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Functional subdivisions in the anterior temporal lobes: a large scale meta-analytic investigation

Jinyi Hung[a,b], Xiaoying Wang[a,b], Xiaosha Wang[a,b], Yanchao Bi[a,b,*]

[a] *State Key Laboratory of Cognitive Neuroscience and Learning & IDG, McGovern Institute for Brain Research, Beijing Normal University, Beijing 100875, China*
[b] *Beijing Key Laboratory of Brain Imaging and Connectomics, Beijing Normal University, Beijing 100875, China*

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ABSTRACT

The anterior temporal lobe (ATL) is involved in a wide range of cognitive processes but its functional specialization remains unclear. In this review, we synthesize evidence from cytoarchitecture, anatomical and functional connectivity, and functional activation to elucidate how subregions in the ATL contribute to various cognitive processes. Two complementary meta-analyses were conducted. We first constructed a comprehensive functional preference profile for all subregions through large-scale neuroimaging meta-analysis, and then employed a coordinate-based activation likelihood estimation analysis to examine such functional preferences by input types. We identified two subregions in the dorsal aspect of the ATL (i.e., superior dorsal, inferior dorsal) and two other subregions (lateral, ventromedial) in the ventral aspect of the ATL, all have distinct anatomical and functional preferences. We proposed sensory, language, and socioemotion as the three dimensions that jointly capture the cognitive components cutting across the four ATL subregions: the superior dorsal ATL was associated with auditory sensory, language (phonological production aspects), and emotion; the inferior dorsal ATL with auditory sensory and language (phonological perception and production aspects); the lateral ATL with visual sensory, language (semantic and episodic aspects), and social processing; and the ventromedial ATL with visual sensory, episodic memory, and emotion. The various functions associated with the ATL can be clustered into subregions, which provides sourceful basis for testing hypothesis-driven cognitive framework.

1. Introduction

The anterior temporal lobe (ATL) refers to the anterior portion of the human temporal lobe and generally encompasses the temporal pole [Brodmann's area (BA) 38] and the anterior segments of temporal gyri, such as BA 20, 21, and 22 (Visser et al., 2012; Wong and Gallate, 2012). It contains association cortices that are frequently shown to be involved in multimodal sensory integration (Skipper et al., 2011; Visser et al., 2012). Historically, as a uniform unit, it is also considered as an enigma due to its involvement in various higher cortical functions without clear function–anatomy correspondence (Olson et al., 2007). It has been shown that the ATL is engaged in language processing (Binder et al., 2011), conceptual/semantic knowledge representation (Binder et al., 2009; Patterson et al., 2007; Rogers et al., 2004), social cognition (Zahn et al., 2007), emotion (Reiman et al., 1997; Royet et al., 2000), memory (Schacter and Wagner, 1999), and recognition of specific entities (e.g., voice, face, name, picture of unique entities) (Damasio et al., 1996, 2004; Gainotti, 2007; Grabowski et al., 2001). What is the underlying mechanism that contributes to the functional heterogeneity in the ATL? Could there be topographical organization, based on its specific functional and anatomical properties, for different cognitive representations/processes? Answers to these questions will deepen our understandings about this brain structure as well as the neurobiological mechanisms of the cognitive processes at stake.

In this review we aim to unravel the potential sub-divisions of ATL across multiple approaches. We first review existing findings from cytoarchitecture, anatomical and functional connectivity studies. We then carry out two complementary meta-analyses to examine the functional activity patterns from both a data-driven approach using a large-scale dataset (Meta-analysis 1: Neurosynth with various research topics) and a theoretical driven approach using a smaller-set of selected studies (Meta-analysis 2: ALE with varying stimulus modalities and contents). Last, we provide a synthesis of evidence from cytoarchitecture, anatomical and functional connectivity, and functional activation patterns to characterize the functional specialization in the ATL.

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[*] Corresponding author.
E-mail address: ybi@bnu.edu.cn (Y. Bi).

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2. ATL Parcellation Based on Cytoarchitecture and Brain Connectivity Patterns

The regional substructures of the ATL have been evaluated based on cytoarchitecture, brain anatomical connectivity, and functional connectivity. The former two have the premise that anatomical microstructure and connectivity constrain brain functions in the primate studies (Passingham et al., 2002) whereas the latter emphasizes on the time-series correlations among regions at rest or during task whose temporal coupling is often considered as meaningful functional units. Below we review each type of results in turn.

2.1. Cytoarchitecture

Localizable substructures were identified in the Brodmann area map for the anterior temporal regions based on the cellular and laminar structures (Brodmann, 1909). The Brodmann's areas we mentioned earlier (i.e., BA 38, 20, 21) were typically characterized by gradual transition among neighboring areas. The temporal pole (BA 38) was particularly diverse in its cross-sectional depth whilst the other two correspond to the gyral nomenclatures. Recent localization technique based on the cellular and chemoarchitectonic structural properties further revealed seven finer divisions in the temporopolar (TP) region, the most anterior tip of the ATL: the mediodorsal (TG), dorsolateral (TAr, TAp), ventromedial (TE, perirhinal areas 35 and 36), and inferomedial (TI) parts of TP, each demonstrates differential processing capabilities at neuronal level (Ding et al., 2009). Depending on each region's neuronal property extension and the comparison with corresponding temporal pole subdivisions in primates, the authors depicted three functional extensions in TP such that ventrally TE extended to anterior segment of the ventral visual stream, dorsally TAr and TAp extended to auditory association areas, medially TI extended to olfactory/insular regions and area 35 and 36 to the medial temporal structures. The localization results in Ding et al. (2009) study are schematically displayed in Fig. 1a.

2.2. Anatomical Connectivity

The ATL also demonstrate diverse anatomical connectivity structures within and outside the human ATL. Within ATL, Binney et al. (2012) identified a pattern of posterior-anterior longitudinal connection with the visual and auditory sensory cortex, and a cross-gyral intra connectivity patterns using diffusion-weighted imaging probabilistic tractography (DWI). The cross-gyral intra connectivity suggested convergence of information across sensory modality. For extra-temporal connections, Binney et al. (2012) identified three association fibers (i.e., uncinate fasciculi, inferior fronto-occipital fasciculi, and arcuate fasciculus) connecting the left anterior segment of the ATL to different frontal and parietal regions of the so-called language network, including inferior frontal gyrus, supramarginal or angular gyri. At a whole-brain network scale, Fan et al. (2013) employed a combination of diffusion tensor imaging (DTI) and resting-state functional connectivity to identify three subregions in the temporal pole coursing through major white matter tracts: a dorsal region (TAr) connected more to the orbital part of inferior frontal gyrus, insular cortex, superior temporal gyrus, and middle temporal gyrus; a ventrolateral region (TGl) connected most to the orbital part of superior frontal gyrus and gyrus rectus; and a ventromedial region (TGm) connected more to ventral and medial temporal cortex (Fig. 1b). Using a larger ROI definition, Papinutto et al. (2016) conducted a ROI-based DTI tracing from ATL to homolateral regions outside the language network to examine the connectivity in the left and right hemispheres. There were two key findings. One was that subregions were dissociated based on their connectivity patterns with target regions: rostral ATL with orbitofrontal regions, ventromedial ATL with paralimbic structures, and lateral ATL with inferior frontal gyrus and posterior temporal regions. Different degree of connectivity strength ipsilaterally was also revealed such that there was a strong connection to the inferior frontal gyrus in the left hemisphere but greater connection to the orbitofrontal cortex in the right hemisphere.

2.3. Functional Connectivity

Resting-state functional connectivity (rsFC) analyses using fMRI data, which test for intrinsic functional coupling across regions (Friston, 1994), have also revealed substructures in the ATL. Yeo et al. (2011) constructed a whole-brain functional connectivity analysis in 1000 healthy subjects via clustering approach and demonstrated that three out of the seven whole-brain functional networks covering the anterior temporal region – the somatomotor, limbic, and default mode networks. The rostral TP region was part of the limbic network, dorsal ATL part of the superior temporal gyrus in the somatosensory network, and many of the lateral ATL in the default mode network. Pascual et al. (2015) specifically investigated brain networks of 40 seed regions in the left temporal pole, which corresponded well to the cytoarchitectonic areas identified by Ding et al. (2009), and showed very similar large-scale network profiles: dorsal (seeds in anterior area TA) with somatosensory auditory association areas, ventromedial (seeds in area 35,

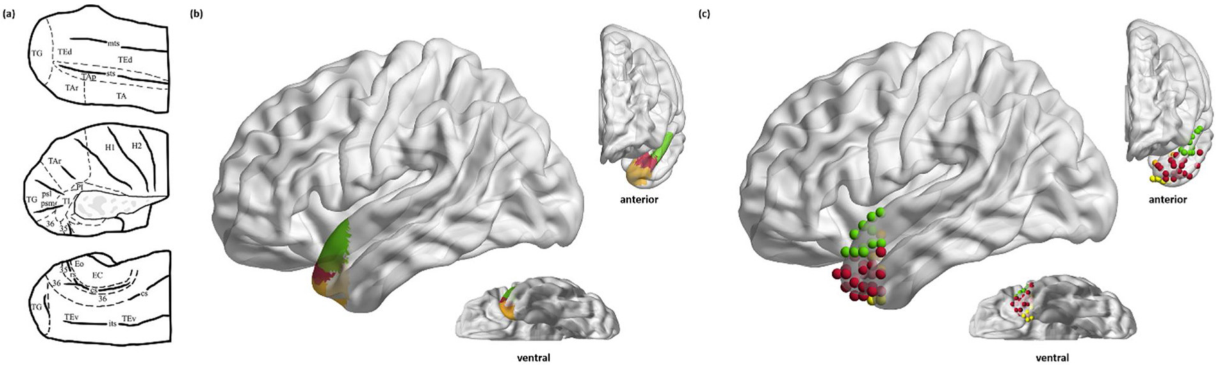


Fig. 1. Schematic depictions of the cytoarchitecture-, anatomical connectivity-, and functional connectivity-based parcellation in the tip of the anterior temporal lobe. (a) Cytoarchitectonic areas in the human temporal pole representing the lateral, dorsal, and medial aspects of TP (top-bottom). Figure obtained from Ding et al. (2009) with permission. (b) Three clusters based on the anatomical connectivity in Fan et al. (2013) study. Green: dorsal TP (TAr), red: lateral TP (TGl), orange: medial TP (TGm). Mask was provided by Dr. Fan. (c) Four clusters based on the anatomical and functional network criteria in Pascual et al. (2015) study. Nodes of the same color were to demonstrate the large-scale functional network they belonged to and thus to approximate each cluster region. Note that the original paper did not draw a hard parcellation in the TP. Here, we demonstrated the seed subregions grouped under the identified functional network. Green: somatosensory-auditory network (anterior area TA), yellow: visual network (area 35, 36), orange: paralimbic network (area EC, TI), red: default-semantic network (area TE, TG).

36) with visual association areas, anterolateral (seeds in area TE, TG) with default and/or semantic network areas, and medial (seeds in area EC, TI) with paralimbic structures (Fig. 1c). These networks were derived from two distinct clusters: the dorsal TP including dorsal and dorsomedial areas and the ventral TP including anterolateral and ventromedial areas. In a study testing the functional parcellation in the temporal cortex, Jackson et al. (2018) found different rsFC patterns with the rest of the brain: one anterior cluster including the temporal pole, anterior interior temporal gyrus (ITG) and the middle temporal gyrus (MTG), and a posterior cluster including the posterior fusiform gyrus, ITG, MTG, and small areas of posterior and anterior STG.

2.4. An Interim Summary

Summarizing the results across cytoarchitectonic boundaries, anatomical connectivity pattern, and functional connectivity differences, at least three functional clusters are consistently reported: (1) a superior dorsolateral part of the ATL that connects to the posterior superior temporal regions anatomically, and is closer to the auditory network; (2) a ventromedial part of the ATL that connects to the medial temporal or posterior temporo-occipital regions, and is typically considered as part of the higher level visual system (Pascual et al., 2015); and (3) a rostromedial part of the ATL that connects to orbitofrontal or paralimbic structures. Additionally, the lateral part of the ATL also contains regions that are functionally linked to distributed cortical regions identified as part of default mode or semantic networks.

Although the consensus is that brain function depends on connection (Passingham et al., 2002), inferring the functional roles of the ATL from these anatomical and intrinsic connectivity structures is not straightforward. For instance, it has been proposed that such division provides evidence for the modality-general vs. modality-specific organization principle in the temporal cortex (Jackson et al., 2018); or its functional connectivity patterns suggest that the ATL is a multisensory integrator that merges information from primary and associative regions. Such inferences still do not directly align with the finer functional activation patterns observed in the literature (e.g., social vs. nonsocial, Skipper et al., 2011), which will be considered below.

3. Functional Specialization Within the ATL

The ATL has been reported to be implicated in a wide range of cognitive processes. How do substructures of the ATL respond to various inputs and tasks? Are there common functional subdivisions underlying these wide range of observations? Two previous studies interested in understanding the role of ATL in semantic cognition have performed meta-analysis via activation likelihood estimation (ALE) to compare the roles of inputs in semantic tasks. Visser et al. (2012) examined the probability of activation likelihood for studies using five stimulus types varying in input modality (visual or auditory) and contents (object properties or language): picture, visual words, auditory words, visual sentences, and auditory sentences. They found that the four stimulus types with language content (together as verbal input), compared to the pictorial input, tended to have more activation peaks in the superior part of the ATL. Rice et al. (2015b) compared the probability of activation likelihood for written and spoken words vs. pictorial inputs in their meta-analysis, and showed verbal preference (both visual and auditory verbal inputs) in the left hemisphere and pictures (visual nonverbal input) in the right hemisphere. In both studies, the suggested division was based on stimulus content (verbal or nonverbal) without inclusive control for stimulus modality (visual or auditory). However, it is unclear whether stimulus modality has additional effect (i.e., lacking direct contrast of same content but different input modality); and critically, whether the broader domains of cognition that have implicated ATL follow the same functional division.

In the following section, we conducted two meta-analyses: one involved coactivation-based meta-analysis via Neurosynth to construct a generic overview of the functional specialization in the ATL via synthesizing the results of neuroimaging studies across as many tasks and studies as possible without a priori assumptions about its function. The other employed coordinate-based meta-analysis via Activation likelihood estimation (ALE), which is based on specific, selected contrasts, to both serves as a validation of the Neurosynth approach (along the overlapping dimensions), and to further examine the unresolved questions of input modality and content in the context of semantic cognition.

3.1. Coactivation-based Meta-analysis via Neurosynth

We examined the generic functional subdivisions within the ATL via a quantitative approach based on Neurosynth (Yarkoni et al., 2011). Using the database, we followed the existing pipeline established by de la Vega et al. (2016, 2018) and the core Neurosynth python tools (https://github.com/neurosynth/neurosynth) to synthesize activation results. This method has successfully decoded the functional subdivisions of the medial prefrontal cortex (de la Vega et al., 2016), the lateral prefrontal cortex (de la Vega et al., 2018), the posterior medial cortex (Huang et al., 2019), and the default mode network (Wang et al., 2018). Codes for the analyses used in this meta-analysis can be accessed at the Github website (https://github.com/jinyihung/ATL_neurosynth).

3.1.1. Dataset and ROI Definition

3.1.1.1. Dataset. We used version 0.6 of the Neurosynth database, released in July 2015 (Yarkoni et al., 2011), a repository automated synthesizing 11,406 fMRI studies in total. The database contains words from the abstract of the included studies from which the developer generated 400 different research topics. These topics were included in our topic-based meta-analysis.

3.1.1.2. ROI Definition. We employed an anatomical ATL mask that covers the anterior portion of the temporal lobe. Six subregions of the MNI-spaced Harvard–Oxford Atlas (probability > 0.2, Xu et al., 2018) were combined as one mask including the temporal pole (TP), the anterior superior temporal gyrus (aSTG), the anterior middle temporal gyrus (aMTG), the anterior inferior temporal gyrus (aITG), the anterior temporal fusiform cortex (aTFC), and the anterior parahippocampal gyrus (aPHG). This ROI definition covers Brodmann area (BA) 38 and the anterior portions of BA 20, 21, and 22. Note that currently there is no explicit border for the ATL regions in the literature. We adapted a broader inclusion as noted in Rice et al. (2015b) ALE meta-analysis. The posterior boundary of the ATL in the current study was approximately marked by the line $y = -24$ along the ventral surface and $y = -14$ on the lateral surface. The total ROI volume was 9706 voxels (voxel size $= 2 \times 2 \times 2$ mm^3). ROIs with stricter probability inclusion were considered in Section 3.1.4.

3.1.2. Neurosynth Methods

There were three processing components in the meta-analysis using Neurosynth. We first identified the ATL subregions based on each ROI voxel's coactivation pattern with the rest of the brain and performed a hard parcellation based on k-means clustering (i.e., coactivation clustering). Each cluster's coactivation pattern was also generated (i.e., coactivation profiles). We then specified how these research topics were linked to activation within distinct ATL subregions using Gaussian naive Bayes classification to establish a multivariate profile of functions regionally (i.e., functional preference profiles). The main rationale follows the Bayes' rule to account for the prior probability of brain activation in a given ROI and the prior probability of each behavioral condition (termed topic in the current analysis) in the Neurosynth database. This allows us to examine the consistency of certain behavioral association across a wide-range of tasks and studies for the ROI, thus establishing a functional preference profile of this region (Genon et al., 2018).

3.1.2.1. Coactivation Clustering. We generated a coactivation matrix among the ROI voxels and those in the rest of the brain. The coactivation pattern of each voxel was represented as a binary vector of length 11,406 (the number of studies) in which a value of 1 means that the voxel falls within 10 mm of the activation coordinate in a study and a value of 0 means the opposite. We eliminated voxels with low activation rates from the rest of the analysis if there were fewer than 60 studies reporting activation of that voxel. The resulting coactivation matrix was then passed through principle component analysis (PCA) to reduce the dimensionality of the whole brain voxels to 100 components, resulting a ROI mask-by-whole brain matrix of 9706 voxels by 100 components. We next applied k-means clustering from scikit-learn Python package (Pedregosa et al., 2011) to this matrix to group the ATL mask into 2–15 clusters. Pearson correlation distance between every voxel in the ATL mask with each whole-brain PCA component was conducted for the silhouette score analysis to select the ideal number of clusters. The Silhouette score is defined as (b–a)/max (a,b), where a is the mean intra-cluster distance for each voxel and b is the mean nearest-cluster distance for each voxel. The greater the Silhouette score, the smaller mean within-cluster distances, suggesting better within-cluster cohesion.

We named the subregions of the cluster resolution based on each cluster's representation on the Harvard-Oxford atlas. We also compared our results to the 40 seed regions in Pascual et al. (2015) study for cytoarchitectonic correspondence and to Fan et al. (2013) study for anatomical connectivity-based substructure comparison. The seed region comparison was done by plotting the coordinates of the seed regions on the resulting subregion mask and identified where those seed regions were located. For the comparison with the anatomical connectivity-based parcellation, we calculated the percentage of significant voxels located in each of the three substructures identified by Fan et al. (2013).

3.1.2.2. Coactivation Profiles. To understand the differences between clusters, we analyzed the differences in whole-brain coactivation patterns between the adjacent resulting clusters. A meta-analytic contrast between studies that activated a given cluster and studies that activated other clusters was conducted. The resulting images identify voxels with a greater probability of coactivating with the cluster of interest than with control clusters. We then conducted a two-way chi-square test between two sets of studies and calculated p values to threshold the coactivation images using False Discovery Rate correction for multiple comparisons such that the included voxels are significant at the $p_{FDR} < 0.01$ level.

3.1.2.3. Functional Preference Profiles. The last part of the analysis aimed to determine the most relevant research topics that best predicted each cluster's activity across studies. The default database contains more than 3100 term-based features, each was extracted from the abstract of all studies. We used a topic-based meta-analysis that contained 400 topics as a result of latent Dirichlet allocation topic modeling (LDA, Blei et al., 2003). Such procedure resolves redundancy among features to sets of topics. Each of the resulting topics was loaded with feature words to a varying extent. For example, an ‘auditory’ topic loads highly on the words ‘auditory’, ‘sound’, ‘sounds’. For our own interest, we focused on cognition-related research topics, which include functions and processes of attention, memory, judgment, reasoning, decision making, comprehension and production of language. Based on the top feature words of each topic, we excluded topics about disorder population/study (e.g., autism; N = 24), methodological terms (e.g., hypothesis; N = 176), and unrelated topics (e.g., smoker; N = 123), leaving 77 topics for the analysis. A schematic view of the inclusion and exclusion procedures is shown in Supplementary Fig. 1.

For the functional preference profile, we determined the likelihood of activation in a given region using selected topics by discriminating between studies that have activated a given region from studies that did not. A study was defined as activating a given region if at least 5 % of voxels in the region was activated in that study (de la Vega et al., 2016, 2018). For each cluster, a Gaussian naive Bayes classifier was trained to discriminate between these two sets of studies and log odds ratios (LOR) for each selected topic was also extracted (Yarkoni et al., 2011; de la Vega et al., 2016). LOR was defined as the log of the ratio between the probability of a given topic in active studies and the probability of the topic in inactive studies. It determined the strength of each topic in indicating the likelihood of being active a given region was. A positive LOR value indicated that a topic was predictive of activation in a given region.

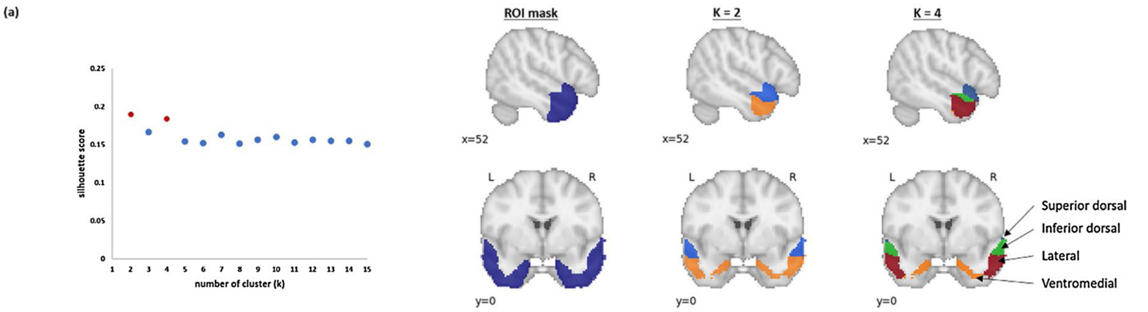
To determine the statistical significance of the region-topic associations, we performed a permutation test for each region-topic log odds ratio for 1000 times (de la Vega et al., 2016). This resulted in a null distribution of LOR for each topic and each region. P values for each pairwise relationship between topics and regions were calculated and adjusted via a False Discovery Rate at 0.01 to account for multiple comparisons. We reported associations significant at the corrected $p < 0.05$ threshold. Additionally, for the overall functional difference between regions, we computed the Pearson's correlation distance between clusters based on the log odds ratio. Correlation distances range from 0 to 1, with 1 indicating highly distant. We also calculated 95 % confidence intervals (CI) of the LOR of a selected topic for one region using bootstrapping by 1000 times for each topic's differential association with subregions. Following de la Vega et al. (2016, 2018), we reported the post hoc comparison results if the 95 % CI of the LOR did not overlap with other subregions for a selected topic.

3.1.3. Neurosynth Results

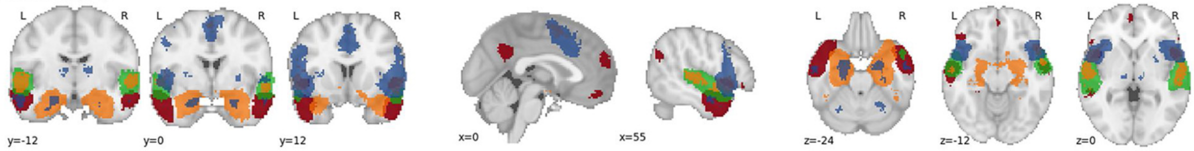
3.1.3.1. Coactivation Clustering. The coactivation profiles of a given region with the rest of the brain across studies via silhouette score analysis initially suggested two cluster distribution (k = 2) with a general border around the superior temporal sulcus that marked the dorsal vs. ventral aspect of the ATL. The model can be further parsed into finer subdivisions based on a similar high silhouette score at k = 4. Two subregions were derived from the dorsal aspect of the ATL (i.e., superior dorsal, inferior dorsal ATL) and the other two from the ventral aspect of the ATL (i.e., lateral, ventromedial ATL) (Fig. 2a).

Anatomically, the superior dorsal ATL cluster fell within the rostral temporal pole of the Harvard-Oxford atlas and corresponded to the anterior area TA (seed N = 5) and TI (seed N = 1) in Pascual et al. (2015) study. The inferior dorsal ATL cluster extended from the temporal pole to anterior superior temporal gyrus and corresponded to the posterior portion of the anterior area TA (seed N = 2). The lateral ATL cluster included temporal pole and the anterior portion of the middle temporal gyrus and inferior temporal gyrus and corresponded to the anterior area TA (seed N = 3), the anterior area TE (seed N = 8), and area TG (seed N = 4). The ventromedial ATL cluster contained Harvard-Oxford atlas' caudal temporal pole, anterior parahippocampal gyrus and anterior fusiform cortex and corresponded to the anterior area 35 (seed N = 1), the anterior entorhinal cortex (seed N = 1), area TI (seed N = 2), and area TG (seed N = 1). Note that the anatomical correspondence between Pascual et al. (2015) study and Ding et al. (2009) cytoarchitecture-based parcellation was slightly different. For instance, TAr and TA were grouped into anterior area TA given their similar cytoarchitectonic structures and TAp was not separated for its lack of reliable localization on MRI. Despite the employment of slightly different classification protocols, the parcellation test-retest and inter-rater reliability between these two studies still remains high (> 90 %). The regional comparison with the seed regions in the Pascual et al. (2015) study thus served as a critical, generic reference to the anatomical segregation for our parcellation results.

Compared to the anatomical connectivity-based parcellation in Fan et al. (2013) study, chi-squared analyses revealed that ATL subregions obtained here were associated with the substructures in the Fan et al. (2013) study ($\chi^2 = 833.64$, $p < 0.001$). The superior dorsal ATL and



(b) Coactivation (K=4)



(c) Superior dorsal ATL

(d) Inferior dorsal ATL

(e) Ventromedial ATL

(f) Lateral ATL

Fig. 2. Functional parcellation in the ATL based on coactivation clustering. (a) The silhouette score for clusters from k = 1 to 15 (p values for all clusters < 0.001) for the ATL ROI mask. k = 2 and 4 (red dots) had the best performance. Cluster names for k = 4 were based on the anatomical correspondence in the Harvard-Oxford atlas: superior dorsal ATL (blue) fell within rostral temporal pole; inferior dorsal ATL (green) extended from the temporal pole to anterior superior temporal gyrus; lateral ATL (red) included temporal pole and the anterior portion of the middle temporal gyrus and inferior temporal gyrus; and ventromedial ATL (orange) contained caudal temporal pole, anterior parahippocampal gyrus and anterior fusiform cortex. (b) Coactivation pattern of all subregions for k = 4 resolution. Bilateral activation was observed for all clusters. (c–f) Coactivation pattern for individual subregions.

inferior dorsal ATL clusters here were mostly associated with area TAr (Pearson residual r superior dorsal ATL = 11.19, inferior dorsal ATL = 5.4), the ventromedial ATL cluster with area TGm (r = 14.89) and TGl (r = 6.36) clusters, and the lateral ATL cluster with area TGl (r = 5.59).

3.1.3.2. Coactivation Profiles. The coactivation patterns of the four clusters were compared to identify voxels with greater coactivation degree with one cluster than the other three. General coactivation patterns for each cluster were bilateral. Coactivation differences were as follows: the superior dorsal ATL cluster coactivated with inferior frontal gyri, precentral gyrus, and anterior cingulate gyri; the inferior dorsal ATL cluster with the superior temporal gyri posteriorly; the lateral ATL cluster coactivated more with the middle temporal gyri, angular gyri, precuneous gyrus, frontal pole, and the left inferior frontal regions; the ventromedial ATL cluster coactivated with medial temporal cortical structures, fusiform gyri, and the frontal orbital cortices (Fig. 2b–f).

3.1.3.3. Functional Preference Profiles. By applying a Gaussian naive Bayes classification, we examined how the 77 topics are related to the activation pattern for each ATL subregions. Permutation results revealed 33 topics that had significant log odds ratio (LOR) after removing topics that were not loaded significantly in any of the four subregions (Table 1). Fig. 3 demonstrated the association strength with the identified ATL subregions (also see Supplementary Fig. 2 for the bootstrapped 95 % CI results).

The superior dorsal ATL and inferior dorsal ATL clusters had short correlation distance (r = 0.22), which may reflect the shared significant topics including *lexical phonology, sentence comprehension, speech (auditory production), music, language,* and *word semantics* based on the permutation results. In addition to these common topics, the

Table 1
Topics significantly associated with anterior temporal lobe.

Topic name	Top words
Auditory sounds	Auditory sound sounds processing tones pitch acoustic tone
Voice identity	Voice identity prosody voices vocal speaker acoustic communication
Speech	Speech auditory production perception sounds listening acoustic phonetic
Music	Music musical musicians pitch auditory listening singing melody
Visuoauditory modality	Visual auditory sensory modality modalities audiovisual integration modal
Language	Language languages linguistic bilinguals native processing bilingual proficiency
Lexical phonology	Phonological lexical words orthographic word processing representations spelling
Sentence processing	Sentences sentence syntactic processing comprehension language linguistic syntax
Comprehension	Comprehension sentences language literal sentence narrative metaphors meaning
Verbal fluency	Verbal fluency tasks nonverbal phonological language rehearsal articulatory
Gesture	Gestures gesture speech communication communicative iconic actor language
Word semantics	Semantic word words processing lexical semantically knowledge meaning
Events	Future events past thinking personal construction experiences episodic
Abstract concrete	Abstract conceptual concrete concepts representations representation concept similarity
Default mode network	Network default mode networks resting deactivation attention spontaneous
Empathy	Empathy empathic affective emotional social responses feeling situations
Mind theory	Mind theory wandering physical thinking mental style mw
Social cognition	Social cognition participants exclusion interaction interactions socially people
Mentalization	Mental mentalizing social belief mind junction beliefs theory
Referential judgment	Referential reference judgments personal appraisal person trait oneself
Memory retrieval	Memory retrieval episodic memories autobiographical reactivation recall semantic
Memory encoding	Memory encoding retrieval recognition subsequent successful episodic encoded
Recognition	Recognition familiar unfamiliar familiarity famous compared person learned
Recollection	Recollection source familiarity information studied test words judgments
Facial expression	Facial expressions emotional emotion processing expression faces neutral
Face processing	Face faces processing identity selective recognition perception sensitive
Emotional face	Faces emotional fearful happy neutral face sad angry
Picture	Pictures picture neutral unpleasant pleasant images processing viewing
Valence	Negative positive valence emotional affect neutral affective responses
Emotion regulation	Emotion regulation emotional negative emotions affect affective regulate
Emotional processing	Emotional processing neutral emotion arousal valence affective emotionally
Fear conditioning	Fear conditioning CS extinction conditioned learning stimulus responses
Threat	Threat fear responses threatening avoidance anxiety cues response

Note: Top keys are taken from https://figshare.com/articles/Neurosynth_LDA_topics_v4_/4893353, shared publicly by Dr. Tal Yarkoni. The table listed eight strongest loading words for each topic based on their association strength in descending order.

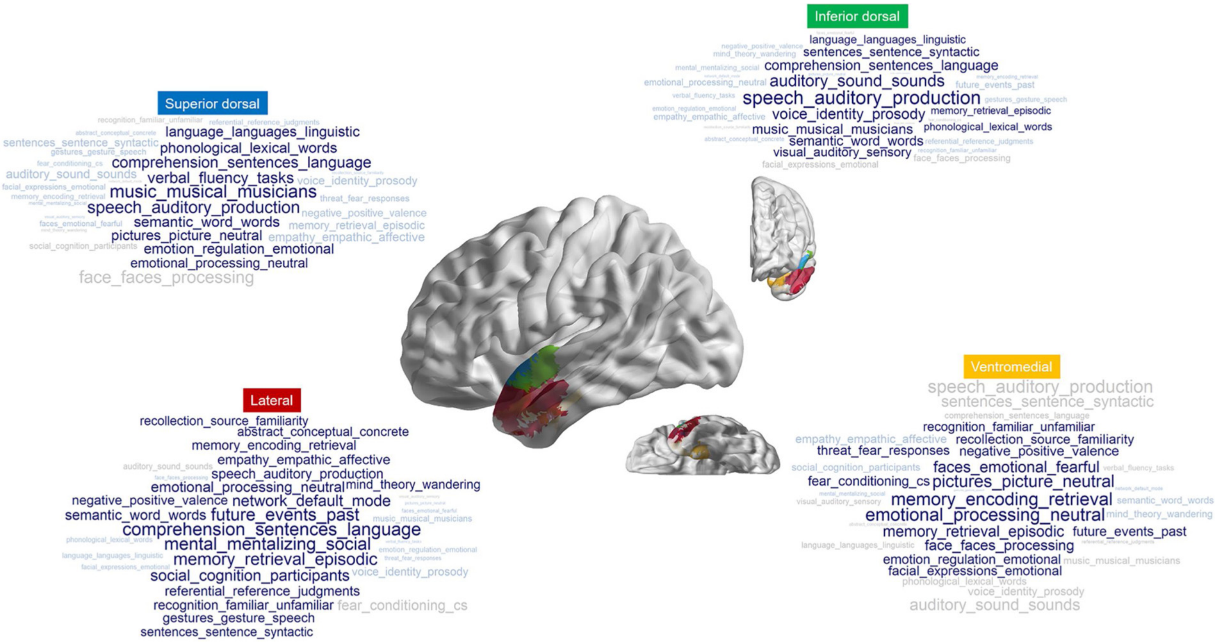


Fig. 3. Functional preference profiles of the four clusters in the ATL via Neurosynth. Word clouds were generated based on the log odds ratio (LOR) in the permutation results for the four subregions. Each feature word list was represented by the top three feature words in the list. Given that the order of the feature words was ranked from high to low frequency loadings in a topic word list, the top words were loaded with the highest frequency to represent a generic topic (Blei et al., 2003). Color was used to mark the significance of the LOR values in the permutation results: blue: significant positive values, lightblue: nonsignificant positive values, and grey: nonsignificant negative values. Font size represented the absolute LOR values. The bigger the font size was, the greater the LOR value was in absolute value. Lastly, the more significant the LOR values were, the closer it was toward the center position in the word clouds.

superior dorsal ATL cluster was associated with *picture, verbal fluency, emotional processing*, and *emotional regulation*. Given the post hoc 95 % CI comparison, the inferior dorsal ATL cluster was more associated with topic *voice identity* (95 % CI LOR = [2.04, 6.73]), *auditory sounds* (95 % CI LOR = [1.51, 7.90]), *visuoauditory modality* (95 % CI LOR = [0.65, 4.90]), and *speech (auditory production)* (95 % CI LOR = [1.86, 10.62]) than the other three clusters.

The lateral ATL cluster was associated with a wider aspect of topics across the other three clusters (functional distance r = 0.53 with the superior dorsal ATL, r = 0.36 with the inferior dorsal ATL, r = 0.44 with the ventromedial ATL cluster). These included *sentence comprehension, mentalization, future/past event, memory retrieval, default mode network, social cognition, emotional processing, word semantics, speech (auditory production), referential judgment, empathy, recognition, memory encoding, gesture, valence, abstract/concrete concept, mind theory, sentence processing*, and *recollection* based on the permutation results. Among these, post hoc 95 % CI comparison showed that it was more associated with topic *default mode network* (95 % CI LOR = [0.85, 4.82]) and *mentalization* (95 % CI LOR = [1.39, 6.03]) than the other three clusters.

The ventromedial ATL cluster had much larger correlation distance from the two dorsal ATL clusters (r = 0.68–80). It was associated with *memory encoding and retrieval, emotion processing, picture, emotional face, face processing, valence, fear, future/past event, emotional regulation, recollection, threat, facial expression*, and *recognition* based on the permutation results. Post hoc 95 % CI comparisondemonstrated that it was more associated with topic *emotional face* (95 % CI LOR = [1.50, 4.82]) than the other three clusters.

To sum up, the four identified clusters were loaded preferentially with various research topics. A strong preference for auditory sound and speech related topics were loaded more in the dorsal aspect of the ATL whereas face, memory, and socioemotion were more associated in the ventral aspect of the ATL. Different components of language-related topics were loaded across the subregions. Phonology was mainly in the dorsal ATL clusters, sentence processing in the inferior dorsal ATL and lateral ATL clusters, and sentence comprehension or word semantics were loaded in both dorsal ATL clusters and the lateral cluster. No language topics were found to be loaded in the ventromedial ATL cluster.

3.1.4. Validation Analyses

3.1.4.1. Specific Consideration of the Basal ATL. A large portion of the basal ATL was not included in the main analysis above because there were not enough studies showing activation here passing the conventional threshold used in previous studies (de la Vega et al., 2016, 2018), which may be due to particular susceptibility to fMRI signal dropouts in this territory. Given the significance of this basal region in semantic cognition (see review in Lambon Ralph et al., 2017; Rice et al., 2015a), we performed an additional analysis to include this region in the validation analysis by lowering the threshold of the minimum number of studies. Using this lower threshold (N = 20 studies), most of the basal part of the ATL was included in the analysis and was clustered into the ventromedial subregion.

The overall functional preference profiles (Supplementary Fig. 3) using lower threshold were very similar to the original setting except that several topics, all associated with the ventromedial subregion, became insignificant in the permutation results despite of its high, positive LOR. Topics still significantly associated with the ventromedial subregions included *memory encoding and retrieval, emotion processing, picture, emotional face, face processing, valence, future/past event*, and *emotional regulation,* which still associated with the visual sensory, episodic memory, and emotion components as in the main results with conventional inclusion threshold. Topics became insignificant were *recollection, fear, threat, facial expression*, and *recognition*.

3.1.4.2. Further Separation of the ATL From the Frontal Cortex. The main results above showed that the superior dorsal cluster shows coactivation with cognitive control regions including anterior cingulate and insula. Give that this region is on the border between the temporal lobe and the inferior frontal cortex, it might be possible that some studies contributing to the superior dorsal cluster were actually reporting frontal activations. To address this concern, we performed additional analyses with reduced ATL ROIs, using the same ROI definition but only by raising threshold to include regions with probability > 0.4 and 0.6. The resulting ATL ROIs were more separated from the frontal lobe (Supplementary Fig. 4a and c). We ran the clustering and coactivation analyses with these ROIs, and still observed that the superior dorsal cluster coactivated with insula and anterior cingulate, although the strength was weaker. Of course, with the nature and resolution of fMRI, the potential contribution of the neighboring frontal cortex is difficult to be fully ruled out, and future more fine-grained studies are warranted regarding the superior–dorsal ATL.

3.2. Coordinate-based Meta-analysis via ALE

We next conducted a coordinate-based meta-analysis using activation likelihood estimation (ALE) (Turkeltaub et al., 2002), focusing on a smaller set of studies that investigated the functional specialization in the ATL in the domain of semantic cognition. Semantic processing is one of the most frequently reported cognitive process here, and in this context the ATL has often been described as the site where multiple sensory modalities are integrated (Lambon Ralph et al., 2017; Plaut, 2002). However, at least two dimensions – stimuli modalities (visual vs. auditory) and stimuli contents (language vs. nonlinguisitc sensory) – were mixed in previous investigations (Rice et al., 2015b; Visser et al., 2012). The goals of this analysis were two-fold: (1) We specifically tested whether ATL is organized by responses to stimuli modalities (visual vs. auditory) and/or stimuli contents (words vs. objects), by selecting studies including these contrasts; (2) to validate results with similar contrasts from the Neurosynth methods above.

3.2.1. Literature Search and Selection Criteria

Two separate literature searches were undertaken – we started from papers included in the Rice et al. (2015b) study and added new papers that were published later. First, Rice et al. (2015b) study included 97 studies that involved semantic processing up till 2012. 74 studies had full-text available to us. We then performed a second literature search to add studies between Jan 2012 to May 2019 in the Web of Science and PubMed, using the following search terms: ("anterior temporal") AND ("PET" OR "fMRI"). This step yielded 524 articles in total after removing duplicates. Titles and abstracts from these articles were then screened to include only healthy adult participants. This step yielded 238 articles.

We then employed the same inclusion and exclusion criteria about semantic memory as in Rice et al. (2015b) and Visser et al. (2012) studies: (1) PET or fMRI studies on semantic memory, (2) the studies included anterior temporal areas explicitly in their data acquisition or analyses, and (3) studies were excluded if the focus was sex differences, task switching, priming, adaptation, metaphoric and idiom comprehension, bilingualism, language development, syntax, working memory, or episodic memory. Further, in our meta-analysis, we only included studies with all task paradigm and extract experiments via whole brain analysis and excluded multivariate analysis following the guidelines given by Müller et al. (2018). This procedure led to 84 studies together from both literature searches (i.e., those in Rice et al., 2015b and the search for later studies). To identify as many potential studies as possible, we also conducted an additional literature through references citing the selected studies and cited in review articles (Engel et al., 2009; Engelien et al., 2006; Samson et al., 2010; Wong and Gallate, 2012). This step yielded an additional 8 articles, resulting a final set of 92 articles. The author JH and another reviewer

Table 2
Number of studies inputted into each analysis.

Study type	ALE peaks	Experiments	Subjects
Auditory language	142	19	220
Visual language	183	31	421
Auditory sensory	87	13	208
Visual sensory	243	28	368

independently extracted relevant data from each of the included studies, including the number of subjects, the type of study, type of task, reported foci (only those in the temporal lobe), and the reported standard space. Disagreements, if any, were discussed and resolved by the reviewers. See Supplementary Table 1 for the summary of studies included in the meta-analysis and their study type.

3.2.2. ALE Methods

ALE analyses were implemented using BrainMap GingerALE 3.02 (Eickhoff et al., 2009). All Talariach coordinates were converted to the MNI space using the Lancaster transform in GingerALE. To disentangle the two dimensions in ATL functionality, namely stimuli modalities (visual vs. auditory) and stimuli contents (words vs. objects), we considered four types of conditions: auditory sensory (object sounds or environmental sounds), auditory language (spoken words or sentences), visual sensory (object pictures or videos), and visual language (written words or sentences). The number of studies in each analysis is listed in Table 2.

We performed single study analyses with two thresholds, one lenient (uncorrected p-value of 0.01) and one more stringent (cluster-level family-wise-error inference, cluster-level of 0.05, threshold permutations of 1000, and uncorrected p-value of 0.001), to present a fuller picture of the general patterns for each of the four input conditions. We then overlaid the ALE maps with the four ATL subregions obtained above using Neurosynth and calculated the percentage of voxel overlaps for comparison purpose. As the results of the two ALE thresholds were comparable in terms of the association between ATL subregions and the input types, except that smaller number of voxel overlaps became zero with the cluster-level inference, we reported all ALE scores using the lenient threshold in the main text and presented the ones under the stringent threshold in Supplementary Fig. 5.

3.2.3. ALE Results

3.2.3.1. Meta-analysis of the Input Type. Single study analyses showed that auditory sensory input was mainly clustered in the bilateral superior and middle temporal gyri including transverse gyrus and insula; auditory language input in the bilateral superior and middle temporal gyri and parahippocampal regions; visual sensory input in the bilateral superior and middle temporal regions, fusiform and parahippocampal regions; and visual language input in the left superior and middle temporal gyri and parahippocampal regions (see Fig. 4a and Supplementary Table 2 for detailed results).

3.2.3.2. ALE Maps in the ATL Subregions. We calculated the percentage of significant voxels located in each of the ATL subregions obtained based on Neurosynth (Fig. 4b). The superior dorsal ATL cluster was similarly strongly associated with auditory sensory, auditory language, visual language inputs ($\chi^2 = 2.05$, $p = 0.91$), and not with visual sensory input (significantly fewer than the other three inputs) ($\chi^2 = 14.1$, $p < 0.005$). The inferior dorsal ATL cluster was similarly associated with auditory sensory, visual language, and visual sensory ($\chi^2 = 0.7$, $p = 0.70$), and was significantly more associated with auditory language ($\chi^2 = 28.4$, $p < 0.001$). The lateral ATL cluster was similarly associated with visual language and auditory language inputs ($\chi^2 = 0.5$, $p = 0.48$), was more associated with visual sensory input ($\chi^2 = 6.6$, $p < 0.05$) but not associated with auditory sensory input (significantly less than all other three, $\chi^2 = 23.8$, $p < 0.001$). The ventromedial cluster was similarly strongly associated with visual sensory and visual language inputs ($\chi^2 = 14.7$, $p < 0.005$), to a lesser extent with auditory language input ($\chi^2 = 25.7$, $p < 0.001$), and further less with auditory sensory input ($\chi^2 = 47.4$, $p < 0.001$). In brief, for nonlinguistic sensory inputs, there seemed to be a stronger dorsal–ventral regional division by stimulus modality; yet, language inputs, visual or auditory, could activate all ATL subregions. That is, ATL functional subdivision may respect both content and modality in an interactive manner.

3.2.3.3. Comparison With the Topic Preference Derived From Neurosynth. These functional preference by stimulus input type was consistent with the topic preference via Neurosynth methods. The dorsal aspects of the ATL showed very strong preference to auditory sensory input, going along with the auditory sound and speech related topics (e.g., auditory sounds, voice identity, music, or speech). The ventral aspects of the ATL showed preference to visual sensory input, which may reflect the stronger loadings of face-related or picture research topics here. Convergently, both meta-analyses revealed a dorsal–ventral division by stimulus modality. Although we were not able to distinguish auditory vs. visual language specific topics in Neurosynth data, language-related research topics were loaded distributedly among the dorsal and ventral aspects of the ATL.

4. Discussion

We conducted a functional parcellation investigation in the anterior temporal lobe (ATL) by aggregating brain activation data from large-scale neuroimaging studies. Consistent with the rsFC based parcellation (Pascual et al., 2015), clustering of whole brain coactivation patterns first revealed two general divisions: dorsal vs. ventral aspects of the ATL, each was further divided into two subdivisions with distinct coactivation patterns and generic functional preferential profiles. The spatial location of these coactivation-based subregions was comparable to previous cytoarchitectonic and connectivity-based parcellation analyses (Ding et al., 2009; Fan et al., 2013; Pascual et al., 2015), resulting in the superior dorsal, inferior dorsal, ventromedial, and lateral aspects of the ATL. These four clusters were associated with different sets of research topics (Meta-analysis 1) and showed different sensitivity to different types of stimulus inputs (Meta-analysis 2).

While meta-analysis is not designed to do specific hypothesis testing, it generates a bigger picture that may unveil broader and/or newer perspectives that are not captured by individual studies. There are inevitably previous studies consistent with the current findings as our meta-analyses are constructed based on synthesizing among previous studies. Thus, in the discussion below instead of going through references being consistent or inconsistent with the current findings, we attempt to characterize the functionality of each subregion by inferring the cognitive component(s) best underlying the 'topics' that most strongly associated with and the types of stimuli input that most consistently activate a subregion (summarized in Fig. 5). We do this conservatively, acknowledging that this practice relies on the cognitive ontologies that are commonly assumed, which can be equivocal (Anderson et al., 2013; Wang et al., 2020). Note that part of the basal ATL was not included in the four identified subregions as it did not reach the voxel inclusion criteria in the first step of the Neurosynth analysis. Validation analysis that included the basal ATL by lowering the inclusion criteria still revealed comparable results to the main analysis, with these basal voxels clustered into the ventromedial subregion. Below we consider jointly the functional results across both meta-analyses, the coactivation, cytoarchitecture and connectivity patterns.

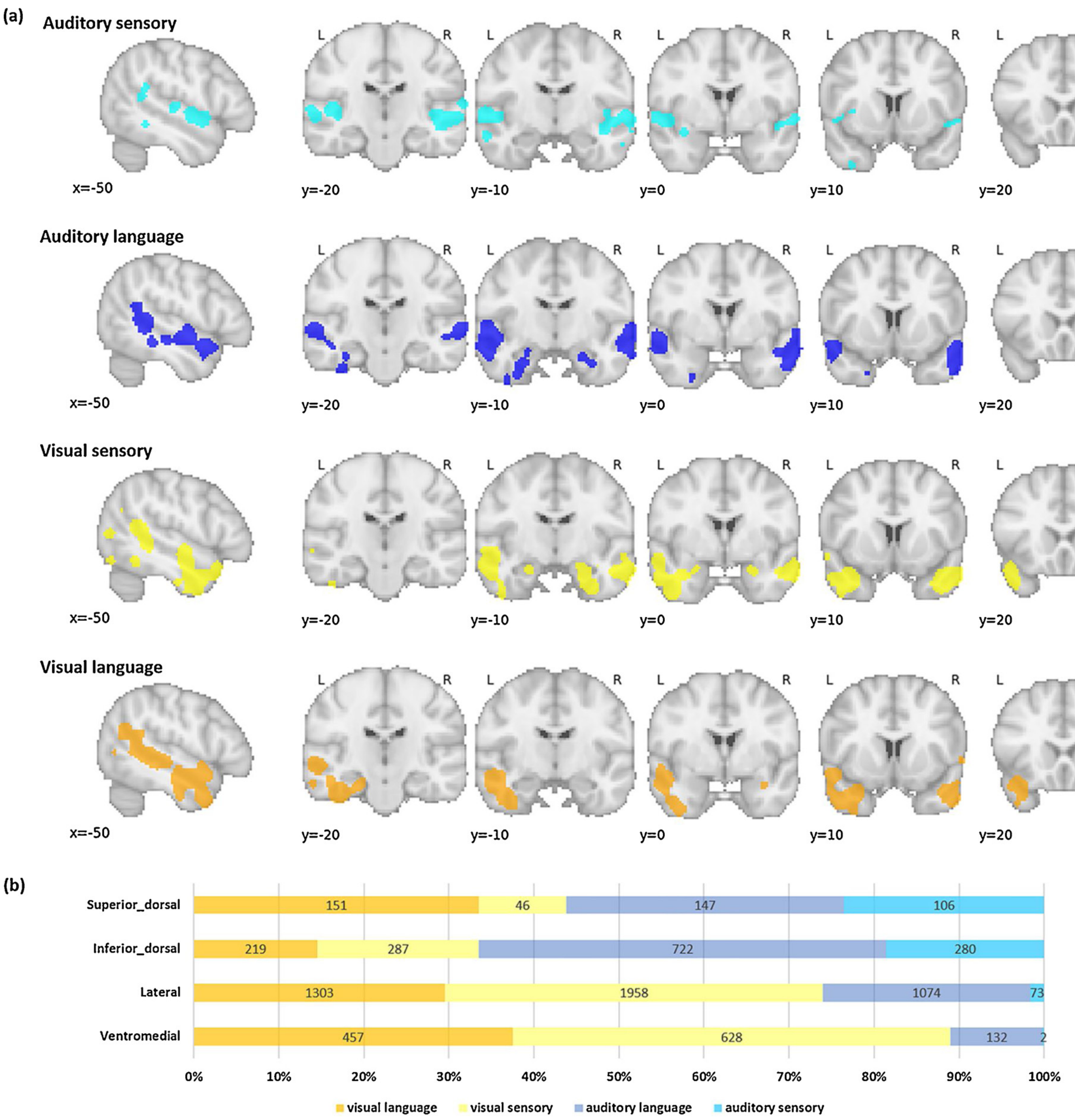


Fig. 4. Influence of input types defined by stimuli modalities and stimuli contents. (a) ALE single study results with uncorrected $p < 0.01$ for auditory sensory (cyan), auditory language (blue), visual sensory (yellow), and visual language (orange). We only included coordinates in the temporal lobe in the ALE analysis. (b) Proportions of probability of activation likelihood of each input type in the ATL subregions obtained based on Neurosynth (i.e., the four clusters in Figs. 2 and 3), with the number of voxel overlaps being marked.

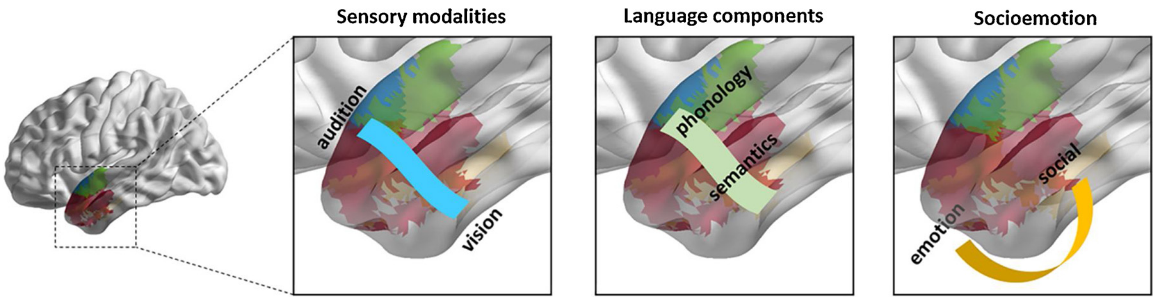


Fig. 5. A schematic framework of the multiple cognitive dimensions underlying the functional specialization in the ATL subregions. A sensory dimension to represent the dissociation between audition- and vision-based information in the dorsal vs. ventral aspects of the ATL. A language dimension to demonstrate the relative functional preference of different aspects of language across the ATL subregions. A socioemotional dimension to demonstrate the relative functional preference of emotional and social processing across the ATL subregions. Curve bands illustrate the direction of the axis for that dimension, with relative/gradients of changes.

4.1. Superior Dorsal ATL Cluster

The superior dorsal ATL cluster is located in the rostral temporal pole, which corresponded mainly to the anterior TA area, located immediately posterior to area TG, and to part of the TI area in Pascual et al. (2015) study. It was congruent with the anatomical connectivity-based dorsal TP (TAr) region in Fan et al. (2013) study. Note that both the superior dorsal and inferior dorsal ATL clusters corresponded to the same region (i.e., TA region) in the previous anatomical parcellation results, but the two dorsal clusters were different in terms of their coactivation patterns and functional preferential profiles. The superior dorsal ATL cluster coactivated with the inferior frontal gyri, precentral gyrus, and anterior cingulate gyri. Neurosynth meta-analysis results showed that it is most strongly associated with topics including *music, speech (auditory production), verbal fluency, sentence comprehension, word semantics, lexical phonology, picture, language*, and *emotion processing/regulation*. The ALE meta-analysis showed that it is consistently activated by auditory sensory inputs (object sounds), both written and spoken language inputs but significantly less so by visual sensory inputs (pictures). Convergently, this area is likely to be related to auditory sensory, language (phonological production aspect), and emotion.

4.2. Inferior Dorsal ATL Cluster

The inferior dorsal ATL cluster is located in the anterior superior temporal gyrus. Similar to the superior dorsal ATL cluster, the inferior dorsal ATL cluster also corresponded to the anterior TA area in Pascual et al. (2015) study, located more posterior to the superior dorsal ATL cluster, and to the dorsal TP (TAr) region in Fan et al. (2013) study. It coactivated greatly with the superior temporal gyri posteriorly. The research topics that it associated most strongly included *speech (auditory production), auditory sounds, voice identity, sentence comprehension, music, word semantics, sentence processing, visuoauditory modality, language, lexical phonology,* and *memory retrieval*. The ALE meta-analysis that it is mostly activated by the auditory language input and to a lesser extent by auditory sensory, visual language, and visual sensory. This area is thus likely to be related to auditory sensory and language (phonological perception and production aspects).

4.3. Lateral ATL Cluster

The lateral ATL cluster included many of the ventrolateral aspect of the ATL, from temporal pole to the anterior superior, middle, and inferior temporal gyri. It corresponded to the mediodorsal, ventromedial and dorsolateral seeds (i.e., area TG, TE, anterior area TA) in Pascual et al. (2015) study, and was more associated with the anatomical connectivity-based ventrolateral TP region (TGl) in Fan et al. (2013) study. The lateral ATL cluster coactivated greatly with the middle temporal gyri, angular gyri, precuneus gyrus, frontal pole, and the left inferior frontal cortex region, consistent with the profile of the default mode network (Buckner et al., 2008; Yeo et al., 2011) and the semantic network (Binder et al., 2009). The topics that are strongly associated with the lateral ATL cluster included *sentence comprehension, mentalization, future/past event, memory retrieval, default mode network, social cognition, emotional processing, word semantics, speech (auditory production), referential judgment, empathy, recognition, memory encoding, gesture, valence, abstract/concrete concept, mind theory, sentence processing,* and *recollection*. The ALE analyses revealed that visual sensory (pictures) and written/spoken languages consistently activated this region but not auditory sensory (object sounds). We tentatively label this area as being related to visual sensory, language (semantic aspect, probably also episodic memory contents expressed by language), and social processing.

4.4. Ventromedial ATL Cluster

The ventromedial ATL cluster is located in the caudal temporal pole including the anterior parahippocampal gyrus and anterior fusiform cortex, and is likely to also include the basal ATL voxels that were considered in the validation analysis. It mainly corresponded to the medial temporal regions in Pascual et al. (2015) study, including ventromedial and inferomedial seeds (i.e., anterior area 35, entorhinal cortex, TI, and TG). It was consistent with two anatomical connectivity-based substructures (i.e., TGm, TGl) with a stronger association with the ventromedial TP cluster in Fan et al. (2013) study. The ventromedial ATL cluster often coactivated with medial temporal cortical structures, fusiform gyri, and the frontal orbital cortices. The topics that most strongly associated with the ventromedial ATL cluster included *memory encoding and retrieval, emotion processing, picture, emotional face, face processing, valence, fear, future/past event, emotional regulation, recollection, threat, facial expression*, and *recognition*. The ALE analyses revealed that visual sensory (pictures) and written language consistently activate this region, to a lesser extent for spoken language, but not auditory sensory (object sounds). The likely cognitive components here are thus visual sensory, episodic memory, and emotion, with some suggestive evidence for language.

4.5. The Overall Principles Across the Subregion Transitions

Based on the above observations, we propose three dimensions (Fig. 5) that jointly capture the cognitive components cutting across the four ATL subregions: a sensory dimension (audition vs. vision), a language dimension (different aspects of language: phonology vs. semantics), and a socioemotional dimension (emotion vs. social vs. neutral). Our proposal reconciled several previous different roles of ATL being offered. In line with the hub-and-spoke semantic theory that input modality from auditory and visual modality-specific region are separated due to its anatomical and functional connectivity (Binney et al., 2012; Lambon Ralph et al., 2017), the sensory dimension emphasizes on the dissociation between auditory and visual sensory functions along the superior–inferior axis. The language dimension reveals multiple kinds of language components spanning across superior and lateral ATL with speech and phonological components being more centered toward the superior portion (Price, 2010; Striem-Amit et al., 2018). The emotional and socioemotional tags in the superior dorsal and lateral ATL are also consistent with its role as a representation and retrieval unit in the social knowledge and cognition framework (Binney and Ramsey, 2019; Olson et al., 2013; Ross and Olson, 2010; Zahn et al., 2007).

It is worth noting that although we used hard parcellation in the analysis, we by no means infer that the functional specialization is discrete rather than graded (e.g., Lambon Ralph et al., 2017). Neither the resolution of fMRI nor the statistical approaches used here are suited to address this issue. The results, suggestive of a multi-dimensional space (also see Lambon Ralph et al., 2017), can also be used to explain effects of unique entities and different categories being represented through incorporating these dimensions (Bi et al., 2015; Mehta et al., 2016; Wang et al., 2016).

5. Conclusion

Our study set out to elucidate the functional divisions in the ATL using large-scale coactivation- and coordinate-based meta-analyses on published neuroimaging studies. We identified separable subregions that corresponded well to previous cytoarchitectonic and connectivity-based parcellation and proposed a three-dimension functional framework to explain the cognitive topography in the ATL. This proposal provides a framework for further hypothesis formulation and testing about the relations among these dimensions, between these dimensions and other specific effects that are not directly explained (e.g., abstract semantic vs. concrete/visual experience based semantics, or sociality vs. emotion valence) (Striem-Amit et al., 2018; Wang et al., 2020, Wang et al., 2019), and between these cognitive dimensions and the corresponding anatomical properties.

Authors' Contributions

YB conceived the research, JH performed research and analyzed data, XYW and XSW assisted with discussion, JH and YB wrote the paper.

Declaration of Competing Interest

The authors declare no competing interests.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.neubiorev.2020.05.008.

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