressive Matrices (25). All participants also provided past psychiatric history (including medications).

Auditory CH Task

Participants completed the CH task 17.04 ± 31 hours after completing the questionnaires. This is a sensory-detection task using principles of psychometric thresholding and Pavlovian associative learning (17,18,26–29) to induce AHs (17,18). Participants press buttons to indicate their detection of a target stimulus, a 1-kHz pure tone embedded in 70-dB sound pressure level white noise and presented concurrently with a flashed white checkerboard on a black background (Figure 1A).

In brief, this paradigm involves presenting the tone at an individually defined threshold intensity concurrently with the

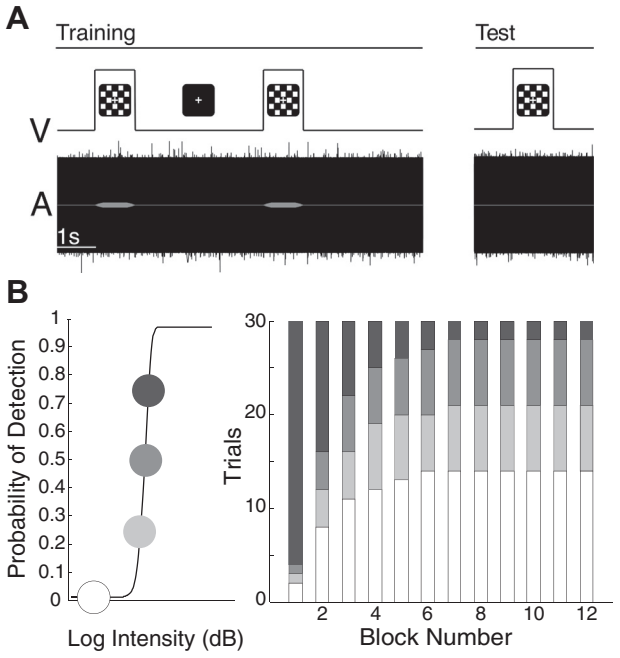

Figure 1. Auditory conditioned hallucination task structure. **(A)** Visual (V) and auditory (A) stimuli and task structure. Trials consisted of simultaneous presentation of a 1000-Hz tone embedded in white noise and a visual checkerboard. **(B)** We estimated individual psychometric curves for tone detection (left) and then systematically varied stimulus intensity over 12 blocks of 30 conditioning trials. Threshold tones were more likely early, and absent tones were more likely later (right).

visual pattern early in the experiment and then presenting subthreshold and tone-absent trials later. Initial presentations promote development of a learned association between the visual pattern and auditory target. As such, in trials during which the flash is presented in isolation, participants will report hearing the tone. We identify this tendency as the CH rate. Prior work indicates that hearing the tone during no-tone trials reflects prior weighting and leads to a hallucination (17). A full description of the task can be found in Supplemental Methods.

Sample Selection

A sample of 458 participants from the Yale Control Over Perceptual Experiences Project were selected after quality control procedures and demographic matching (see Supplemental Methods for details). To understand how a generally increased susceptibility to AHs affected CH rate, we used the CHAT-AH score to classify individuals as either AH^+ or AH^-. Any endorsement of CHAT-AH items 4 to 8 was considered as AH^+ (Table S1) (30), because items 1 to 3 ("Have you ever thought you heard someone call your name, but then realized you must have been mistaken?"; "Have you ever heard your phone ringing, but then realized the phone hadn't actually rung?"; and "Do you ever hear strange noises when you are falling asleep or waking up in the morning?") are very commonly endorsed in the general population (31–33). As such, the AH^+ group reflects a heterogeneous group of clinical and nonclinical individuals who have a propensity toward a diverse set of abnormal auditory experiences in the form of hallucinations.

A random sample, balanced in age, sex, and total score on the Raven's Progressive Matrices between the AH^+ and AH^- groups, was selected for between-group analyses. The AH^+ group was further divided based on the frequency of the hallucinations reported (daily, weekly, monthly or less), based on the highest frequency endorsed for any CHAT-AH items 4 to 7.

Hierarchical Gaussian Filter Analysis

To identify the latent states driving behavior on the CH task, we fitted parameters of a three-tiered hierarchical Gaussian filter (HGF) using trialwise data on stimulus intensity and responses (34,35). The HGF is a computational Bayesian hierarchical model of learning and inference in a changing environment (36). This model has been adapted for CH data (17,18). Full details regarding the HGF can be found in Supplemental Methods.

Retest Sample and Procedures

To determine whether changes in task performance may relate to changes in clinical status, all Control Over Perceptual Experiences Project participants who completed initial assessments were invited to complete an additional follow-up assessment. The final retest sample characteristics are outlined in Table 1. To minimize the transfer of prior learning (37–39), follow-up versions of the CH task used novel stimulus pairs (e.g., different auditory tones and different visual stimuli) matched for luminance, complexity, and contrast, which were dependent on time elapsed (first follow-up: <8 months; second follow-up: >8 months) since initial assessment. Red horizontal stripes and a 1250-Hz tone were used for individuals at first follow-up. Blue stripes at 45° and a 1500-Hz tone were used at the second follow-up. All follow-up participants had one follow-up data point (before or after the 8-month mark), which was used in final analyses. Similar detection rates were reported between these stimulus sets, supporting their general equivalence (Figure S5). Otherwise, the structure and procedure of the task were as outlined above in the original task.

Participants also recompleted the CHAT and LSHS-R 14 ± 3.78 days before the follow-up tasks. As was done for the initial dataset, participants were grouped into different frequency groups (daily, weekly, monthly or less, or never), based on the CHAT-AH questionnaire. Figure S5 shows initial and follow-up hallucination frequency for participants included in

Table 1. Sample Demographic and Clinical Characteristics of Original and Follow-up Samples

Sample Demographic and Clinical Characteristics	AH^- (n = 209)	AH^+ (n = 249)	p	Follow-up (n = 40)
Age, Years, Mean (SD)	37.78 (10.95)	38.17 (13.75)	.741	39.5 (15.81)
Total LSHS Score, Mean (SD)	5.91 (6.12)	16.28 (9.38)	<.001	11.18 (11.07)
Total PDI Score, Mean (SD)	1.96 (2.65)	6.63 (4.17)	<.001	6.18 (4.67)
Self-Reported Mental Illness, n (%)	18 (10.2%)	88 (36.1%)	<.001	15 (37.5%)
Race, n (%)			.384	
American Indian/Alaskan Native	5 (2.4%)	2 (0.8%)	–	0 (0.0%)
Asian	19 (9.1%)	28 (11.2%)	–	7 (17.5%)
Black or African American	6 (2.9%)	8 (3.2%)	–	0 (0.0%)
More than one race	7 (3.3%)	18 (7.2%)	–	3 (7.5%)
Native Hawaiian or other Pacific Islander	1 (0.5%)	2 (0.8%)	–	0 (0.0%)
White	164 (78.5%)	185 (74.3%)	–	30 (75.0%)
Unknown/prefer not to say	7 (3.3%)	6 (2.4%)	–	0 (0.0%)
Sex, F, n (%)	121 (57.9%)	166 (66.7%)	.066	28 (70.0%)
Current Medication Use, n (%)	10 (4.8%)	58 (23.3%)	<.001	9 (22.5%)
Self-Reported Psychosis Spectrum Illness, n (%)	1 (0.5%)	28 (11.2%)	<.001	3 (7.50%)
Total Raven Score (Out of 9), Mean (SD)	6.36 (1.69)	6.07 (1.83)	.079	5.00 (0.41)

AH, auditory hallucination; F, female; LSHS, Launay-Slade Hallucination Scale; PDI, Peters et al. Delusion Inventory.

the final analysis. Changes in groups between initial and follow-up periods were used to categorize individuals into one of three groups: decrease (e.g., daily to weekly or monthly), no change (e.g., daily to daily), or increase (e.g., never or monthly to weekly or daily). For purposes of quantifying changes in hallucination frequency on follow-up assessment, hallucination frequency categories (e.g., "once per week") were converted to minimum occurrence rates over days (e.g., 1/7 for weekly). Relative changes were calculated as log ratios of final rates over initial rates. Ratios instead of differences between rates were used to avoid divide-by-zero errors.

Statistical Analysis

Differences between AH^- and AH^+ groups were computed using two-sample *t* tests. For comparisons of means across frequency groups, one-way analysis of variance was used. To control for confounds related to hallucination status, we used analysis of covariance. Correlations were computed using Pearson correlations. We used nonparametric measures (Mann–Whitney *U* tests and rank-based linear correlation) for follow-up analyses due to the small sample size and outliers. All statistical analyses were completed using the R packages *tableone*, *plotrix*, *car*, *nlme*, and *afex* performed with RStudio version 1.4.1717 (http://www.rstudio.com/) and SPSS.

RESULTS

Sample Characteristics

Table 1 reports the summary of the demographic and clinical features of our final balanced sample. The AH^+ group ($n = 249$) obtained significantly higher scores in propensity for hallucinations (LSHS) ($t_{135} = 10.0$, $p < .001$) and delusions (Peters et al. Delusion Inventory) ($t_{426} = 14.5$, $p < .001$) than the AH^- group ($n = 209$). AH^+ also reported a higher frequency of psychosis spectrum illness ($\chi^2_1 = 20.4$, $p < .001$) and mental illness in general ($\chi^2_1 = 35.1$, $p < .001$). AH^+ were more likely to use psychiatric medication ($\chi^2_1 = 29.3$, $p < .001$) than AH^-, specifically serotonin ($\chi^2_1 = 10.5$, $p = .001$) and norepinephrine ($\chi^2_1 = 4.5$, $p = .034$) reuptake inhibitors, serotonin agonists ($\chi^2_1 = 4.2$, $p = .039$), second-generation antipsychotics ($\chi^2_1 = 24.1$, $p < .001$), stimulants ($\chi^2_1 = 5.09$, $p = .024$), and mood stabilizers ($\chi^2_1 = 8.54$, $p = .003$; Table S4). The final, balanced groups did not differ significantly in age, sex, or reported race.

CH Rates and Confidence Are Higher in Patients With AHs

AH^+ and AH^- groups did not differ on the QUEST-derived threshold (Figure 2A), but AH^+ participants were more likely to report hearing a tone on no-tone trials (i.e., CH rate; $t_{450} = 2.71$, $p = 6.9 \times 10^{-3}$) (Figure 2B). We explored if CH rate reflected hallucination status differences in other sensory modalities and found that it did not (see Supplemental Results). These results also persisted after controlling for delusional ideation, Raven total score, presence of psychotic-spectrum illness, and medication use. Recruitment source (Table S3) significantly predicted hallucination status and, accordingly, CH rate. Please see Supplemental Results for full details.

Significant differences between AH^+ and AH^- groups emerged early during the fourth block of the experiment at the 26th presentation of a no-tone trial (Figure 2D). Maximal statistical difference was noted at trial 62 ($t_{455} = 3.27$,

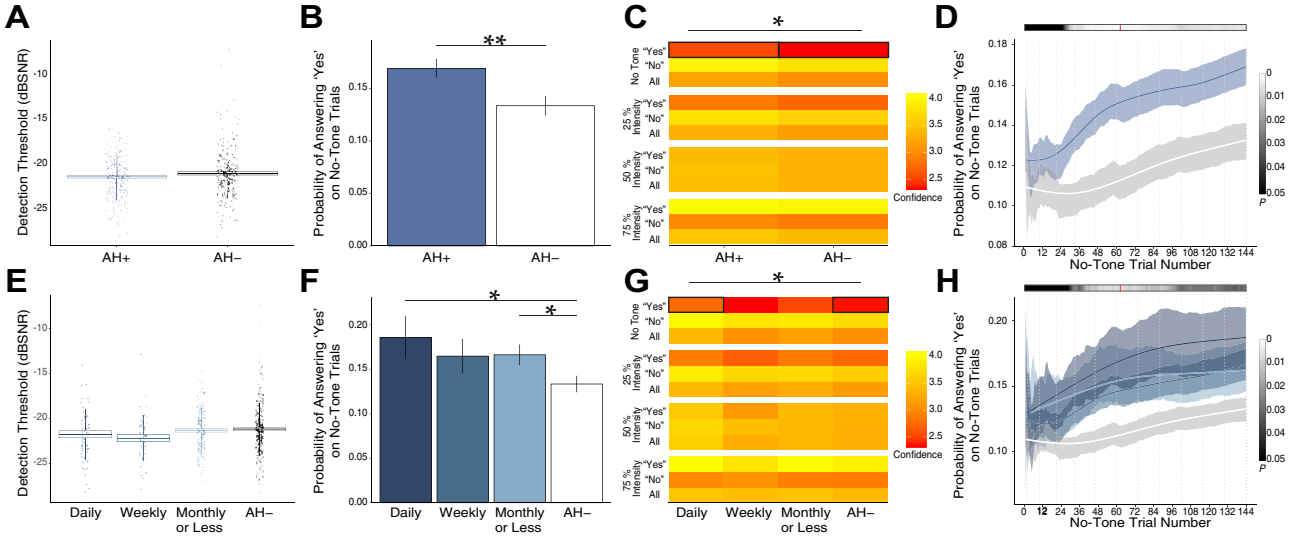

Figure 2. Behavioral results. **(A)** Calculated thresholds for tone detection were similar to those previously reported (17,18) and did not differ between auditory hallucination (AH^+) and nonhallucination (AH^-) groups. **(B)** Probability of reporting conditioned hallucinations was significantly higher in AH^+ than in AH^- groups. **(C)** Confidence in reporting conditioned hallucinations was also higher in AH^+ than in AH^- groups. **(D)** Trialwise analysis of the emergence of behavioral effects demonstrated early differences in means that became significant in experimental block 4 and reached their maximum in early block 7 of 12. AH^+ was divided into three groups based on reported hallucination frequency: daily ($n = 49$), weekly ($n = 43$), and monthly or less ($n = 146$). **(E–G)** Results parsed by frequency of clinical hallucinations demonstrated a similar lack of differences in threshold **(E)**, but showed that probability of **(F)** and confidence in **(G)** reporting conditioned hallucinations differed significantly by frequency of voice-hearing. **(H)** Emergence of behavioral effects showed a similar profile to groupwise effects in **(D)** and means effects in **(F)**. dbSNR, decibel signal-to-noise ratio.

$p = 1.2 \times 10^{-3}$). Performance did not differ significantly on any other conditions (Figure S2).

There was a significant interaction between confidence ratings, answer choice, and condition ($F_{6,4966} = 529$, $p = 2 \times 10^{-16}$). Participants were more confident reporting detection and less confident reporting nondetection with increasing target loudness. There was a significant interaction between hallucination status and condition ($F_{3,4966} = 2.7$, $p = .045$). Participants with hallucinations had higher confidence in answering "yes" on no-tone trials ($t_{427} = 2.23$, $p = .026$) (Figure 2C).

CH Rates and Confidence Ratings Scale With Severity of AHs

CH rate varied significantly according to the frequency of reported hallucinations ($F_{3,445} = 7.68$, $p = 5.0 \times 10^{-3}$; $r_{445} = 0.13$, $p = 6.0 \times 10^{-3}$) (Figure 2F). Significant differences emerged early (no-tone trial 28) and hit their maximum again at no-tone trial 62 ($F_{3,445} = 12.1$; $p = 5.9 \times 10^{-3}$) (Figure 2H). Post hoc differences were evident between individuals with daily hallucinations and the AH$^-$ group ($t_{62} = 2.14$, $p = .036$) as well as between those with monthly hallucinations and the AH$^-$ group ($t_{304} = 2.15$, $p = .032$). We further investigated if the relationship between CH rate and hallucination status reflected current or overall susceptibility to hallucinations within participants who reported having hallucinations and completed detailed phenomenological surveys about their hallucinations ($n = 220$). CH rates significantly correlated with hallucination frequency within the two days prior to survey completion ($r_{218} = 0.13$, $p = .042$) and not with the frequency of hallucinations at the worst time in their history ($r_{173} = 0.12$, $p = .12$).

Confidence ratings for hearing the tone on no-tone trials were significantly different between frequency groups ($F_{3,435} = 4.98$, $p = .026$). Post hoc analyses showed that the difference between daily and AH$^-$ was significant ($t_{70} = 4.98$, $p = .021$).

Relative Prior Weighting Is Higher in Those Who Hallucinate and Is Associated With Frequency of AHs

To evaluate latent factors driving performance on the CH task, we fit participants' behavioral data to a three-tiered model of perception, the HGF (34,35), which we have done in past work (17,18) (Figure 3A). The HGF is particularly useful in its ability to directly model the degree to which participants rely on their priors when making perceptual judgments (ratio of precision of priors to precision of incoming sensory evidence, or relative prior weighting, ν). The AH$^+$ group exhibited higher prior weighting ($t_{451} = 2.3$, $p = .021$) (Figure 3C) but did not differ in belief trajectories (μ_1, μ_2, μ_3) (Figure 3B) or decision noise (β^{-1}) (Figure 3C).

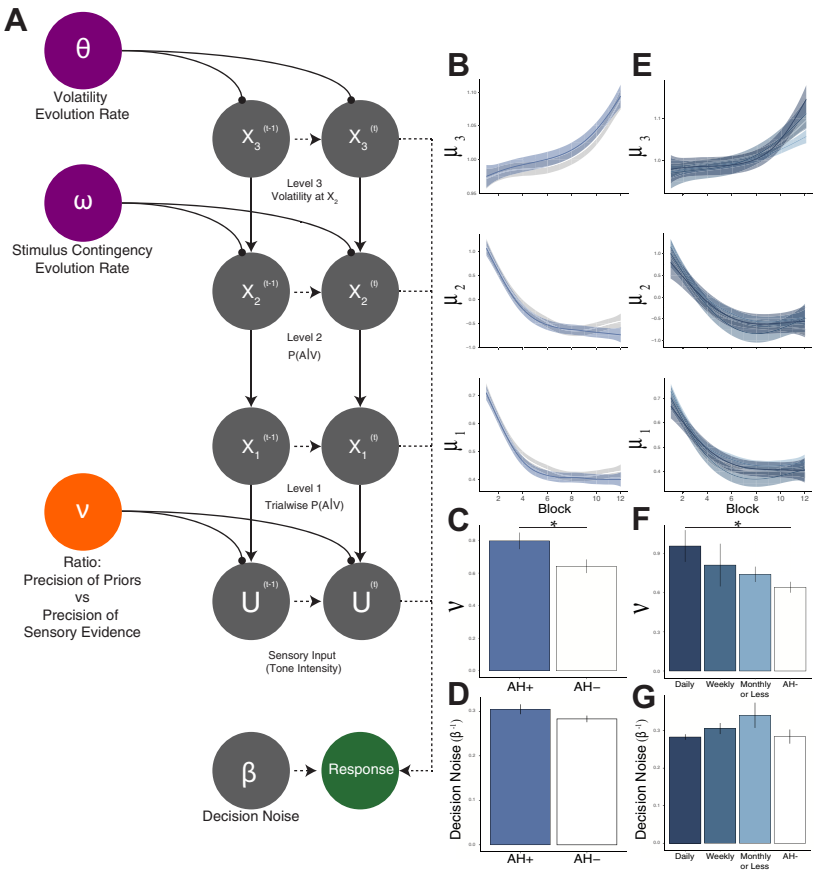

Figure 3. Hierarchical Gaussian filter analysis. **(A)** Hierarchical Gaussian filter model, mapping the combination of latent states (e.g., trajectories X_1, X_2, X_3, relative prior weighting ν, inverse decision temperature/decision noise β^{-1}, evolution rates ω and θ) to recorded responses, taking into account trialwise stimulus strength (U). The first level (X_1) represents the target tone's presence on trial t. The second level (X_2) represents the contingency between the visual and auditory stimuli. The third level (X_3) represents the volatility of the relationship between the visual and auditory stimuli over the course of the experiment. Critically, responses are modeled allowing for individual variation in weighting between sensory evidence and perceptual beliefs (parameter ν). **(B–G)** Belief trajectories do not differ between auditory hallucination (AH$^+$) and nonhallucination (AH$^-$) groups at any level **(B)**, nor did decision noise **(D)**, whereas prior weighting was greater in AH$^+$ than in AH$^-$ **(C)**. A similar pattern of results was seen when participants were divided into frequency groups, which did not differ in belief trajectories **(E)** or decision noise **(G)**. By contrast, relative prior weighting **(F)** scaled with hallucination frequency.

The relative prior weighting parameter (ν) was found to vary according to frequency of AHs ($F_{1,445} = 7.42$, $p = 6.6 \times 10^{-3}$; $r_{445} = 0.13$, $p = 7.0 \times 10^{-3}$). Conversely, there was no difference in decision noise (β^{-1}) between frequency groups.

Changes in CHs and Prior Weighting Vary With Changes in AH Frequency

A subset of participants (n = 40; see Table 1 for sample characteristics) completed a repeated-measures version of the CH task several months (mean ± SD = 375.54 ± 113.99 days) after initial performance. Those who did not report AHs at baseline or during follow-up assessments (n = 6) were excluded from final analyses. Mann–Whitney U tests illustrated that those who reported an increase in hallucination frequency during follow-up sessions showed larger increases in CH rates than those with decreased hallucination frequency (r = 0.377, p = .026) (Figure 4A), while those with no change in frequency exhibited no change in CH rate. Rank-based correlation analyses confirmed this relationship: changes in AH frequency were associated with both changes in CH rate (r_{28} = 0.45, p = .014) (Figure 4B) and changes in relative prior weighting (r_{28} = 0.39, p = .022) (Figure 4C), adjusted for baseline CH rates. Consistent with Figure 3, changes in CH rate correlated with changes in relative prior weighting (rank-based correlation; $r_{33} = 0.51$, $p = 1.6 \times 10^{-3}$) (Figure 4D). As with preliminary results, we explored different potential confounds and their relationship with changes in hallucination frequency and did not find significant effects (see Supplemental Results for details).

DISCUSSION

In a large, heterogeneous sample of individuals with hallucinations, we have provided evidence for a link between CHs, relative prior weighting in perception, and recent hallucination frequency. Previous work has highlighted the relationship between relative prior weighting and AHs in small subgroups of people who frequently heard voices with distinctly clear acoustic qualities (14,17). The sample here includes individuals with a broad range of phenomenological characteristics, daily functioning, and clinical needs, allowing us to examine the performance data and model parameter estimates for relationships to each of these quantities. As we have done in prior work (17), we relate auditory CH rates to a propensity toward hallucinations in our diverse sample, both categorically and dimensionally, as measured by CHAT-AH and LSHS-R scores. Rates of CH were lower in this diverse AH$^+$ sample compared with previous, highly selected samples; however, examining CH rates and estimated relative prior weighting in subgroups of individuals with daily hallucinations (Figures 2 and 3) yields values that closely approximate previously

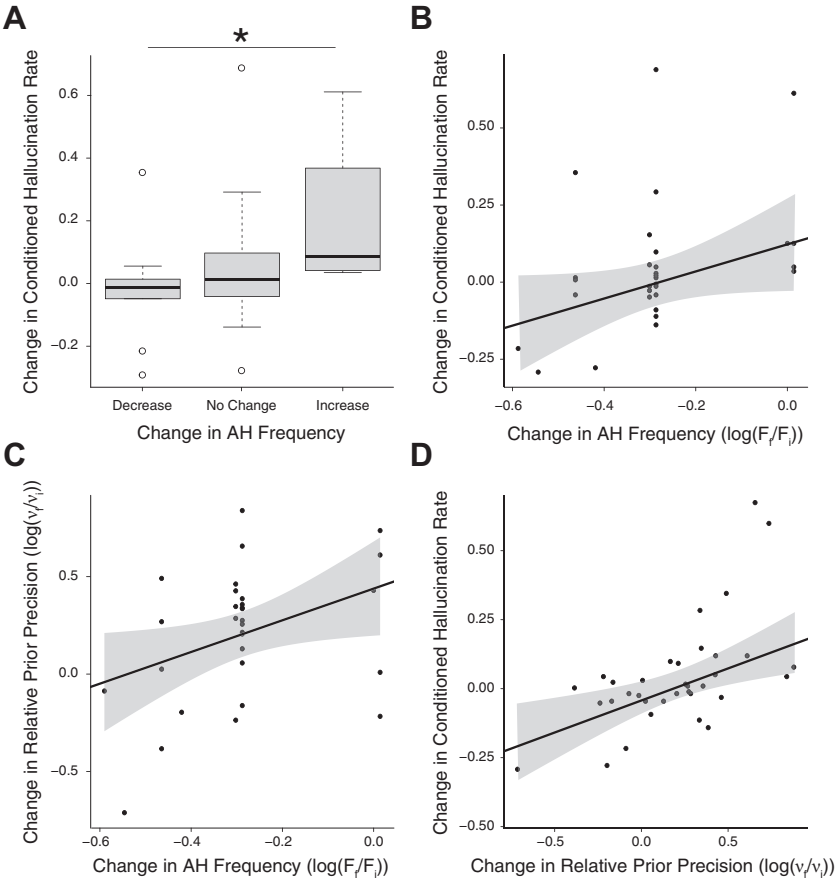

Figure 4. Changes in conditioned hallucinations (CHs) and prior weighting vary with changes in auditory hallucination (AH) frequency. **(A)** In a subsample of AH$^+$ participants who performed a repeated-measures version of the CH task again after several months, those with an increase in hallucination frequency showed a higher rate of CHs than those with a decrease, while those without a change in frequency demonstrated no change in CH rate. **(B–D)** Correlations demonstrating both CH rate **(B)** and relative prior weighting **(C)** track with changes in AH frequency on follow-up, and changes in CH rate are attributable to changes in prior weighting **(D)**. *$p < .05$.

reported rates (17) despite variance in software and hardware implementation as well as stimulus set (Figures S3–S5).

Relationships between prior weighting, CHs, and frequency of hallucinations are evident throughout the dataset. CH rates and prior weighting are higher in high-frequency hallucinating groups on cross-sectional analysis (Figures 2 and 3). In addition, changes in CH rate and priors track with changes in frequency of hallucinations during follow-up sessions even after adjustment for baseline frequency (Figure 4). Group differences in CH rate and prior weighting also vary within the experiment itself, as reflected by both raw (Figure 2D, E) and simulated (Figure S6) trial data. These patterns indicate that individuals with hallucinations acquire audiovisual contingency beliefs as quickly as those without but weigh these beliefs more strongly during perception. Thus, differences arise when the beliefs are strongest, earlier in the experiment, and weaken as the experiment continues and beliefs are updated in all groups.

Our findings that the relative weighting of priors is both higher in individuals who hallucinate and sensitive to changes in symptom severity suggests that relative prior weighting captures both static and dynamic elements of hallucinations. If increased prior weighting increases the likelihood of experiencing hallucinatory events, it may represent a latent brain state or mode of functioning that leads proximally to those events. This may be contrasted against other factors that, although increasing lifetime risk of having hallucinations (e.g., a history of trauma), do not translate to symptom severity on a more granular scale. Future interventional studies are required to understand the exact temporal relationships between prior weighting and hallucination expression and if differences in CH rate are sensitive to other psychotic symptoms (e.g., delusions) before hard conclusions can be drawn.

Our results contribute to the growing literature exploring computationally derived biomarkers in psychiatry (4,40,41). Biomarkers with some sensitivity to current symptom severity are able to track dynamic changes in symptomatology (41,42). We have recently demonstrated that individuals at high risk for psychosis tend to rely on their priors (18,43), which supports the potential utility of measures like this in identifying risk for symptom development before the onset of frank psychosis. Similarly, our results indicate that prior weighting is higher in individuals who hallucinate, regardless of clinical status, and is susceptible to changes in hallucination frequency over time. This may lead to the development of similar measures capable of tracking changes in latent states driving symptom expression among those who already exhibit risk for disease development (44). This latter approach would allow for a more nuanced understanding of pathophysiology, where the interplay between static risk factors (such as gene expression) lead to a worsening of dynamic, state-sensitive markers of symptom susceptibility.

From the perspective of computational neuroscience, the fact that relative prior overweighting can vary significantly over time yields important clues as to its neural instantiations. Although aberrations in cortical morphology (45–47) and white matter integrity (48) increase psychosis risk, it is unlikely that these processes directly drive prior weighting. Rather, these factors may predispose to the development of neural states in which prior weighting is dynamically heightened, either absolutely or relative to degraded and unreliable sensory evidence. Due to the short timescales over which changes in Bayesian inference have been observed, any neural mechanisms underlying these changes (e.g., phasic neuromodulator release) must also be dynamic (5,7,49). Further research is needed to assess the relationship between these processes and other known dynamic factors at play in psychosis.

There are some limitations to our study to consider. Having hallucinations may increase the tendency of participants to report CHs, regardless of whether those reports reflect true perceptual experience. Our data do not suggest that there are differences in overall target detection between AH^+ and AH^- groups. Reported detection on 25%, 50%, and 75% conditions did not significantly differ between groups nor did threshold (which is defined by rates of reported detection) (Figure 2 and Figure S2). We also consider the possibility of demand characteristics, because participants are asked to report hallucination status and severity, although observed changes in CH rates along with changes in hallucination frequency (Figure 4) are less easily explained by demand characteristics. However, the role of demand characteristics in motivating behavior cannot be entirely ruled out. Finally, despite having controlled for the groupwise clinical differences, it is not possible to completely rule out the influence of recruitment sources on CH rates.

The identification of a computationally driven method of identifying risk factors and underlying pathophysiological differences in individuals with hallucinations is the first step toward individualized risk and treatment prediction based on distinct etiologies (50). This work extends these efforts by identifying parameters within a specific, formalized model of perception that may lead to hallucination expression. We anticipate that subgroup identification based on such a formal system may take advantage of emerging knowledge of the neural (16,17) and biochemical (51) underpinnings of precision-weighting to identify biologically based interventions most likely to alter the pathophysiological processes leading to initial symptom expression.

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ARTICLE INFORMATION

From the Yale University School of Medicine and the Connecticut Mental Health Center (EK, VLF, BQ, AH, HJ, CM, ES, ADS, CL, ARP), New Haven, Connecticut; School of Naturopathic Medicine (RT), Southwest College of Naturopathic Medicine and Health Sciences, Tempe, Arizona; Faculty of Science (LG), University of British Columbia, Vancouver, British Columbia, Canada; Department of Psychiatry (AI), St Elizabeth's Hospital, Washington, DC; Cincinnati Veterans Affairs Medical Center (AMN), Cincinnati, Ohio; Istanbul Faculty of Medicine (ES), Istanbul University, Istanbul, Turkey; Max

Planck Institute for Psychiatry (ES), Munich, Germany; Department of Psychiatry (VP), All India Institute of Medical Sciences, New Delhi, India; McGill University School of Medicine (DB), Montreal, Quebec, Canada; Interacting Minds Centre (CM), Aarhus University, Aarhus C, Denmark; Translational Neuromodeling Unit (CM), Institute for Biomedical Engineering, University of Zürich and ETH Zürich, Zürich, Switzerland; and Neuroscience Area (CM), Scuola Internazionale Superiore di Studi Avanzati, Trieste, Italy.

EK and VLF contributed equally to this work.

Address correspondence to Albert R. Powers, M.D., Ph.D., at albert.powers@yale.edu.

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