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# The Cerebellum Links to Positive Symptoms of Psychosis: A Systematic Review and Meta-analysis

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***Background:*** **Positive symptoms of psychosis may be the result of faulty coordination and automatization of motor and higher order cognitive functions, partly due to cerebellar dysfunction. Specifically, auditory verbal hallucinations (AVH) have been related to altered processing of sensory feedback to one's own action. Such alterations highlight the role of dysfunctional cerebellar circuitry in psychosis. However, how exactly the cerebellum contributes to AVH remains unclear.** ***Methods:*** **A systematic search of electronic databases identified a broad range of cerebellar neuroimaging studies in psychotic patients, reporting volume, structural connectivity, or resting-state functional connectivity data. A total of 22 studies were selected for review: 11 focused on the specific effects of AVH and 11 probed the effects of aggregated positive symptom scores. Meta-analysis was used to probe the consistency of cerebellar differences and their relationship with sociodemographic and clinical measures. An exploratory activation likelihood estimation (ALE) analysis tested the regional specificity of cerebellar differences in patients with such symptoms.** ***Results:*** **Cerebellar differences were more consistently associated with AVH than with aggregated positive symptom measures, particularly when considering resting-state functional connectivity data. These differences were not moderated by age, sex, medication, or symptom severity. The ALE meta-analysis revealed a spatial convergence of these differences in lobules V–VI and crus I.** ***Conclusions:*** **Cerebellar dysconnectivity might indicate a specific liability for AVH, particularly in sensorimotor (lobules V–VI) and cognitive (crus I) cerebellar zones. These abnormalities may contribute to altered sensory feedback processing and, consequently, affect higher level cognitive functions (eg, cognitive control) in AVH.**

*Key words:* auditory verbal hallucinations (AVH)/meta-analysis/cerebellum/structural neuroimaging/diffusion-weighted imaging/resting-state fMRI/connectivity

## Introduction

The human cerebellum is a large brain structure that represents about 10% of total brain volume and has almost 80% of the surface area of the cerebral cortex.[1–4] It is densely interconnected with the thalamus, subcortical regions, and the cerebral cortex via parallel closed-circuit loops.[5,6] Although the cerebellum has traditionally been implicated in sensorimotor control,[7] converging evidence also suggests a role in non-motor functions such as cognitive[8–13] and affective processing.[11,14,15] Recent studies have revealed a functional differentiation of cerebellar sub-regions and cortico-cerebellar circuits[6,16–18] that involve sensorimotor (anterior lobe [extending into medial regions of lobule VI] and lobule VIII) and cognitive zones (posterolateral lobe). Lesions in topographically distinguishable cerebellar sub-regions also are known to give rise to distinct syndromes: for example, malfunctioning of the posterolateral cerebellum may impact cognitive processing in the absence of motor symptoms.[11]

The cerebellum is also central to the cognitive dysmetria model of psychosis,[19–21] which posits that faulty coordination and automatization of mental processes (eg, memory, attention, and motor activity) can account for the broad diversity of psychotic symptoms. Accordingly, abnormalities in cerebellar morphology[22] and connectivity[23,24] have been identified as the most significant predictors of psychotic symptoms. In addition, functional and anatomical cerebellar changes have been

related to sensorimotor deficits (eg, increased postural sway[25–27]), cognitive dysfunction,[28] and sensory modality (ie, auditory) of hallucinations.[29,30] However, the specific role of the cerebellum in positive symptoms such as auditory verbal hallucinations (AVH) remains understudied and only a small number of cerebellar findings are discussed in meta-analyses of structural MRI (sMRI) data obtained from hallucinating patients.[31–34]

AVH are a cardinal symptom of schizophrenia and related spectrum disorders,[35,36] presenting in approximately 60%–90% of patients and persisting in approximately 30% of cases despite treatment with antipsychotic medication.[37] Despite numerous attempts to explain the mechanisms underlying AVH, their neural substrates are yet to be clarified. However, an increasing number of behavioral,[38,39] electroencephalography,[40,41] and functional magnetic resonance imaging (fMRI) studies[42,43] suggests that AVH are associated with altered sensory feedback processing resulting from one's own action (eg, speaking). These alterations could be explained by changes in the cerebellum and altered functioning of its key role in forward modeling,[44] ie, the mechanistic computations that rely on a copy of the motor command to predict the sensory consequences of an action.[45–48] However, notwithstanding this causal link, research on the neural mechanisms underpinning AVH has mostly focused on cerebral regions with only scant attention to cerebellar contributions. Consequently, the consistency and regional specificity of cerebellar differences in AVH remain unknown.

As each cerebellar sub-region seems to connect to cortical regions through input and output projections,[16] distinct cortico-cerebellar circuits and cerebellar sub-regions could be differentially affected in AVH. This calls for more differentiated conceptual and methodological explanatory approaches. Specifically, cerebellar-thalamo-temporal cortical connectivity (sensorimotor circuitry recruiting the anterior cerebellar lobe and putatively engaged in auditory feedback processing) and cerebellar-thalamo-prefrontal cortical connectivity (cognitive circuitry recruiting the posterolateral cerebellum and putatively engaged in increased cognitive control demands) could be particularly disrupted in AVH.[44]

Among the available methods to study neural connectivity, diffusion tensor imaging (DTI) provides information on white matter architecture and integrity,[49,50] ie, structural connectivity. Cerebellar white matter tracts defined by tractography might indicate alterations in the neuronal architecture of the cerebellum and in cerebro-cerebellar connections.[51] In addition to structural connectivity, functional connectivity can be quantified during rest by correlating variations of blood oxygen-level

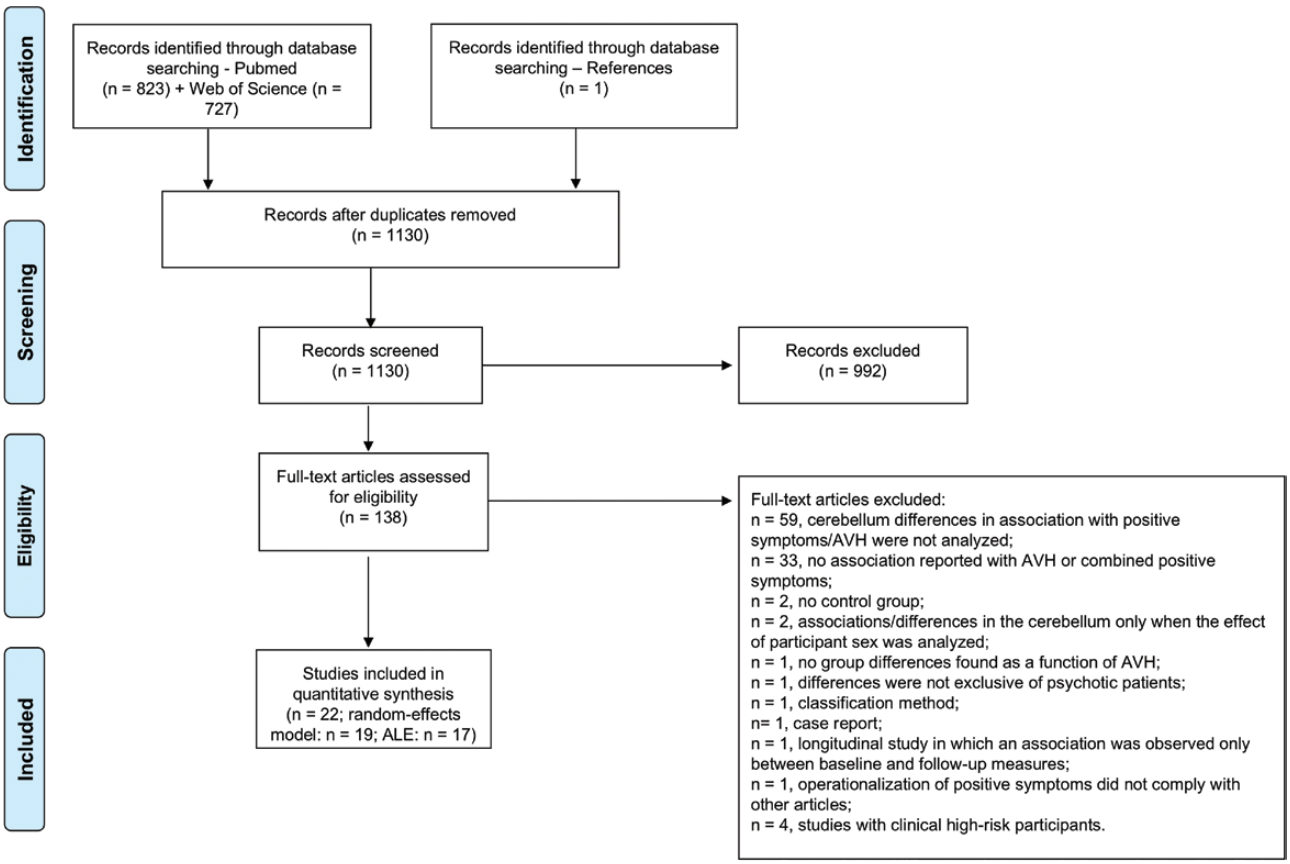


**Fig. 1.** Meta-analysis flowchart.

dependent (BOLD) signal across different brain regions over time.[52,53] Hence, it represents a promising measure to categorize cerebellar sub-regions into distinct functional networks[54,55] and to map the organization of cerebro-cerebellar circuits.[6] As AVH emerge in the absence of corresponding external input, the study of DTI and resting-state connectivity patterns might be more suitable to reveal differences in network connectivity underlying AVH compared to task-specific sensory stimulation.[56–58]

### *The Current Study*

The current study presents a systematic review and first quantitative meta-analysis of task-free sMRI, DTI, and resting-state fMRI (rs-fMRI) studies with a focus on the cerebellum in patients reporting psychotic-like symptoms such as AVH, and their matched controls. Using this approach, we examined the robustness and regional specificity of cerebellar differences in patients with such symptoms by specifying the possible concordance between findings across datasets and samples, and by determining possible heterogeneity factors, namely effects of age or symptom severity.[59]

To this end, the current study followed a two-step meta-analytic procedure. First, a random-effects model was applied to estimate the consistency of cerebellar differences in psychotic patients vs controls and their relationship with sociodemographic and clinical measures. Second, a primary activation likelihood estimation (ALE) meta-analysis, focusing on cerebellar coordinates, was conducted in an exploratory manner to define which cerebellar sub-regions are more reliably affected by positive symptoms such as AVH, as well as the symptom-specificity of these findings (AVH vs aggregated positive symptom scores). In doing so, we aimed to shed light on specific contributions of cerebellar sub-regions to the experience of hearing voices in the absence of corresponding sensory input.

## Methods and Materials

### *Literature Search Strategy*

First, a literature search of sMRI, DTI, and rs-fMRI studies, reporting specific AVH effects on cerebellar volume or structural and functional connectivity, published up to December 31, 2020, was performed using PubMed (https://www.ncbi.nlm.nih.gov/pubmed), Web-of-Science (htpps://webofknowledge.com), and Google Scholar (https://scholar.google.com) search engines, following established guidelines for systematic reviews and meta-analyses (ie, the PRISMA Statement[60]). We note that our meta-analysis was not registered at the protocol stage in a database such as PROSPERO, which may be considered a limitation of our study.

A combination of the following relevant keywords was used: cerebellum, AVH, psychosis/psychotic, schizophrenia, DTI, tractography, diffusion-weighted, and resting-state. A literature search was completed with reference tracing in already identified articles and in review articles.[61] After removing duplicates, titles and abstracts were reviewed independently by three authors (A.P.P., J.J., and M.A.). In a first step, studies were considered eligible if they: (1) were published in English peer-reviewed journals; (2) compared psychotic patients with AVH with controls and/or psychotic patients without AVH; (3) reported cerebellar differences in voice hearers vs controls; (4) used MRI; and (5) reported findings in either Montreal Neurological Institute (MNI) or Talairach space. Studies that conducted voxel-based analyses in which the cerebellum was reported as part of a region of interest analysis were also included. A total of 11 studies testing psychotic patients were included in the review (figure 1). Due to the limited number of available studies, which would not allow performing an ALE analysis (recommended minimum number of experimental entries = 17 [62]), we extended our search criteria to include studies reporting cerebellar differences in association with aggregated positive symptoms (eg, Positive and Negative Syndrome Scale [PANSS]-Positive subscale) without further specification. This led to the identification of 11

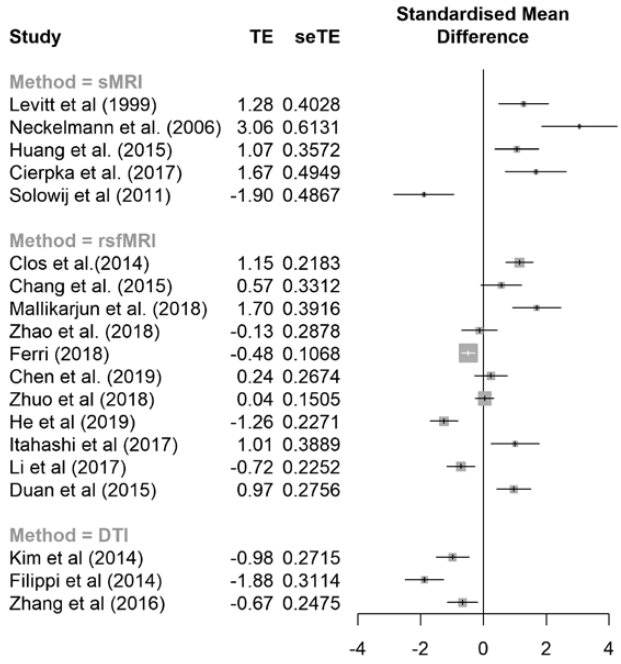


**Fig. 2.** Synthesis forest plot for the meta-analysis showing effect sizes for cerebellar measures in participants reporting positive symptoms such as AVH compared to matched healthy controls, as a function of imaging method. *Note.* DTI, diffusion tensor imaging; rs-fMRI, resting-state fMRI; sMRI, structural MRI. The size of the box is directly related to the weight of the study in the meta-analysis. Boxes on the left of the vertical line indicate reduced volume or connectivity in participants reporting positive symptoms compared to controls; boxes on the right of the vertical line indicate increased volume or connectivity in participants reporting positive symptoms compared to controls.

additional studies. Data from all studies ($n$ = 6 sMRI; 3 = DTI; 13 = rs-fMRI) were extracted by one of the authors and verified independently by two others (see figure 1; see supplementary table S1 for a list of all data extracted from each article). Any discrepancies were resolved through discussion and mutual consensus.

### *Data Analysis*

All eligible studies were pooled for the meta-analysis with a random-effects model. Due to effects dependence (ie, several effects nested within the same study), the meta-analytic model was estimated using robust variance estimation (a method that provides more weight to studies with smaller variance) with correction for small samples.[63] Effect sizes were computed using Hedges' $g$ (an unbiased standardized effect measure) and converted from $z$, $r$, $F$, and $t$ test statistics for cerebellar measures used in each study (see Supplementary materials and Supplementary table S1 available at https://osf.io/fut6y/?view_only=2de89d1cdf4542e2b4d576dbb93b7f1f). Heterogeneity was assessed with the $I^2$ statistic: $I^2$ values higher than 50% suggest relevant heterogeneity.[64] Further, a sensitivity analysis was performed to evaluate the estimated effect stability across different correlation values.[65] The impact of distinct sources of variability on volume or connectivity measures was also examined. Meta-regression models tested the effects of age,[66] sex, illness duration,[67] severity of positive (PANSS Positive subscale) and negative symptoms (PANSS Negative subscale), and chlorpromazine (CPZ) medication equivalents. In two studies, PANSS scores were estimated based on the Scale for the Assessment of Positive Symptoms (SAPS) and the Scale for the Assessment of Negative Symptoms (SANS) scores using a validated conversion equation.[68] Publication bias was assessed with a funnel plot and complemented with an additional sensitivity analysis[69] following a weight-model function. Analyses were conducted with robusta,[63] meta,[70] and metaphor[71] packages.[72] The R script used for the computation of the meta-analysis is available at https://osf.io/fut6y/?view_only=2de89d1cdf4542e2b4d576dbb93b7f1f, as well as the weightr shiny app[73] in the R environment (R3.4.3. GUI 1.70); effect sizes were converted using esc.[74]

Subsequently, an exploratory analysis was conducted to examine the convergence of cerebellar zones across studies testing the effects of AVH or aggregated positive symptom scores. An ALE analysis was conducted using the GingerALE package (3.0.2; www.brainmap.org/ale/) in the BrainMap environment (BrainMap

**Table 1.** Studies Included in the Meta-analyses

| # | Study | Method | Sample Size (N) | | | |
|---|---|---|---|---|---|---|
| | | | SZ (Undifferentiated) | pAVH | nAVH | HC |
| 1 | **Levitt et al.**[90] | sMRI | 15 | – | – | 15 |
| 2 | **Neckelmann et al.**[89]* | sMRI | 12 | – | – | 12 |
| 3 | Yoshihara et al.[92]* | sMRI | 18 | – | – | 18 |
| 4 | Solowij et al.[93a] | sMRI | 9 | – | – | 16 |
| 5 | **Huang et al.**[83]* | sMRI | – | 18 | 18 | 18 |
| 6 | **Cierpka et al.**[84]* | sMRI | – | 10 | 10 | 14 |
| 7 | **Kim et al.**[129] | DTI | 25 | – | – | 36 |
| 8 | **Filippi et al.**[91]* | DTI | 43 | – | – | 17 |
| 9 | **Zhang et al.**[130] | DTI | 39 | – | – | 30 |
| 10 | **Clos et al.**[57]* | rs-fMRI | – | 49 | – | 49 |
| 11 | **Chang et al.**[131]* | rs-fMRI | – | 18 | 18 | 20 |
| 12 | Alonso-Solis et al.[80]* | rs-fMRI | – | 19 | 14 | 20 |
| 13 | Duan et al.[96] | rs-fMRI | 28 | – | – | 31 |
| 14 | Cui et al.[82]* | rs-fMRI | – | 17 | 15 | 19 |
| 15 | **Li et al.**[99] | rs-fMRI | 42 | – | – | 42 |
| 16 | **Ferri et al.**[132]* | rs-fMRI | 183 | – | – | 178 |
| 17 | **Itahashi et al.**[81]* | rs-fMRI | 25 | – | – | 25 |
| 18 | **Mallikarjun et al.**[133]* | rs-fMRI | – | 18 | – | 18 |
| 19 | **Zhao et al.**[86]* | rs-fMRI | – | 28 | 20 | 38 |
| 20 | **Zhuo et al.**[97] | rs-fMRI | 95 | – | – | 93 |
| 21 | **Chen et al.**[87]* | rs-fMRI | – | 31 | 26 | 33 |
| 22 | **He et al.**[98]* | rs-fMRI | 42 | – | – | 52 |
| | | **Total** | **576** | **208** | **121** | **794** |

*Note.* HC, healthy controls; nAVH, psychotic patients without AVH; pAVH, psychotic patients with AVH; SZ, schizophrenia.
[a]The sample size refers specifically to cannabis non-users. Studies marked with an asterisk were included in the ALE meta-analysis (these studies reported MNI coordinates or replied to the authors' request for providing the coordinates). Studies highlighted in bold were included in the estimation of Hedges' $g$ index (these studies provided the necessary statistical information for the computation of Hedges' $g$ index).

**Table 2.** Inclusion Criteria of Voice Hearers in the Studies Included in the Meta-analyses That Specifically Compared Participants With vs Without AVH

| Study | pAVH Clinical Group—Inclusion Criteria | nAVH Clinical Group—Inclusion Criteria | Other Relevant Features | Control of AVH During Scanning? |
|---|---|---|---|---|
| Huang et al.[83] | Reported AVH at least once a day for the past 4 weeks | Never experienced AVH or have not experienced them within 2 years before recruitment | 1st episode and drug-naive at time of scanning | Information not provided |
| Cierpka et al.[84] | Medication resistant for AVH (>6 weeks of treatment for at least two clinically ineffective drug trials), without pronounced formal thought disorder symptoms, with sufficient insight into AVH | Never experienced AVH during the illness course or experienced AVH in the past but were fully remitted from AVH at least 12 months before the study | Schizophrenia patients (paranoid subtype); no group differences (pAVH vs nAVH) in CPZ equivalents | Information not provided |
| Clos et al.[57] | Experienced AVH several times a day for at least 1 year | n.a. | Chronic psychosis | Yes. Post-scan assessment of AVH: spontaneous reports did not yield reliable information on specific features of AVH |
| Chang et al.[131] | Reported AVH at least once a day for the past 4 weeks | Never experienced AVH or have not experienced them within 2 years before recruitment | 1st episode and drug-naive at time of scanning. Participants not included if they reported a history of significant neurological or systematic illness, substance abuse, or prior electroconvulsive therapy | Information not provided |
| Alonso-Solis et al.[80] | Daily presence of AVH in the past year (quantified with PANSS), in face of at least 2 adequate trials of antipsychotic drugs at equivalent doses to 600 mg/day if clozapine | Did not show acute psychotic symptoms (quantified with PANSS) in the last 12 months | Patients not included in the study if presenting substance use (except alcohol, tobacco or cannabis), neurological disease or mental retardation | Information not provided |
| Cui et al.[82] | Reported AVH at least once a day for the past 4 weeks | Not specified | 1st episode and drug-naive at time of scanning. Patients not included if they reported a history of significant neurological or systematic illness | Information not provided |
| Mallikarjun et al.[133] | At least one episode of AVH every other day | n.a. | 1st episode psychosis | Participants pressed a button during scanning during the experience of AVH: symptom capture analysis served a seed-based FC analysis |
| Zhao et al.[86] | A score of ≥3 on P3 item of PANSS | Not specified | 1st episode and drug-naive at time of scanning. Patients not included if they reported a history of significant neurological or systematic illness, mental retardation, were pregnant, planning to be pregnant within the following 6 months, lactating | Information not provided |

**Table 2.** Continued

| Study | pAVH Clinical Group—Inclusion Criteria | nAVH Clinical Group—Inclusion Criteria | Other Relevant Features | Control of AVH During Scanning? |
|---|---|---|---|---|
| Chen et al.[87] | Reported AVH of spoken speech at least 5 times per day during the preceding 8 weeks; refractory AVH (at least 12 weeks) | Had not experienced AVH (or olfactory, gustatory, tactile hallucination) since the diagnosis of schizophrenia or within 5 years before MRI | Patients with refractory schizophrenia; no group differences (pAVH vs nAVH) in CPZ equivalents. Patients not included if they reported a history of significant neurological or systematic illness, head trauma, recent aggression or other forms of behavioral dysfunction, or substance abuse. | No |
| Neckelmann et al.[89] | BPRS Hallucinations score | n.a. | Patients not included if they reported a history of significant neurological or systematic illness, or substance abuse. | Information not provided |
| Itahashi[81] | Auditory hallucination severity was evaluated using the AHRS and the PANSS hallucination item (P3) | n.a. | Patients not included if they reported a history of significant neurological or systematic illness, or substance abuse. | Information not provided |

*Note.* AHRS, Auditory Hallucination Rating Scale; AVH, auditory verbal hallucinations; BPRS, Brief Psychiatric Rating Scale; CPZ, chlorpromazine; FC, functional connectivity; n.a., not applicable; nAVH, psychotic patients without AVH; PANSS, Positive and Negative Syndrome Scale; pAVH, psychotic patients with AVH.

Project, San Antonio, TX). Experimental coordinates were entered into the database in Montreal Neurological Institute (MNI) space, irrespective of the imaging modality. Results reported in Talairach space[75] were converted to MNI[76] using the GingerALE (2.3.6) icbm2tal conversion algorithm.[77] An "experiment" was defined as a single mapwise contrast between subjects presenting AVH (or an aggregated positive symptoms score) and control subjects (healthy controls or psychotic patients without AVH, in separate contrasts). Following prior recommendations,[78,79] ALE maps were derived using a cluster-level familywise error thresholding inference ($p < .05$) with 5000 random permutations and an uncorrected cluster forming threshold ($p < .001$).[62] Secondary ALE analyses examined the reported coordinates for effects that were specifically related to AVH to test the symptom-specificity of these findings.

## Results

In the following sub-sections, we first describe the literature search results: the demographic and other descriptive data of the samples included in the meta-analyses are presented, and the main findings per imaging modality are summarized. Finally, we present the results of the meta-analyses, including the random-effects models and meta-regression, as well as the exploratory ALE analysis.

### *Literature Search Results*

A total of 22 studies were selected (table 1; $n = 6$ sMRI, 3 DTI, 13 rs-fMRI studies). Across studies, there were 794 healthy controls, 208 psychotic patients with persistent AVH, 121 psychotic patients without AVH, and 576 psychotic patients characterized on the basis of an aggregated positive symptom score. The latter number refers to studies that did not discriminate how many patients experienced AVH but, instead, reported an aggregated positive symptom score (eg, PANSS positive subscale score); that is, patients with different positive symptom profiles were grouped on the basis of a positive subscale score. These studies were included to reach the minimum number of studies required to conduct an ALE meta-analysis. Among the full set of studies, 11 studies specifically included participants with AVH: 9 involved a comparison of voice hearers with patients without AVH and healthy controls[80–87] or with healthy controls only[57,88]; 2 tested a correlation with AVH measures.[81,89] Supplementary table S1 lists demographic and other descriptive data for each study. The mean age was 28.50 years for the group of psychotic patients with AVH, 26.55 for the group of psychotic patients without AVH, 32.98 for the group of psychotic patients characterized on the basis of an aggregated positive symptom score, and 30.71 for healthy control subjects.

**Table 3.** Main Findings of Volumetric (sMRI) Studies

| | Method | | ROI | | |
|---|---|---|---|---|---|
| Author (Year) | Measure | Restriction | Determination | Cerebellar Findings | |
| A. Group Findings | | | | Groups | Increase or Decrease |
| Huang et al.[83] | GM | Whole-brain | Regions of significant difference in group analysis (pAVH, nAVH, HC) | pAVH vs HC | ↓ GM: L pCE, R aCE |
| Cierpka et al.[84] | GM | Cerebellum | Lobule parcellation with probabilistic atlas of human cerebellum[1] | pAVH vs HC | ↓ GM: R CE (VIIb) |
| | | | | pAVH vs nAVH | ↓ GM: R CE (VIIIa) |
| B. Correlation Findings | | | | Measure | Positive or Negative |
| Levitt et al.[90] | WM | Cerebellum vermis | Regions of significant difference in group analysis (SZ, HC) in whole, hemispheric, and vermis regions-of-interest | SAPS | ↑ WM: CE vermis |
| Yoshihara et al.[92] | WM | Whole-brain | At each intracerebral voxel (for each tissue class separately) | PANSS(P) | ↑ WM: CE vermis/↓ WM: B CE(h) |
| Neckelmann et al.[89] | GM | Whole-brain | Regions from regression model with clinical scores as a covariate (same dataset) | BPRS(H) | ↓ GM: L, R pCE |
| Solowij et al.[93] | WM | Cerebellum | Regions of significant correlation in only schizophrenic non-cannabis users group | SAPS | ↓ WM: CE |
| Cierpka et al.[84] | GM | Cerebellum | Regions of significant difference in group analysis (pAVH, nAVH, HC) | PANSS(P) | ↓ GM: R CE (VIIIa) |

*Note:* Anatomical and neuroimaging: aCE, anterior cerebellum; CE, cerebellum; GM, gray matter; L, left; pCE, posterior cerebellum; R, right; ROI, region of interest; WM, white matter. Clinical scales: BPRS, Brief Psychiatric Rating Scale; PANSS, Positive and Negative Syndrome Scale; SAPS, Scale for the Assessment of Positive Symptoms. *Sample*: HC, healthy controls; nAVH, psychotic patients not reporting AVH; pAVH, psychotic patients reporting AVH; SZ, schizophrenia.

The studies that specifically tested participants with vs without AVH varied in the inclusion criteria of voice hearers (table 2): whereas most included patients who reported AVH at least once a day,[57,80,82,83,85,87] others were less strict (eg, experience of AVH every other day[88]; medication-resistant for AVH for at least 6 weeks of treatment[84] without specification of AVH frequency; selection of AVH participants based on clinical scale scores without specification of current AVH frequency—a score of at least 3 on PANSS hallucinatory behavior,[86] Brief Psychiatric Rating Scale Hallucinations score,[89] or Auditory Hallucination Rating Scale and PANSS-P3 score[81]). All but five studies[81,89–92] relied on the same scan acquisition magnetic field strength (3T) (table 3). The quality of each study was evaluated based on criteria that considered aspects related to both sample composition/characterization and imaging procedures (see Supplementary Material). The main findings of these studies are summarized in tables 3–5 (see also Supplementary table S1).

*Structural MRI*. Six studies[83,84,89,90,92,93] were included ($n$ = 110 patients, 93 controls; table 3), with mixed results. *Reduced* gray matter volume in both anterior and posterior lobes[83] was observed in psychotic patients with AVH compared to healthy controls. A specific gray matter volume reduction was identified in psychotic patients with AVH in lobules VIIb (compared to healthy controls) and VIIIa (compared to psychotic patients without AVH) using cerebellum-optimized segmentation techniques.[84] Positive symptom scores were negatively correlated with cerebellar gray matter volume in the posterior lobe[89] or with total cerebellar white matter volume.[93] However, *increased* vermis white matter was found to be positively correlated with positive symptom severity in psychotic patients.[90,92]

*Diffusion Tensor Imaging*. Three studies[91,94,95] ($n$ = 107 patients, 83 controls; table 4) were included. *Reduced* fractional anisotropy[94,95] and mean diffusivity[91] were found to be associated with increased positive symptom severity. These alterations involved both anterior[95] and posterior[91,94] lobes of the cerebellum.

*Resting-state fMRI*. A total of 13 studies[57,58,80–82,85–88,96–98] were included ($n$ = 688 patients, 618 healthy controls; table 5). Patterns of both increased and decreased connectivity were identified. Functional connectivity was *decreased* between the cerebellum and the thalamus,[57] putamen, and claustrum[82] in psychotic patients with AVH, as well as between the left and right hemispheres of the anterior cerebellar lobe.[85] Effective connectivity between

**Table 4.** Main Findings of Structural Connectivity (DTI) Studies

| Author (Year) | Method | | ROI | | | Cerebellar Findings | |
|---|---|---|---|---|---|---|---|
| | Measure | Restriction | Determination | # | Cerebellar Location | | |
| Correlation Findings | | | | | | Measure | Positive or Negative |
| Kim et al.[129] | FA | Cerebellum | Spatially unbiased cerebellar lobules | 28 | L, R CE (I–V, V, crus I, II, VIIb, VIIIa, VIIIb, IX, X), CE Vermis (crus I, II, VIIb, VIIIa, VIIIb, IX, X) | PANSS(P) | ↓FA: CE (crus I) |
| Filippi et al.[91] | FA, MD | Whole-brain | Voxels of significant correlation with clinical features (same dataset) | n/a | n/a | PANSS(P) | FA: *n.s.* ↓MD: R m/iCEP |
| Zhang et al.[130] | FA | Whole-brain | Regions of significant difference in group analysis (SZ, HC) | 1 | L CE | PANSS(P) | ↓FA: L CE |

*Note:* Anatomical and neuroimaging: aCE, anterior cerebellum; CEP, cerebellar peduncles; CE, cerebellum; FA, fractional anisotropy; L, left; MD, mean diffusivity; pCE, posterior cerebellum; R, right; ROI, region of interest. Clinical scales: BPRS, Brief Psychiatric Rating Scale; PANSS, Positive and Negative Syndrome Scale; SAPS, Scale for the Assessment of Positive Symptoms. Sample: HC, healthy controls; SZ, schizophrenia.

the posterior cerebellum and posterior cingulate cortex was also decreased in psychotic patients with AVH.[86] In contrast, functional connectivity was *increased* between the cerebellum and both temporal pole[80] and insula[88] in psychotic patients with AVH. In addition, effective connectivity was found to be increased between the posterior cerebellum and anterior middle prefrontal cortex[86] in psychotic patients with AVH compared to healthy controls.[86]

Different studies reported negative correlations between positive symptom scores and functional connectivity between the right cerebellar lobule VI and left crus I,[97] and between the thalamus and the right posterior cerebellar lobe.[58] Dynamic functional connectivity between sensorimotor cerebellar zones (bilateral lobules V, VI, VIIb, VIIIa, VIIIb) and the fronto-parietal and sensorimotor networks was also found to be negatively correlated with positive symptom scores.[98] In addition, a negative correlation between resting-state amplitude of low frequency fluctuation in the left posterior lobe of the cerebellum and positive symptom severity was also observed.[99] Positive correlations between positive symptom scores and functional connectivity of the cerebellum were also identified, namely between the cerebellum and the left caudate nucleus,[96] or between the posterior cerebellum and the rest of the brain.[81]

### *Random-Effects Models and Meta-regression*

A total of 19 pooled studies with 30 within effects (see figure 2) were included in the correlated random-effects model with small-sample corrections separately per imaging modality: 5 sMRI (8 within effects), 3 DTI (4 within effects), and 11 rs-fMRI (18 within effects). Three (out of 22) studies were excluded because they did not provide the necessary statistical information to compute an effect size.[80,82,92]

Results revealed nonsignificant estimates for sMRI ($g$ = 1.04, SE = 0.82, $p$ = .275, 95% CI [−1.24, 3.31]), DTI ($g$ = −1.16, SE = 0.36, $p$ = .083, 95% CI [−2.69, 0.38]), and rs-fMRI ($g$ = 0.25, SE = 0.27, $p$ = .366, 95% CI [−0.34, 0.85]) cerebellar measures when pooling data from studies testing specific effects of AVH and of aggregated positive symptoms. Heterogeneity values were high ($I^2_{sMRI}$ = 92.6%, $I^2_{DTI}$ = 78.7%, $I^2_{rs\text{-}fMRI}$ = 94.4%). In a subsequent analysis, we tested whether effect sizes differed between studies reporting cerebellar differences specifically as a function of AVH (9 studies, 17 within effects) or as a function of an aggregated positive symptom score (10 studies, 13 within effects). A significant pooled large effect size was observed for studies focusing on AVH only ($g$ = 1.08, SE = 0.29, $p$ = .006, 95% CI [0.42, 1.74], $I^2$ = 87.5%; figure 3). For studies reporting cerebellar differences as a function of an aggregated positive symptom score, the estimate was not significant ($g$ = −0.55, SE = 0.32, $p$ = .118, 95% CI [−1.27, 0.17], $I^2$ = 92.9%). Effects remained unchanged for different correlation values. The prediction interval (PI) for the significant effect suggested a similar pattern for future studies (95% $PI_{AVH}$ [0.39, 1.77]) ($p$-values included .001, .01, .05, .10, .20, and .30 with the following weights: 1 for $p$ <.05; 0.80 for $p$-values between .05 and .10; 0.70 for $p$-values between .10 and .20; 0.60 for $p$-values between .20 and .30; and 0.50 for $p$-values between .30 and 1.). We also explored the effects of AVH for each imaging modality separately: a significant effect size was observed for rs-fMRI studies (6 studies, 11 within effects—$g$ = 0.74, SE = 0.27, $p$ = .039, 95% CI [0.05, 1.43]; $I$ = 89.3%); the effect was only marginally significant in the case of sMRI

**Table 5.** Main Findings of Resting-state fMRI Studies

| | Method | ROI (Seeds) | | | | | Cerebellar Findings | | |
|---|---|---|---|---|---|---|---|---|---|
| Author (Year) | Measure | Restriction | Determination | # | Location | Size | | | |
| A. Group Findings | | | | | | | Groups | Increase or Decrease | |
| Clos et al.[57] | FC | Seed | Regions active during AVH | 4 | L MTG, L IFG, L AG, L Thal | 5mm radius | pAVH vs HC | ↓ FC: L Thal ↔ R CE | |
| Alonso-Solis et al.[80] | FC | Seed | Hubs and subsystem regions of DMN | 11 | DMN hubs (PCC, aMPFC), subsystem 1 (DMPFC, TPJ, LTC, TempP), subsystem 2 (VMPFC, pIPL, Rsp, PHC, HF) | 4mm radius | pAVH vs HC/pAVH vs nAVH | ↑ FC: TempP ↔ CE | |
| Chang et al.[131] | VMHC | Whole-brain | Bilateral areas of significant difference in group analysis (pAVH, nAVH, HC) | n/a | n/a | *n/a* | pAVH vs HC / pAVH vs nAVH | ↓ VMHC: R aCE ↔ L aCE | ** |
| Cui et al.[131] | FC | Seed | Regions of significant ALFF and ReHo modulation (same dataset) | 2 | L Put, R Put | 6mm radius | pAVH vs HC | ↓ FC: R Put ↔ CE (B IV, B V, L VIII)<br>↓ FC: L Put ↔ CE (B VIII, R IV, R V) | |
| Mallikarjun et al.[131] | FC | Seed | Regions active during AVH (same dataset) | 15 | Cluster 1 (L LG, L LG, L pHIP), 2 (L Ins, L STG, L STG), 3 (R Ins, R STG, R STG), 4 (L Ins, L CL, L CL), 5 (R PCC, R PCu, R PCu) | 4mm radius | pAVH vs HC | ↑ FC: L Ins ↔ B CE<br>↑ FC: L CL ↔ L CE | |
| Zhao et al.[86] | EC (GCA) | Seed | Hub regions of DMN | 2 | PCC, aMPFC | 6mm radius | pAVH vs HC<br>pAVH vs nAVH | ↑ EC: pCE → aMPFC<br>↓ EC: PCC → L pCE | |
| Chen et al.[87] | FC(S) | Whole-brain | Regions of significant difference in group analysis (pAVH, nAVH, HC) | 7 | B Cu, L CS, L MTG, B CE, L SMG, B Thal, R MPFC | *not given* | pAVH vs HC<br>pAVH vs HC / pAVH vs nAVH | ↑ FC(S): R CE ↔ rest of brain<br>↑ FC(S): L CE ↔ rest of brain | |
| B. Correlation Findings | | | | | | | Measure | Positive or Negative | |
| Li et al.[99] | ALFF | Whole-brain | Regions of significant difference in group analysis (SZ, HC) | 5 | B pCE, B Put, R MTG, R FFG, R Ins | *not given* | PANSS(P) | ↓ ALFF: L pCE | *** |
| Duan et al.[96] | FC | Seed | Regions of significant difference in group analysis (SZ, HC) | 2 | L CN, R CN | 141, 71 voxels | PANSS(P) | ↑ FC: L CN ↔ CE | |

**Table 5.** Continued

| Author (Year) | Method | ROI (Seeds) | | | | | Cerebellar Findings | | |
|---|---|---|---|---|---|---|---|---|---|
| | Measure | Restriction | Determination | # | Location | Size | | | |
| Ferri et al.[132] | FC | Seed | Bilateral thalamic region of thalamo-cortico-cerebellar network | 1 | B Thal | *not given* | SAPS(P) | ↓ FC: Thal ↔ R pCE | |
| Itahashi et al.[81] | FC | Whole-brain | Regions of significant difference in group analysis (SZ, HC) | 1 | R CE (crus I) | 84 voxels | PANSS(P3) | ↑ FC: CE (crus I) ↔ rest of brain | * |
| Zhuo et al.[97] | FC(D) | Cerebellum | Regions of significant difference in group analysis (SZ, HC) | 1 | R CE (VI) | *not given* | PANSS(P) | ↓ FC: R CE (VI) ↔ L CE (crus II) | * |
| He et al.[98] | (d)FC | Cerebellum | Regions of significant coupling between FC and changes in GM in SZ (same dataset) | 2 | CBCc (B crus I/II), CBCm (B V/VI/VIIb/VIIIa/VIIIb), | *not given* | PANSS(P) | ↓ (d)FC: CBCm ↔ FPN (L DLPFC)<br>↓ (d)FC: CBCm ↔ SM (SMA) | *<br>* |

*Note:* Anatomical: AG, angular gyrus; AIns, anterior insula; aMPFC, anterior middle prefrontal cortex; aPFC, anterior prefrontal cortex; B, bilateral; CBCc, cerebellar cognitive cluster (defined as bilateral crus I and crus II); CBCm, cerebellar motor cluster (defined as bilateral lobules V, VI, VIIb, VIIIa, VIIIb); CE, cerebellum; CEN, cerebellar network; CL, claustrum; CN, caudate nucleus; CON, cingulo-opercular network; CS, central sulcus; Cu, cuneus; DLPFC, dorsolateral prefrontal cortex; DMN, default mode network; DMPFC, dorsomedial prefrontal cortex; FFG, fusiform gyrus; FPN, fronto-parietal control network; HF, hippocampal formation; IFG, inferior frontal gyrus; IPL, inferior parietal lobule; Ins, insula; L, left; LG, lingual gyrus; LTC, lateral temporal cortex; MTG, middle temporal gyrus; MPFC, medial prefrontal cortex; PCC, posterior cingulate cortex; PHC, parahippocampal cortex; pHIP, parahippocampal gyrus; pIPL, posterior inferior parietal lobule; PCu, precuneus; Put, putamen; R, right; Rsp, retrosplenial cortex; SM, sensorimotor network; SMA, supplementary motor area; SMG, supramarginal gyrus; STG, superior temporal gyrus; TempP, temporal pole; Thal, thalamus; TPJ, temporo-parietal junction; VMPFC, ventral medial prefrontal cortex. *Clinical scales:* PANSS = Positive and Negative Syndrome Scale; SAPS = Scale for the Assessment of Positive Symptoms; BPRS = Brief Psychiatric Rating Scale; BPRS(H). Neuroimaging measures: ALFF, amplitude of low frequency fluctuation; (d)FC, dynamic functional connectivity; EC, effective connectivity; FC, functional connectivity; FC(S), functional connectivity strength; FCA, granger causality analysis; ReHo, regional homogeneity; ROI, region of interest; VHMC, voxel-mirrored homotopic connectivity (bilateral functional connectivity). Sample: HC, healthy controls; nAVH, psychotic patients not reporting AVH; pAVH, psychotic patients reporting AVH; SZ, schizophrenia.
Cerebellar Findings:
*Result from a cerebellar seed; **Result between cerebellar seeds; ***Result within a cerebellar seed.

studies (3 studies, 6 within effects—$g$ = 1.85, SE = 0.57, $p$ = .084, 95% CI [−0.62, 4.31]; $I^2$ = 74.5%).

Regarding publication bias, the visual inspection of the funnel plot suggested asymmetry (figure 4), which was supported by a sensitivity analysis revealing an adjusted model with a slight decrease in the point estimate ($g_{AVH}$ = 0.90).

Meta-regression models were performed for AVH pooled estimates. No associations were observed with the mean age of the experimental and the control group, symptom severity, medication (CPZ equivalents), illness duration, or proportion of female participants ($p$ > .05).

### *ALE Results*

A total of 18 out of 22 studies ($n$ = 4 sMRI,[83,84,89,92] 2 DTI,[91,95] 12 rs-fMRI[57,58,80–82,85–88,96,98,99]) were included in the exploratory primary ALE (4 studies did not provide anatomical coordinates[90,93,94,97]). Four clusters were identified showing convergence of neuroimaging

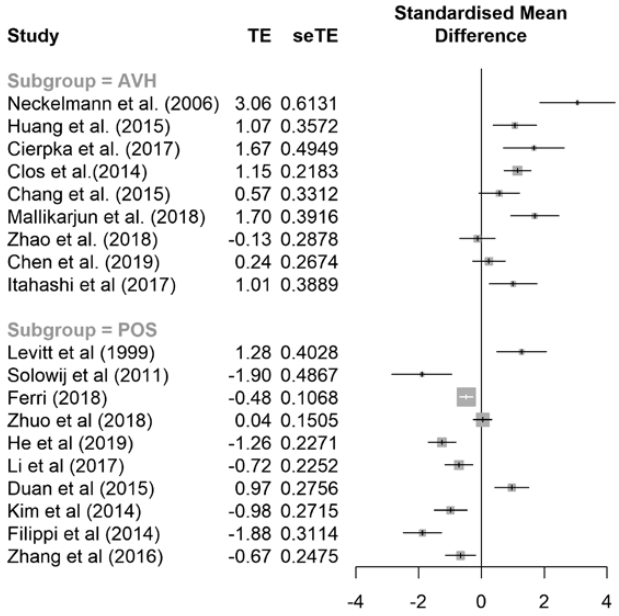


**Fig. 3.** Synthesis forest plot for the meta-analysis showing effect sizes for cerebellar measures in studies probing the specific effects of AVH or aggregated positive symptoms (POS).

findings (table 6; figure 5). The two largest clusters were found in (left) crus I and (left) lobule VI. The third and fourth clusters were located in (right) lobules V/VI and (right) lobule X.

Subsequently, we attempted to define which clusters were specifically associated with AVH, by conducting a secondary ALE with studies reporting effects dependent on AVH. The ALE revealed three clusters that were specific of AVH (table 5): the first centered in left crus I, the second centered in right lobule V/VI, and the third centered in right crus I.

## Discussion

The current meta-analyses provide the first quantification of the location and extent of structural and connectivity differences in cerebellar regions related to positive symptoms and, specifically, AVH, combining data from 1699 participants. We observed that cerebellar dysconnectivity might indicate a specific liability for AVH, particularly in sensorimotor (lobules V–VI) and cognitive (crus I) cerebellar zones.

The random-effects model suggests that cerebellar alterations are more consistently associated with AVH than with aggregated positive symptom measures: studies focusing specifically on AVH produced a significant and large effect size ($g$ = 1.08), whereas the effect size of studies reporting cerebellar differences on the basis of an aggregated positive symptom score was not significant. These differences were more robust when considering measures derived from resting-state fMRI studies and were not moderated by age, sex, illness duration, medication, or symptom severity. Therefore, sources other than these factors may be causing significant heterogeneity in the reported studies. We note, though, that the number of studies included in our meta-analyses is relatively small, which may have contributed to the lack of statistically significant effects in the meta-regression. Therefore, these findings should be replicated in future studies and meta-analyses.

The ALE analysis complemented the random-effects model by showing that not all cerebellar sub-regions seem to be equally affected by AVH. The spatial convergence was stronger in the cerebellar hemispheres, particularly in (left and right) crus I and (right) lobule V/VI. However, considering the limitations of including different imaging modalities in the same statistical model, the ALE results should be considered as exploratory.

Recent studies suggest a spatial compartmentalization of sensorimotor and cognitive functions within the cerebellum.[100] The anterior cerebellum (eg, lobules V and VI) is primarily connected to motor and pre-motor cortical regions,[18,101] supplementary motor area, and lateral thalamic regions that project to primary sensorimotor regions.[102] These sub-regions are consistently activated during planning and execution of simple actions[103] as part of a primary sensorimotor zone.[104] Specifically, lobule V was found to engage in predicting the sensory consequences of action[105] and in signaling unexpected changes in sensory feedback.[106–108] The right-lateralized anterior cerebellar coordinate is consistent with the observation of motor and somatosensory representations in right-handed participants, showing ipsilateral cerebellar somatotopy.[73] The posterolateral cerebellum (eg, crus I) is connected to the prefrontal cortex[16,18,109] and engages in executive functions such as cognitive control.[101,110,111] Specifically, crus I has also been implicated in the sensory processing of sounds at shorter latencies than the auditory cortex[112] in line with a sensory function of the cerebellum.[113] The current findings may suggest that AVH, in particular, are related to abnormalities in cerebellar regions engaged in sensorimotor and cognitive control functions. These findings further indicate it is relevant to differentiate positive symptom profiles, which may imply distinct neurocognitive mechanisms.[114,115] This aligns with the notion that the factor structure of positive symptoms is more complex than it is generally acknowledged.[116–119]

### *Methodological Considerations and Future Directions*

The interpretation of the current results needs to consider limitations of meta-analytic methods that pool studies varying in sample size, magnetic field strength, or data analysis. Even though we used a random-effects model (robust to between-study variations), several limitations regarding sample composition should be noted.

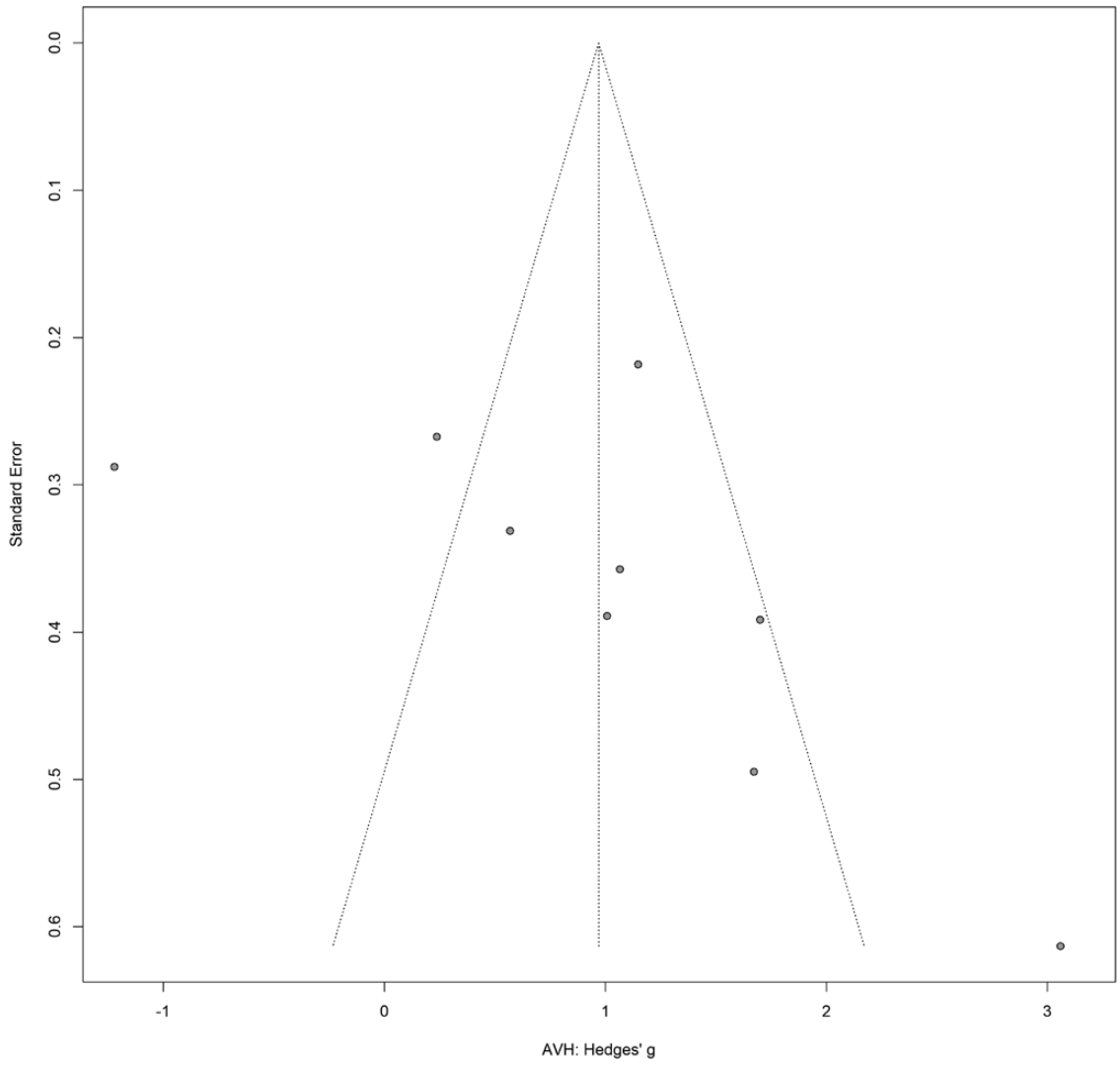


**Fig. 4.** Funnel plot of potential ascertainment bias in studies focused specifically on AVH.

The lack of a comparison group of non-hallucinating psychotic patients in some of the studies[57,88] does not allow definite conclusions about the selectivity of the reported abnormalities in AVH. Due to the limited number of studies examining differences in cerebellar volume or structural and functional connectivity in patients reporting AVH, we added studies reporting an association with an aggregated positive symptom score. However, we note that AVH rarely occur as isolated mental events but often co-occur with delusional thoughts; also, AVH and delusions may not be clearly separable under certain circumstances.[120] The relatively small number of studies may have accounted for the nonsignificant effects of moderators such as age, sex, illness duration, medication, or symptom severity as well as for the nonsignificant estimates for sMRI studies. Therefore, we note that the absence of evidence for a statistically significant effect of these variables should not be regarded as evidence of absence of an effect. More studies are clearly warranted to explore this lack of an effect.

Technical and methodological limitations should also be pointed out. Most advanced methods for the analysis of structural brain imaging data are optimized for the cerebrum but not the cerebellum. This may be related to a cortico-centric bias in neuroscience research,[121] reflected in optimized scanning protocols and analysis tools for the cerebral cortex. The cerebellum is often not included in standard scanning or analysis protocols and, therefore, its involvement in AVH is likely underreported. Most structural studies have used relatively crude segmentation techniques to examine the cerebellum (eg, voxel-based morphometry[83,89]), which do not pick up functional sub-regions within cerebellar lobes.[6,18] As for DTI, we should note that current fiber extraction algorithms do not optimally disentangle unique axonal pathways based on their cerebellar origin.[94] Additionally, seed-based approaches to resting-state functional

**Table 6.** ALE Meta-analysis Results

| | | Coordinates (Center) | | | | Localization | | | Main Contributors | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Analysis | Cluster # | X | y | z | **Size (mm³)** | Hemisphere | Lobe | Label of Center | Ref. | Method | Main Results |
| SSA ALL | 1 | −40 | −71.9 | −38.5 | 952 | Left | Posterior | Crus I | [1] | sMRI | AVH↓ |
| | | | | | | | | | [2] | rs-fMRI | AVH ↑ |
| | | | | | | | | | [3] | rs-fMRI | AVH ↑ |
| | | | | | | | | | [4] | sMRI | AVH↓ |
| | 2 | −27.8 | −58.7 | −28.9 | 904 | Left | Anterior | Lobule VI | [5] | DTI | POS ↓ |
| | | | | | | | | | [6] | rs-fMRI | POS ↓ |
| | | | | | | | | | [7] | DTI | POS ↓ |
| | 3 | 22.8 | −46.9 | −22.2 | 864 | Right | Anterior | Lobule V/VI | [1] | sMRI | AVH↓ |
| | | | | | | | | | [8] | rs-fMRI | AVH↓ |
| | | | | | | | | | [9] | rs-fMRI | AVH↓ |
| | 4 | 22.6 | −39.2 | −46.1 | 736 | Right | Posterior | Lobule X | [10] | rs-fMRI | POS ↓ |
| | | | | | | | | | [11] | rs-fMRI | AVH ↑ |
| SSA AVH | 1 | −40.1 | −72.3 | −38.4 | 1152 | Left | Posterior | Crus I | [1] | sMRI | AVH↓ |
| | | | | | | | | | [2] | rs-fMRI | AVH ↑ |
| | | | | | | | | | [3] | rs-fMRI | AVH ↑ |
| | | | | | | | | | [4] | sMRI | AVH↓ |
| | 2 | 22.8 | −46.7 | −22.1 | 960 | Right | Anterior | Lobule V/VI | [1] | sMRI | AVH↓ |
| | | | | | | | | | [8] | rs-fMRI | AVH↓ |
| | | | | | | | | | [9] | rs-fMRI | AVH↓ |
| | 3 | 39.7 | −78 | −31.3 | 552 | Right | Posterior | Crus I | [2] | rs-fMRI | AVH ↑ |
| | | | | | | | | | [12] | rs-fMRI | AVH ↑ |
| SSA POS | 1 | −28.1 | −58.9 | −29 | 1080 | Left | Anterior | Lobule VI | [5] | DTI | POS ↓ |
| | | | | | | | | | [6] | rs-fMRI | POS ↓ |
| | | | | | | | | | [7] | DTI | POS ↓ |
| | 2 | 29.5 | −59.3 | −41.8 | 624 | Right | Posterior | Non-lobular[a] (white matter) | [10] | rs-fMRI | POS ↓ |
| | | | | | | | | | [13] | rs-fMRI | POS ↑ |
| AVH ∩ POS | 0 | - | - | - | - | - | - | - | - | - | - |
| AVH > POS | 0 | - | - | - | - | - | - | - | - | - | - |
| POS > AVH | 1 | −25.9 | −57.7 | −28.2 | 664 | Left | Anterior | Lobule VI | [5] | DTI | POS ↓ |
| | | | | | | | | | [6] | rs-fMRI | POS ↓ |
| | | | | | | | | | [7] | DTI | POS ↓ |

*Note*. ALE analyses: cluster-forming threshold of $p < .001$ and 5000 random permutations with a cluster-level correction of $p < .05$. ALE, activation likelihood estimation; SSA, single study analysis; Ref., reference.
[a]Non-lobular white matter finding adjacent to right hemispheric lobule VIIIa/VIIb and crus I/II. Contributors to clusters: [1] Huang et al. (2015); [2] Mallikarjun et al. (2018); [3] Zhao et al. (2018); [4] Neckelmann et al. (2006); [5] Filippi et al. (2014); [6] He et al. (2019); [7] Zhang et al. (2016); [8] Chen et al. (2019); [9] Cui et al. (2016); [10] Ferri et al. (2018); [11] Alonso-Solis et al. (2015); [12] Itahashi et al. (2018); [13] Duan et al. (2015).

connectivity have relied on *a priori* restrictions on seed regions or specific networks, resulting in potential biases.[97] Hence, cerebellar alterations in AVH may be more common than previously reported.

Resting-state fMRI data also tends to be noisy, which may obscure the sources of BOLD signals, particularly in subcortical regions.[122–124] Resting-state fMRI connectivity analyses are particularly vulnerable to physiological noise (eg, cardiac or respiratory signals) and motion-related artifacts. These artifacts could have been enhanced in the patients sample (for a review see[56]). Moreover, not all of the rs-fMRI studies included in the current review reported specific attempts to control for AVH presence during scanning.[58,85–87] These methodological aspects make the generalizability of the current effects questionable.

The studies reviewed in this article suggest that it is critical to more systematically explore the role of the cerebellum in positive symptoms such as AVH. Therefore, optimized scanning protocols and analysis tools for the cerebellum should be consistently used in future studies (eg, SUIT[125]). Additionally, we recommend a more thorough and standardized characterization of AVH features

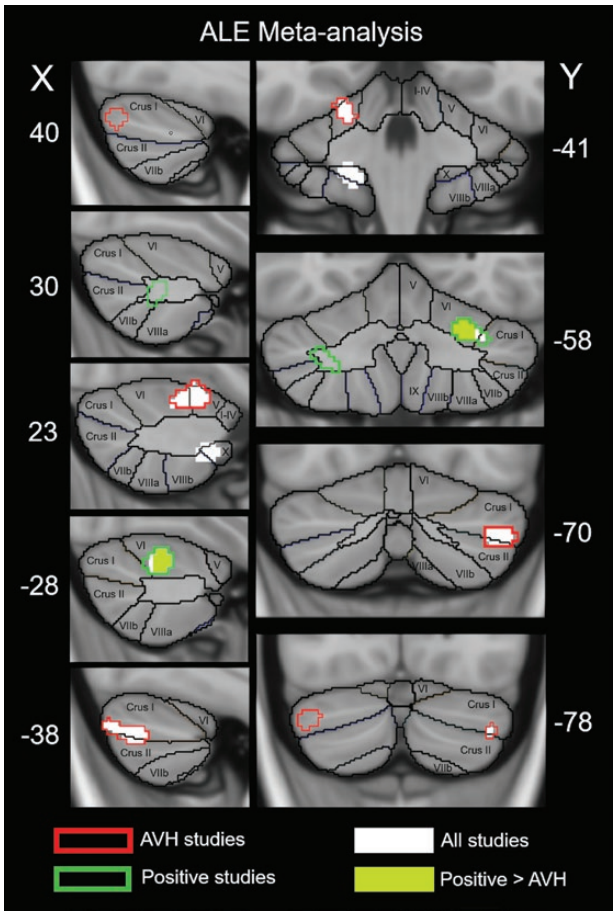


**Fig. 5.** ALE meta-analysis results. *Note.* Cluster-forming threshold of $p < .001$ and 5000 random permutations with a cluster-level correction of $p < .05$. AVH studies (red outline), single experiment ALE of combined AVH dataset; positive symptoms studies (green outline), single experiment ALE of combined positive symptoms dataset (ie, studies examining the effects of aggregated positive symptom scores); all studies (white fill), single experiment ALE of combined AVH and positive symptoms dataset; positive > AVH (light green fill), contrast analysis between single experiment AVH and combined positive symptoms ALE results. Images (MNI space): five slices at x-axis 40, 30, 23, −28, −38, and four slices at y-axis −41, −58, −70, −78. There were no significant effects in contrast analysis of positive symptoms > AVH, or in conjunction analysis of positive symptoms ∩ AVH.

in samples of voice hearers (eg, duration, frequency, and state vs trait features of AVH experience determining sample composition) as well as of AVH history (if applicable) in control samples of patients who are not currently hallucinating. Furthermore, the presence of other clinical symptoms (eg, delusions and negative symptoms) should be described and the corresponding clinical scores should be provided to allow for an adequate control of the effects of concomitant symptoms[126,127] when examining cerebellar abnormalities in AVH. It is also critical to dissociate between structural and functional differences in the cerebellum in voice hearers compared to their controls. Moreover, AVH are not limited to persons with psychosis but are experienced along a spectrum of hallucination proneness in healthy individuals without requiring psychiatric care, also in association with disrupted sensory feedback processing.[41,128] Therefore, future studies should test the hypothesis of cerebellar involvement in nonclinical voice hearing.

## Conclusions

The current meta-analyses summarize the existing evidence reporting volumetric and connectivity abnormalities in the cerebellum and their association with positive symptoms such as AVH, underscoring the need for a topographically informed approach to investigate the cerebellum. Even though cerebellar alterations may be characteristic of positive symptoms in general, disconnected sensorimotor and cognitive cerebellar zones could reflect a specific liability for AVH, particularly regarding lobule V/VI and crus I. Cerebellar dysconnectivity could contribute to altered sensory feedback processing and consequently to increased cognitive control demands in AVH. These are testable hypotheses for future studies, aiming to specify the role of the cerebellum in psychotic symptoms such as AVH across the psychosis continuum.

## Supplementary Material

Supplementary data are available at *Schizophrenia Bulletin Open* online.

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