Supplementary Materials for

Decoding emotional prosody: a unified brain network integrating gender and task type effect

Pinyuan Hu *et al*.

* Suyu Zhong. Email: zhongsuyu@bupt.edu.cn

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Supplementary Text

Supplementary methods

Scan parameters of HCP dataset

The T1-weighted MRI and resting-state Functional MRI in HCP were used in our study. For T1-weighted MRI, the parameters were as follows: Repetition Time (TR) = 2400 ms, Echo Time (TE) = 2.14 ms, Inversion Time (TI) = 1000 ms, flip angle = 8 degrees, Field of View (FOV) = 224×224 mm, voxel size = 0.7 mm isotropic, bandwidth = 210 Hz/Px, and total acquisition time = 7 minutes 40 seconds. The resting-state fMRI section were scanned by a gradient-echo EPI sequence with the following parameters: TR = 720 ms, TE = 33.1 ms, flip angle = 52 degrees, FOV = 208×180 mm, matrix size = 104×90, slice thickness = 2.0 mm, 72 slices, multiband factor = 8, echo spacing = 0.58 ms, and bandwidth = 2290 Hz/Px.

Preprocessing of the gene expression data

To identify the gene foundation of emotional prosody, the public gene expression data, Allen Human Brain Atlas (AHBA) (http://human.brain-map.org) were used. It offers transcriptomic data of 58,692 probes corresponding to 29,131 genes, derived from 3702 spatially distinct tissue samples collected from six postmortem adult brains. The gene expression data was processed as follows： First, probes without valid EntreZ ID (total 12,871 probes) and those with expression values below the 50% of all probes (14,252 probes) were excluded, resulting in 31,569 probes for 15,633 genes. To identify a representative probe for each gene, we computed the Spearman correlation of expression values across brain regions for each donor pair and selected the probe with the highest average correlation, resulting in 15,633 representative probes. Subsequently, samples were matched to parcels in the Atlas of Intrinsic Connectivity of Homotopic Areas (AICHA, www.gin.cnrs.fr/en/tools/aicha). Parcels that did not match any samples were assigned the expression values of the tissue sample closest to the centroid of that region. Finally, expression values for each sample across genes for each donor were normalized using a scaled robust sigmoid normalization function, followed by normalization of expression values for each gene across samples for each donor. The expression values for all samples assigned to a region were averaged independently for each donor and then averaged across donors.

Activation network derived from "t test" approach

In "t test" approach, the Fisher Z maps were generated similarly to "overlap" approach in main study. However, the normative functional connectivity map for each experiment was identified in a different way. Specifically, the Fisher Z maps of LR and RL were averaged independently for each subject in HCP, and then averaged across subjects. Then we smoothed this average Fisher z map with a 6 mm FWHM Gaussian kernel to get normative functional connectivity map, while excluding white matter regions. Finally, these normative functional connectivity maps were compared against zero using a voxel wise one-sample t-test, with multiple comparisons corrected at cluster-level FWE $P <$ 0.05 (cluster-forming threshold at voxel-level $P < 0.001$) via non-parametric permutation tests implemented in Statistical non-Parametric Mapping (SnPM13, http://warwick.ac.uk/snpm, 10,000 permutations). The suprathreshold clusters were brain regions significantly connected to activation seeds across experiments.

To investigate the differences between EEP and IEP in three cohorts, or the differences between corresponding activation networks of male and female, voxel wise two-sample t-tests, with multiple comparisons corrected at cluster-level FWE $P < 0.05$ (cluster-forming threshold at voxel-level $P < 0.001$, 10,000 permutations) were conducted.

Supplementary results

Activation networks of emotional prosody calculated by "t test" approach

For overall cohort, the activation network t map of EP was widespreadly distributed, mainly in brain regions including bilateral SFG, right PcC, bilateral FP, bilateral MFG, bilateral Insular, bilateral LG, right OcP, bilateral TP, bilateral OFC, bilateral PreCG and bilateral PostCG (Supplementary Figure 3). Notably, the spatial distribution of activation network t map of EEP was quite similar to that of EP (r = 0.98, $p < 0.001$) (Supplementary Figure 4). However, for IEP, the activation network was mainly focused on bilateral TP, bilateral OFC, left PT.

The activation network t maps of EP and EEP for female and male were spatial correlated to that of overall cohort (correlation between F-EP and O-EP: r = 0.94, $p < 0.001$; correlation between F-EEP and O-EEP: r = 0.93, $p < 0.001$; correlation between M-EP and O-EP: r = 0.91, $p < 0.001$; correlation between M-EEP and O-EEP: r = 0.90, $p <$ 0.001) (Supplementary Figure 4). For IEP, the activation network t maps of female and male were quite focused, mainly on bilateral TP, bilateral OFC and left PT (Supplementary Figure 3).

Additionally, we compared EEP and IEP in overall, female and male cohorts respectively. The comparison results were showed in Supplementary Figure 5B illustrated that for three cohorts, brain regions including left MFG, left SFG, left PreCG showed significantly stronger functional connectivity to activation seeds for EEP.

As shown in Supplementary Figure 5C, the activation network of EEP was broader than IEP, suggests that EEP requires the involvement of more brain regions for deeper processing.

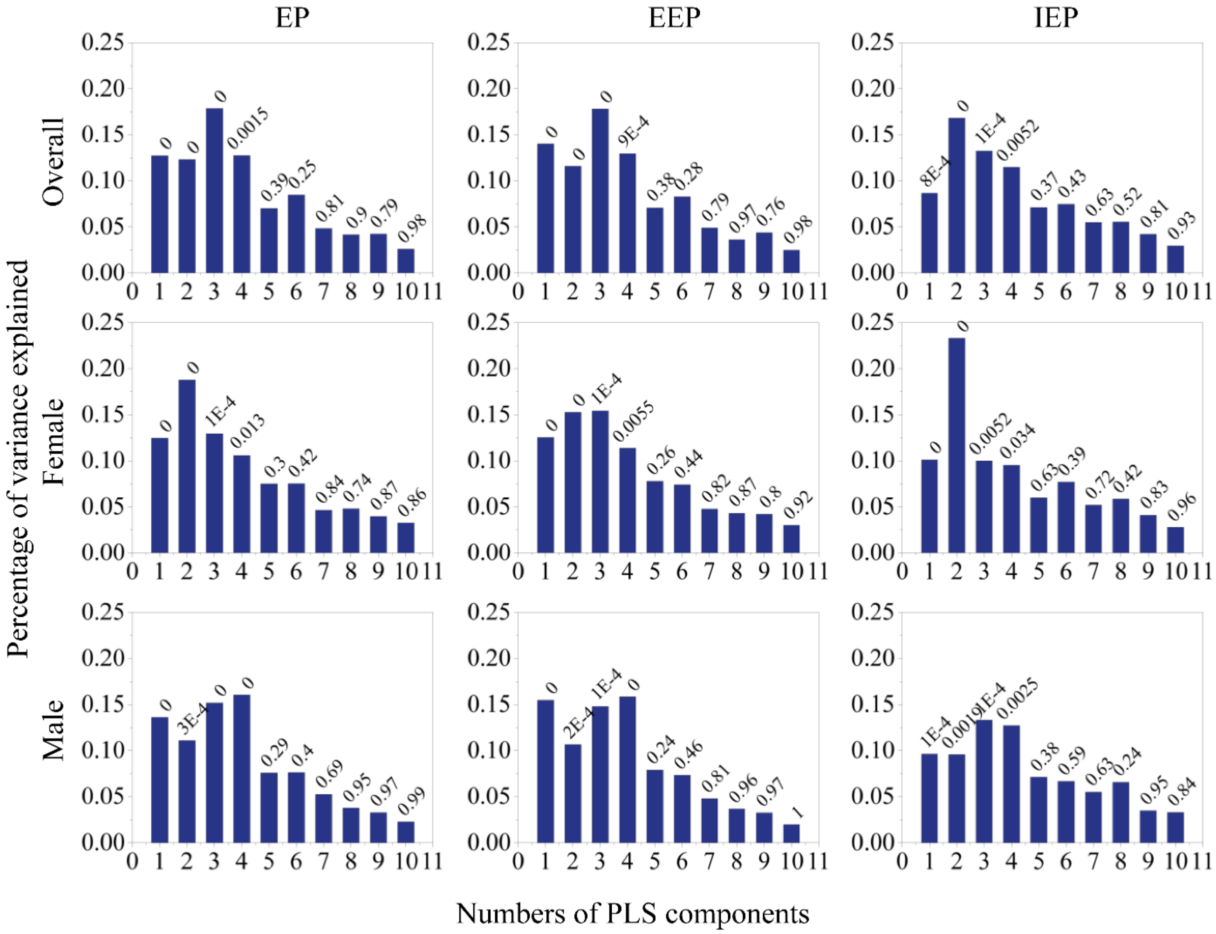
Gender effects on activation networks calculated by "t test" approach

The comparison analysis showed in Supplementary Figure 5A illustrated that, for EP and EEP, there were a set of brain regions whose functional connectivity to activation seeds for female were significantly stronger than that for male (mainly distributed in bilateral PcC, right AG, right Insular, bilateral LG, bilateral OcP, bilateral OFG, bilateral TOF, bilateral lcC, left TFCp, left PreCG, right COpC, bilateral Put). However, no brain region showed significant gender effect for IEP.

Additionally, the overlap analysis showed broader activation network t maps in female for EP and EEP. However, the gender-specific effect in IEP was not prominent due to the localized distribution of activation network for female and male. (Supplementary Figure 5D)

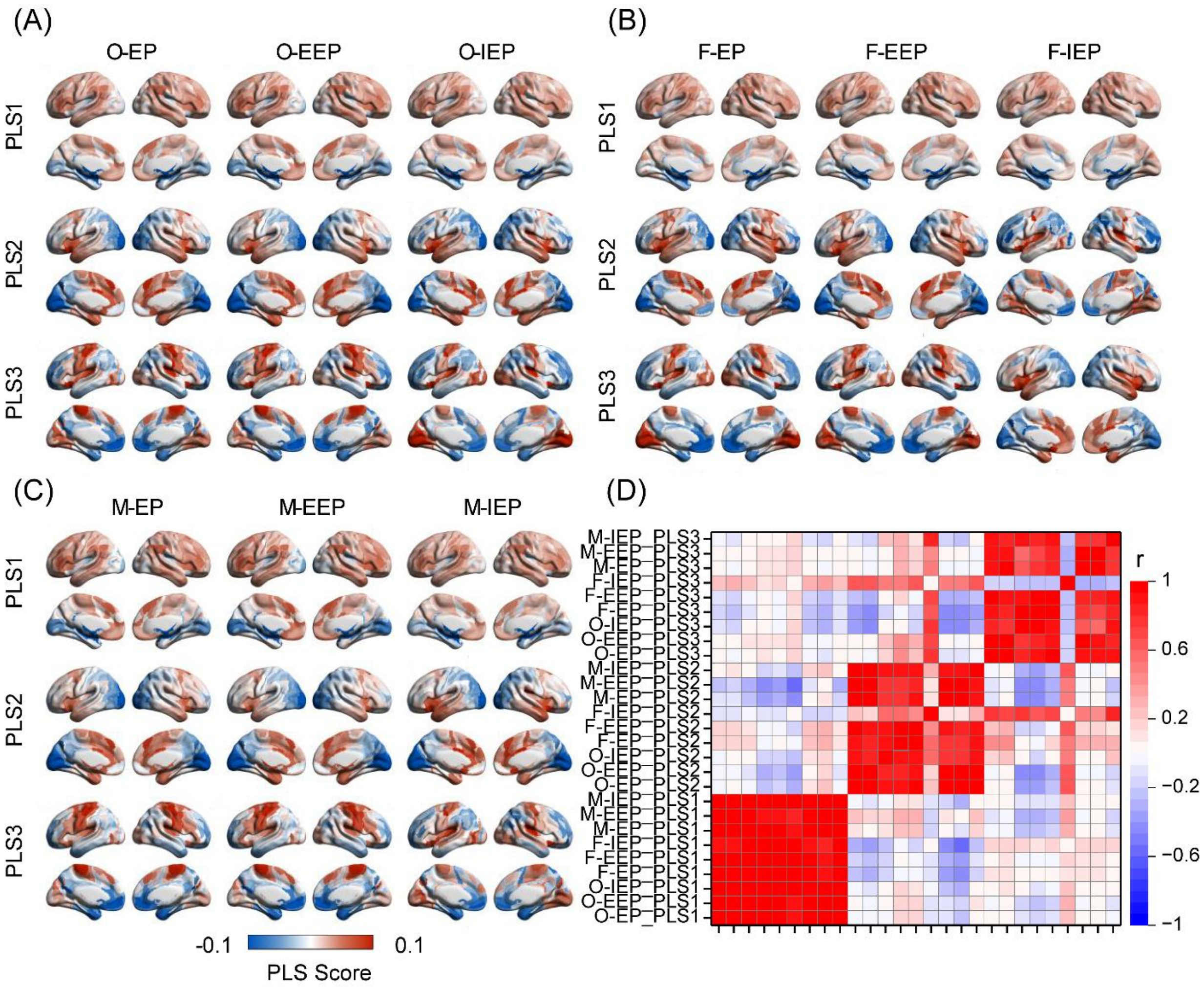
Consistent findings of "overlap" and "t test" approach

The activation networks calculated by "overlap" and "t test" approach were consistently widespread and mainly distributed in Amygdala, bilateral IFG, bilateral Insular, bilateral STG, bilateral PreCG, bilateral PostCG, and these brain regions were demonstrated in previous studies to be involved in emotional prosody processing. Furthermore, the broader activation networks in female calculated by "overlap" approach showed in main study were also found in supplementary results calculated by "t test" approach. This demonstrated that female requires the involvement of more brain regions to process emotional prosody.



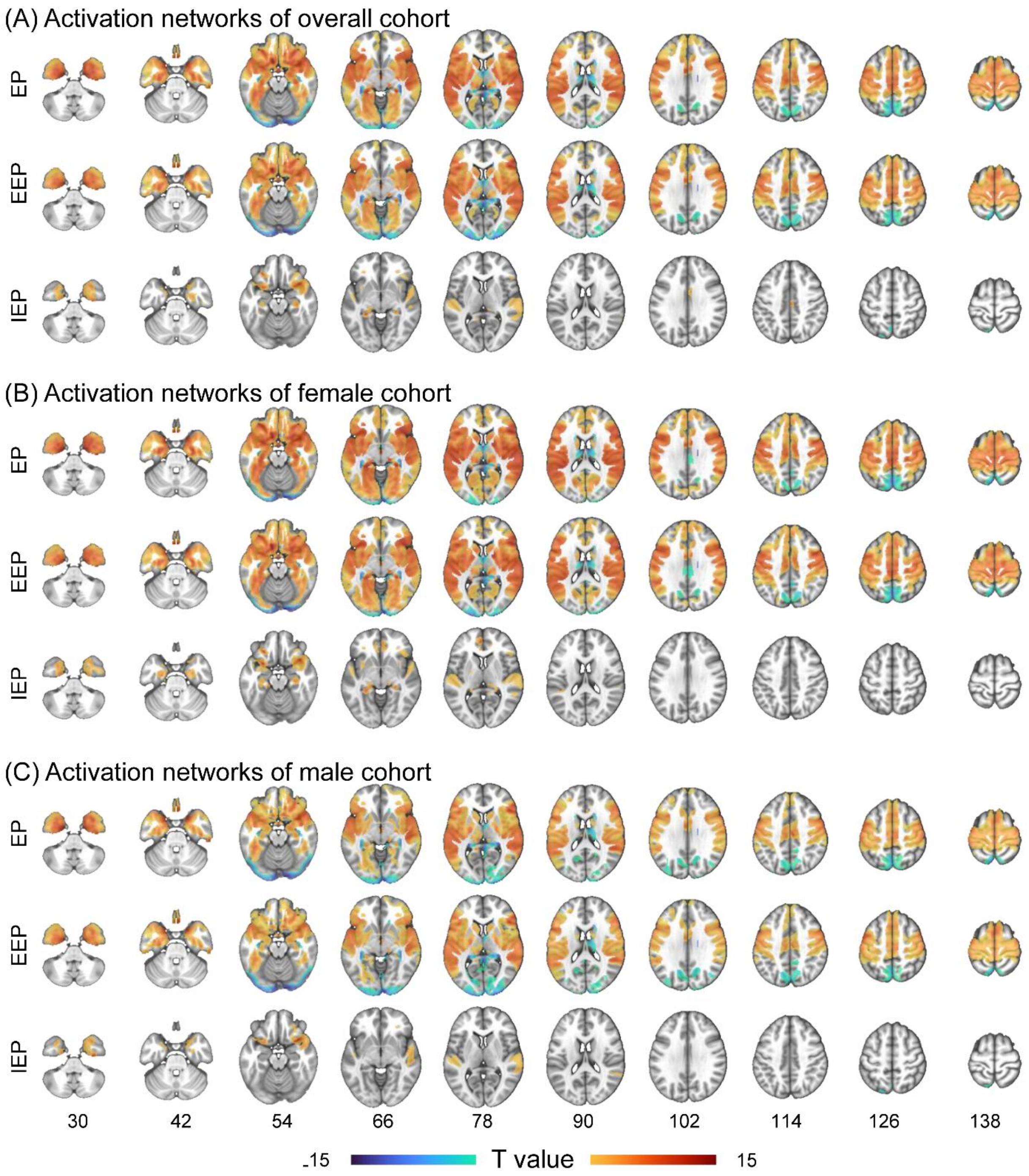
Supplementary Figure 1.

Percentage of variance explained for 15 PLS components of each activation network. The number displayed at the top of the bars represent the permutation p-value for this component.



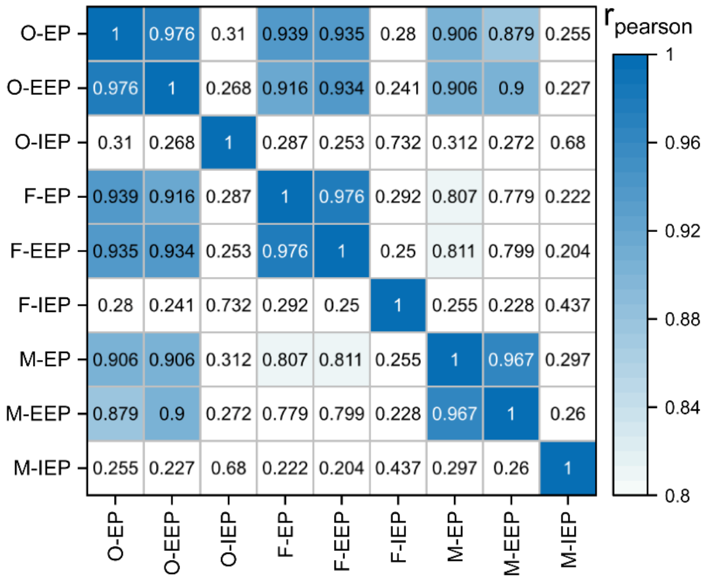
Supplementary Figure 2.

The distribution of each significant PLS component of activation networks dependent on "overlap" approach. For overall (A), male (B) and female (C) cohort. (D) The correlation between significant PLS components for EP, EEP and IEP for overall, female and male.



Supplementary Figure 3.

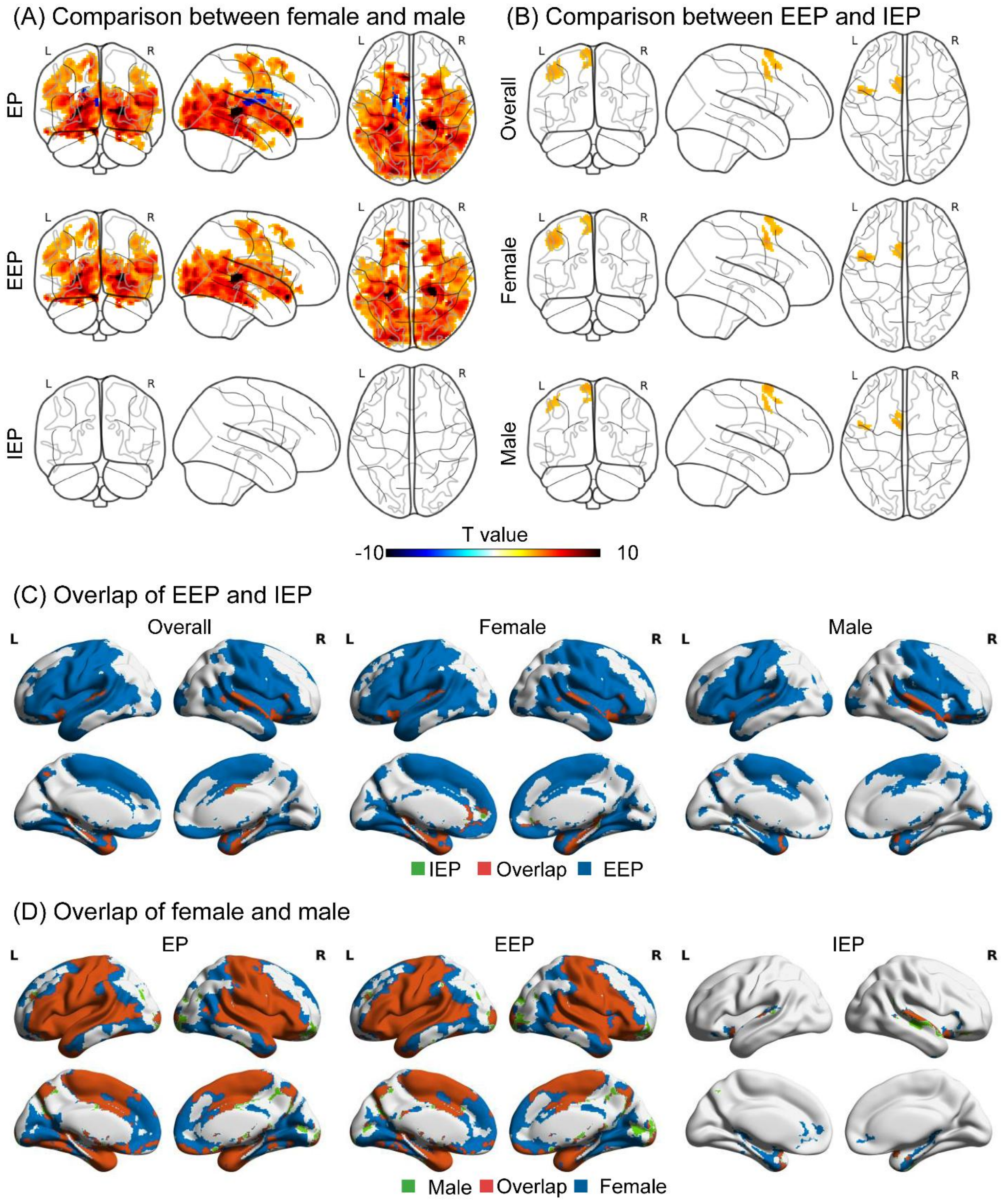
Activation networks calculated by "t test" approach. EP, EEP and IEP activation network of overall (A), female (B) and male (C) cohorts.



	O-EP	O-EEP	O-IEP	F-EP	F-EEP	F-IEP	M-EP	M-EEP	M-IEP
O-EP	1	0.976	0.31	0.939	0.935	0.28	0.906	0.879	0.255
O-EEP	0.976	1	0.268	0.916	0.934	0.241	0.906	0.9	0.227
O-IEP	0.31	0.268	1	0.287	0.253	0.732	0.312	0.272	0.68
F-EP	0.939	0.916	0.287	1	0.976	0.292	0.807	0.779	0.222
F-EEP	0.935	0.934	0.253	0.976	1	0.25	0.811	0.799	0.204
F-IEP	0.28	0.241	0.732	0.292	0.25	1	0.255	0.228	0.437
M-EP	0.906	0.906	0.312	0.807	0.811	0.255	1	0.967	0.297
M-EEP	0.879	0.9	0.272	0.779	0.799	0.228	0.967	1	0.26
M-IEP	0.255	0.227	0.68	0.222	0.204	0.437	0.297	0.26	1

Supplementary Figure 4.

Correlation between activation networks based on "t test" approach.



Supplementary Figure 5.

Comparison analysis results based on “t test” approach. (A) Gender difference networks of EP, EEP and IEP based on "t test" approach for overall, female and male. (B) Task type difference networks of overall, female and male dependent on "t test" approach for EP, EEP and IEP. (C) Overlap of activation networks of EEP and IEP based on "t test" approach for overall, female and male. (D) Overlap of activation networks of female and male dependent on "t test" approach for EP, EEP and IEP.

Supplementary Table 1.

Information of selected papers.

Study	Year	Task Type	Experimental task	Control task	Contrasts	No./Language of participants	No. of Foci	Stereotaxic Space
Alba-Ferrara et al.	2011	Explicit	Categorization	Neutral	Emotion > Neutral	19/English	12	MNI
Aryani et al.	2018	Implicit	Passive listening	Semantic	Emotion (high arousal) > Emotion (low arousal)	28/German	4	MNI
Bach et al.	2008	Explicit	Discrimination	Neutral + Gender discrimination	Emotion > Neutral	16/German	9	MNI
Beaucousin et al.	2007	Explicit	Discrimination	Grammar discrimination	Emotional prosody > No prosody	23/French	20	MNI
Beaucousin et al.	2011	Explicit	Categorization	Grammar discrimination	Emotion > Grammar	23/French	20	MNI
Belyk et al.	2016	Explicit	Discrimination	Pitch contour discrimination	Emotion > Rest	12/English	26	TAL
Brück et al.	2011	Explicit	Discrimination	Semantic + Vowel	Emotion > Neutral	24/German	4	MNI
Buchanan et al.	2000	Explicit	Detect Target	Phonetics	Sad > Verbal Happy > Verbal Emotion > Verbal	10/English	2 1 3	TAL
Castelluccio et al.	2016	Implicit	Passive listening	Neutral	Angry > Neutral	8/French	8	TAL
Ceravolo et al.	2016	Implicit	Distance judgement	Neutral	Aggressive > Neutral	14/French	11	MNI
Ceravolo et al.	2021	Explicit	Same / Different	Neutral	Emotion > Neutral Angry > Neutral Happy > Neutral	19/French	17 33 16	MNI
Dietrich et al.	2008	Implicit	Passive listening	Neutral	Emotion > Neutral	16/German	4	MNI
Elizalde Acevedo et al.	2022	Explicit	Label	Neutral	Negative > Neutral	20/Spanish	7	MNI
Escoffier et al.	2013	Explicit	Discrimination	Pitch	Emotion > Pitch	16/English	2	MNI
Ethofer et al.	2006	Explicit	Rate Discrimination + Rate	Rate semantic emotion semantic	Emotion > Neutral Affective prosody > Emotional word content	24/German	2 3	MNI
Ethofer et al.	2009	Explicit	Discrimination	Neutral + Word class	Angry > Neutral Emotional classification > Word classification	24/German	9 4	MNI
Ethofer et al.	2012	Explicit	Discrimination	Neutral	Emotion > Neutral	22/German	2	MNI
Frühholz et al.	2012	Explicit & Implicit Explicit	Discrimination Prosody discrimination Gender discrimination	Neutral	angry > neutral	17/French	14 19 11	MNI
Gandour et al.	2003	Explicit	Same / Different	Passive listening	Emotion > Passive listening	10/Mandarin 10/English	7 7	TAL
George et al.	1996	Explicit	Discrimination	Semantics, Repetition	Emotion > Neutral	13/English	1	TAL
Goerlich-Dobre et al.	2014	Explicit	Stress + Emotion discrimination	Neutral	Emotion > Neutral	22/Dutch	6	MNI
Hervé et al.	2013	Explicit	Categorization	Grammar + Plausible judgement	Emotion - Semantics > TOM-Semantics	42/French	9	MNI
Imaizumi et al.	1997	Implicit vs Explicit	Discrimination	Speaker Identity	Implicit > Explicit, Emotion > Speaker	6/Japanese	11	TAL
Koch et al.	2017	Explicit	Rate	Neutral	Emotion > Neutral	30/German	9	MNI

Supplementary Table 1 (continued).

Information of selected papers.

Study	Year	Task Type	Experimental task	Control task	Contrasts	No./Language of participants	No. of Foci	Stereotaxic Space
Kotz et al.	2003	Explicit	Discrimination	Neutral	Prosody speech > Normal speech	12/German	8	TAL
Maurage et al.	2013	Explicit	Emotion judgement	Rest	Anger > Rest Fear > Rest	24/English	7 8	MNI
Mitchell et al.	2003	Implicit	Passive listening	Neutral Rest	emotion > neutral emotion > rest	13/English	6 5	TAL
		Explicit	Attend to prosody	Attend to semantic	attention to prosody > attention to semantics		3	
Park et al.	2014	Implicit	Passive listening	Neutral	Emotion > Neutral	24/German	2	MNI
Péron et al.	2016	Explicit	Discrimination	Gender + Neutral	Emotion > Neutral	15/French	14	MNI
Quadflieg et al.	2008	Explicit	Discrimination	Neutral	Angry > Neutral	12/German	11	TAL
Razafimandimby et al.	2016	Explicit	Categorization	Grammar discrimination	Emotion > Grammar	25/French	6	MNI
Rosenblau et al.	2016	Explicit	Label	Gender	Emotion > Neutral	20/German	13	MNI
Rota et al.	2008	Explicit	Categorization	Neutral	Emotion > Rest	10/German	9	MNI
Seydell-Greenwald et al.	2020	Explicit	Discrimination	Neutral	Emotion > Neutral	20/English	9	TAL
Smith, et all.	2015	Implicit	Active Reasoning	Neutral	Emotion > Neutral Sad > Neutral	17/French	2 2	MNI
Wiethoff, et al.	2008	Implicit	Passive listening	Neutral	Emotion > Neutral	24/German	4	MNI
Wildgruber	2004	Explicit	Discrimination	Linguistic	Emotion > Rest	10/German	13	MNI
Wildgruber et al.	2002	Explicit	Identification, Relative expressiveness	2nd > 1st stimulus	Sentence 1 (emotion) > Neutral	12/German	11 9	MNI
Wildgruber et al.	2005	Explicit	Identification	Phonetics Rest	Emotion > Vowel Emotion > Rest	10/German	2 17	MNI

Supplementary Table 2.

Wilcoxon rank-sum test between female and male (female-male) for the overlap proportion in 7 Yeo sub network.

	VN	SMN	DAN	VAN	LN	FPN	DMN
EP z value (p)	-	33.43 (4.69e-245)	7.45 (9.20e-14)	12.95 (2.47e-38)	-	21.49 (1.78e-102)	26.23 (1.09e-151)
EEP z value (p)	5.53 (3.24e-08)	41.51 (0)	13.11 (2.83e-39)	17.73 (2.54e-70)	-	32.34 (1.93e-229)	30.18 (4.36e-200)
IEP z value (p)	-	16.50 (3.98e-61)	0.57 (0.57)	6.34 (2.23e-10)	-	0.39 (0.70)	5.99 (2.10e-09)

note: for the cells marked with '-', there was no voxel involved in the corresponding subnetwork in the activation network for male, the Wilcoxon rank-sum test cannot be performed.

Supplementary Table 3.

Corresponding terms of each enrichment ID.

Dataset	Index	ID	Term
BP	1	GO:0070646	protein modification by small protein removal
BP	2	GO:0016072	rRNA metabolic process
BP	3	GO:0022613	ribonucleoprotein complex biogenesis
BP	4	GO:0034470	ncRNA processing
BP	5	GO:0003018	vascular process in circulatory system
BP	6	GO:0007264	small GTPase mediated signal transduction
BP	7	GO:0009410	response to xenobiotic stimulus
BP	8	GO:0015711	organic anion transport
BP	9	GO:0033865	nucleoside bisphosphate metabolic process
BP	10	GO:0015850	organic hydroxy compound transport
BP	11	GO:0006720	isoprenoid metabolic process
BP	12	GO:0030258	lipid modification
BP	13	GO:0006790	sulfur compound metabolic process
BP	14	GO:0010876	lipid localization
BP	15	GO:1901293	nucleoside phosphate biosynthetic process
BP	16	GO:0006520	amino acid metabolic process
BP	17	GO:0016053	organic acid biosynthetic process
BP	18	GO:0007188	adenylate cyclase-modulating G protein-coupled receptor signaling pathway
BP	19	GO:0006066	alcohol metabolic process
BP	20	GO:0072522	purine-containing compound biosynthetic process
BP	21	GO:0019693	ribose phosphate metabolic process
BP	22	GO:0016042	lipid catabolic process
BP	23	GO:0044282	small molecule catabolic process
BP	24	GO:0006631	fatty acid metabolic process
CC	1	GO:0009897	external side of plasma membrane
CC	2	GO:0031253	cell projection membrane
CC	3	GO:0098857	membrane microdomain
CC	4	GO:0098984	neuron to neuron synapse
CC	5	GO:0099572	postsynaptic specialization
CC	6	GO:1990351	transporter complex
CC	7	GO:1904949	ATPase complex
CC	8	GO:0098978	glutamatergic synapse
CC	9	GO:0043292	contractile fiber
CC	10	GO:0031983	vesicle lumen
CC	11	GO:0045177	apical part of cell
CC	12	GO:0072562	blood microparticle
CC	13	GO:0044309	neuron spine
CC	14	GO:0045178	basal part of cell
CC	15	GO:0042579	microbody
CC	16	GO:0097060	synaptic membrane
CC	17	GO:0062023	collagen-containing extracellular matrix
CC	18	GO:0031252	cell leading edge
CC	19	GO:0005759	mitochondrial matrix
MF	1	GO:0001217	DNA-binding transcription repressor activity
MF	2	GO:0001216	DNA-binding transcription activator activity
MF	3	GO:0019783	ubiquitin-like protein peptidase activity
MF	4	GO:0016755	Aminoacyl transferase activity
MF	5	GO:0008234	cysteine-type peptidase activity
MF	6	GO:0032182	ubiquitin-like protein binding
MF	7	GO:0140313	molecular sequestering activity
MF	8	GO:0005178	integrin binding
MF	9	GO:0016298	lipase activity
MF	10	GO:0016874	ligase activity

Supplementary Table 3 (continued).

Corresponding terms of each enrichment ID.

Dataset	Index	ID	Term
MF	11	GO:0019001	guanyl nucleotide binding
MF	12	GO:0016776	phosphotransferase activity, phosphate group as acceptor
MF	13	GO:0046982	protein heterodimerization activity
MF	14	GO:0016903	oxidoreductase activity, acting on the aldehyde or oxo group of donors
MF	15	GO:0016810	hydrolase activity, acting on carbon-nitrogen (but not peptide) bonds
MF	25	GO:0060589	nucleoside-triphosphatase regulator activity
MF	26	GO:0022804	active transmembrane transporter activity
MF	27	GO:0016887	ATP hydrolysis activity
Pathway	1	hsa05168	Herpes simplex virus 1 infection
Pathway	2	hsa00230	Purine metabolism
Pathway	3	hsa04024	cAMP signaling pathway
Pathway	4	hsa04261	Adrenergic signaling in cardiomyocytes
Pathway	5	hsa04270	Vascular smooth muscle contraction
Pathway	6	hsa04530	Tight junction
Pathway	7	hsa04936	Alcoholic liver disease
Pathway	8	hsa01232	Nucleotide metabolism
Pathway	9	hsa04666	Fc gamma R-mediated phagocytosis
Pathway	10	hsa04976	Bile secretion
Pathway	11	hsa04914	Progesterone-mediated oocyte maturation
Pathway	12	hsa00640	Propanoate metabolism
Pathway	13	hsa01240	Biosynthesis of cofactors
Pathway	14	hsa04714	Thermogenesis
Pathway	15	hsa04913	Ovarian steroidogenesis
Pathway	16	hsa04072	Phospholipase D signaling pathway
Pathway	17	hsa00280	Valine, leucine and isoleucine degradation
Pathway	18	hsa04211	Longevity regulating pathway
Pathway	19	hsa04926	Relaxion signaling pathway
Pathway	20	hsa04146	Peroxisome
Pathway	21	hsa05132	Salmonella infection
Pathway	22	hsa01212	Fatty acid metabolism
Pathway	23	hsa04022	cGMP-PKG signaling pathway
Pathway	24	hsa00071	Fatty acid degradation
Pathway	25	hsa02010	ABC transporters
Pathway	26	hsa01100	Metabolic pathways
Disease	1	umls:C0027765	nervous system disorder
Disease	2	umls:C0242656	Disease Progression
Disease	3	umls:C0003130	Anoxia
Disease	4	umls:C0002395	Alzheimer's Disease
Disease	5	umls:C0004352	Autistic Disorder