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Review article

The neurobiology of sex differences during language processing in healthy adults: A systematic review and a meta-analysis

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ABSTRACT

The neurobiology of sex differences during language processing has been widely investigated in the past three decades. While substantial sex differences have been reported, empirical findings however appear largely equivocal. The present systematic review of the literature and meta-analysis aimed to determine the degree of agreement among studies reporting sex differences in cortical activity during language processing. Irrespective of the modality and the specificity of the language task, sex differences in the BOLD signal or cerebral blood flow was highly inconsistent across fMRI and PET studies. On the temporal side, earlier latency of auditory evoked responses for female compared to male participants were consistently observed in EEG studies during both listening and speaking. Overall, the present review and meta-analysis support the theoretical assumption that there are much more similarities than differences between men and women in the human brain during language processing. Subtle but consistent temporal differences are however observed in the auditory processing of phonetic cues during speech perception and production.

1. Introduction

In the past three decades, dozens of studies have explored sex differences in the neurobiology of language, in terms of both brain structure and functions, in normal and clinical populations, across the life span. Sex differences in language processing have been abundantly reported, with the ultimate objective to correlate cortical activity differences with, putative, verbal ability differences. Yet, the available empirical evidence appears largely equivocal and its functional interpretation controversial (for reviews and meta-analyses, see Kansaku and Kitazawa, 2001; Sommer et al., 2004, 2008; Kaiser et al., 2009; Wallentin, 2009; Fine, 2013; Rippon et al., 2014).

Probably the most emblematic example, often cited as well-established in scientific textbooks and articles, is the long-standing hypothesis that "the male brain may be more symmetrically organized than the female brain both for verbal and non-verbal functions" (Harris, 1980). With the advent of brain imaging research and following the seminal study by Shaywitz and colleagues (1995), many studies investigating sex differences in language processing have claimed to provide evidence for sex differences in the functional lateralization of the brain for language. Two meta-analyses however provided clear counter-evidence against functional laterality differences by combining and weighting effect sizes observed in previous brain imaging studies (Sommer et al., 2004, 2008). The resulting mean weighted effect size appeared to be so weak that, according to the authors, "the putative sex difference in language lateralization may be absent at the population level, or may be observed only with some, as yet not defined, language tasks" (Sommer et al., 2004). In line with this interpretation, several reviews and meta-analyses also failed to find sex differences in lateralization in behavioral studies using divided visual field paradigms (Boles, 1984; Chiarello et al., 2009) and dichotic listening (Hiscock and Mackay, 1985; Sommer et al., 2008; see also Hirnstein et al., 2013).

Not restricted to language lateralization, a number of paradigmatic, methodological and statistical issues, as well as publication and theoretical biases have been identified as critically interfering in the evaluation of sex-related differences on brain activity and functioning, likely explaining the lack of generalization and replication of many past findings (for reviews, see Kaiser et al., 2009; Fine, 2013; Rippon et al., 2014). Among the main issues identified are the limited sample sizes, the task heterogeneity, the weak relationship (if any) between the observed cortical activity and behavioral performance, and the absence of a direct contrast between men and women when evaluating brain activity differences. A publication bias - that is the greater probability of publishing significant differences compared to null findings - has also been

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suggested to favor differences rather than similarities when investigating neurobiological differences between men and women (see Kaiser et al., 2009). Another important point is the absence of a clear-cut distinction between sex and gender. According to gender studies, sex is indeed deeply interwoven with social and cultural constructions of gender through the life span. Since the great majority of neurobiological studies did not take into account gender characteristics, such as gender identity, gender role and/or sexual orientation (but see Smith et al., 2019), caution must be taken when discussing results in order to avoid "stereotype-consistent functional interpretations of sex differences in the brain as fixed, implicitly supportive of a gender essentialist perspective" (Fine, 2013).

Apart from the neurobiology of language, substantial sex differences however exist. Large sex differences have indeed been reported on motor performance, particularly after puberty and depending on muscle mass and bone size (Thomas and French, 1985), and on handedness, with 25% higher prevalence of non-right handedness in males skills (albeit with significant differences between countries; Sommer et al., 2008). Regarding cognitive abilities, one of the first major reviews on behavioral sex differences also argued for clear differences in verbal ability, visual-spatial ability and mathematical ability (Maccoby and Jacklin, 1974; see also Gur et al., 2012; Halpern, 2007). Overall, much evidence for sex similarities was however observed in this review, as confirmed in a subsequent meta-analysis (Hyde and Plant, 1995) and reviews of meta-analyses (Hyde, 2005, 2014). Even the observed sex differences in Maccoby and Jacklin's review (1974) were partly nuanced in these studies. Based on contemporary data, they reported a moderate sex difference favoring males in 3D mental rotation, but no difference on mathematical tests (although with large variability across countries in the magnitude and even the direction of sex difference; see Else-Quest et al., 2010), small to moderate effect sizes favoring females on verbal tests, notably on verbal fluency and reading comprehension, and ambiguous evidence regarding sex differences in social and sexual behaviors, critically depending on cultural and educational factors. Regarding brain structural dimorphisms, an influential meta-analysis reported that men have larger crania, proportionate to their larger body size, and larger absolute grey matter (GM), white matter (WM), cerebrospinal fluid (CSF) and total intracranial (TIV) volumes (from +8% to 13%), with larger WM and CSF fractions (i.e., fractional cerebral compartment volumes as the ratios of tissue absolute volumes to TIV), while women have larger GM fractions (Lemaitre et al., 2005). Recent meta-analysis and large-scale studies also suggest regional sex differences in GM volume and tissue density mostly including brain areas that are part of the limbic and language systems (Ruigrok et al., 2014), in GM density throughout the brain (Gennatas et al., 2017), on grey matter asymmetry in several brain regions (Núñez et al., 2018; but see Watkins et al., 2001, and, Sommer et al., 2008, for counter-evidence), some of which are typically involved in language production, and on anatomical connectivity obtained with diffusion imaging, with greater within-hemispheric connectivity observed in men and greater between-hemispheric connectivity in women (Ingalhalikar et al., 2014). Finally, sex differences are also observed in developmental language-related disorders such as stuttering and dyslexia, with a higher prevalence for men compared to women, as well as in parkinson's disease, autism and schizophrenia, in which speech, language and/or communicative deficits are considered negative symptoms (Wallentin, 2009).

Previous reviews and meta-analyses on sex-related neurobiological differences in language processing primarily focused on language lateralization (Kansaku and Kitazawa, 2001; Sommer et al., 2004, 2008), on a broad overview of sex differences in language performance and in the underlying brain structure and processing (Wallentin, 2009), and/or on crucial criteria and issues from fMRI examinations (Kaiser et al., 2009; see also Rippon et al., 2014). Independent of language lateralization, the present systematic review of the literature and meta-analysis aims to characterize the degree of agreement between previously reported spatial and temporal neurobiological activity differences between men and women during language processing. This systematic review will determine which modality, task and verbal material were studied using fMRI, PET, EEG and MEG, and which of these parameters, if any, led to conclusive findings. The meta-analysis will quantify the consistency of previously reported sex differences in brain activity across fMRI and PET studies.

2. Neurobiology of sex differences in language processing: a systematic review

2.1. Search strategy

A comprehensive electronic literature search was performed using PubMed in December 2018. The search identified neurobiological language studies investigating sex differences. The key search terms (in the title and/or the abstract) included: (sex difference(s) or gender difference(s)) and (language or speech or voice) and (neuroimaging or brain imaging or fMRI or functional MRI or functional magnetic resonance imaging or MEG or magnetoencephalography or EEG or ERP or electroencephalography). The title and abstract of all articles were screened. The pre-selected articles were then assessed thoroughly. Additional references were retrieved from selected articles.

2.2. Selection criteria

Only English publications from peer-reviewed journals were selected. We first identified 59 studies (40 fMRI, 15 EEG, 3 PET and one MEG studies) that met the following criteria: (i) sex-related neurobiological differences were assessed using either fMRI, PET, MEG or EEG (ii) in healthy female and male participants (iii) during a language task (see Appendix).

Several qualitative historical observations can be made (see Fig. 1) based on the 59 studies that were identified (including non-elderly healthy adults but also newborns, infants, children and/or teenagers, and elderly; see below. First, the number of neurobiological studies per year investigating sex differences in language processing increased from the seminal study by Shaywitz et al., in 1995–2006, and then decreased until today (with a peak in 2012). The mean impact factor per year of the scientific journals (based on the current impact factor of the journals) where these studies were published shows a decrease from 1995 to 2006, and then reaches a plateau. Finally, the percentage of studies that directly contrasted men and women when evaluating brain activity differences increased until 2009, to finally represent the majority of the studies. Altogether, these observations appear to reflect the rising interest that was triggered by early reports of sex differences in language processing, with high impact publications. Then came the first critical reviews and discussions of important methodological issues in the mid-2000s, which were followed by careful examination of sex differences since then (i.e. directly contrasting female vs. male).

In the present study, we focus on right-handed non-elderly healthy adults. Studies involving newborns aged 1–5 days (Cheng et al., 2012), infants aged 3–6 months (Pivik et al., 2011), children and/or teenagers aged 5–18 years (Gaillard et al., 2003; Plante et al., 2006; Szaflarski et al., 2006; Burman et al., 2008; Spironelli et al., 2010; Scheerer et al., 2013; Yu et al., 2014; Sugiura et al., 2018), elderly aged 60–73 years (Li et al., 2018) or left-handed adults (Pujol et al., 1999; Szaflarski et al., 2002) were thus removed from the review. When a study included one group of right-handed non-elderly adults (Pujol et al., 1999; Gaillard et al., 2003; Szaflarski et al., 2006; Scheerer et al., 2013; Li et al., 2018), the study was kept. When participants' handedness was not indicated (given the preponderance of right-handers in the world's population; Ahrens et al., 2014; Schirmer et al., 2007; Smith et al., 2019), or when the study involved very few left-handed participants (two of thirty-nine participants; Junger et al., 2013), the study was also included in the review.

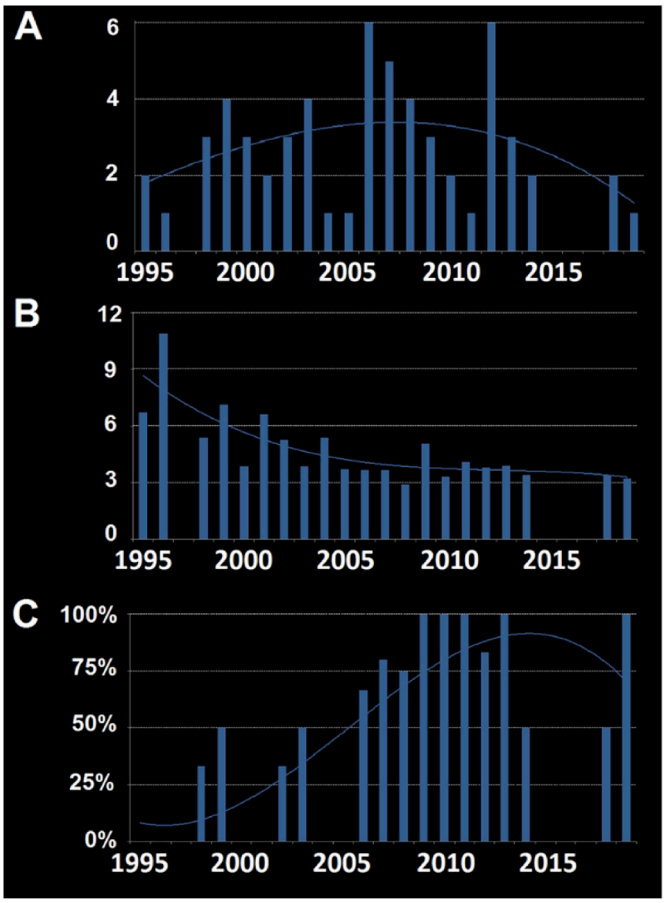


Fig. 1. (A) Number of neurobiological studies (fMRI, PET, MEG, EEG) per year investigating sex differences in healthy participants, (B) mean impact factor per year of the scientific journals in which these studies were published, and (C) percentage per year of studies that directly contrasted men and women when evaluating brain activity differences. Polynomial tendency curve of the 3rd order are indicated.

For the 51 remaining studies, a final criterion was the use of direct contrast between men and women when assessing brain activity differences (i.e. not assessing sex differences in men and women separately). With these criteria, 28 studies (17 fMRI, 9 EEG and 2 PET studies) were identified (see Table 1; note that four studies included two distinct tasks; Harrington et al., 2008; Ihnen et al., 2009; Swink and Stuart, 2012; Allendorfer et al., 2012).

2.3. Data extraction

For each selected study, the observed differences in cortical activity between men and women, the sample size and mean age of female and male participants were extracted. In order to examine the degree of agreement across the selected studies, they were classified according to (i) the imaging technique (fMRI, PET, EEG, MEG) (ii) the modality of the task (passive perception, active perception with manual responses, covert production, overt production), (iii) the language task (listening, reading, counting, picture naming, gender judgment, rhyme judgment, anagram judgment, lexical judgment, semantic judgment, sentence comprehension, free narration, word generation, verb generation, past-tense generation), (iv) the verbal material (vocal sounds, vowels, syllables, words/pseudowords, sentences or stories), and (iv) the modality of presentation (sound, text, logogram, picture, face).

2.4. Results

The resulting 28 studies (i.e., those that directly contrasted non-elderly healthy men and women), included a median number of 31 female and male participants (range: 12–272; SD: ±45) with a median age group of 26 years (range: 20–55; SD: ±8). They mostly used fMRI (n = 17) but also EEG (n = 9) and PET (n = 2). The modality of the tasks was similar across studies with eight tasks involving passive listening/reading, eight involving active listening, eight involving covert production and eight involving overt production (note that four studies included two distinct tasks; Harrington et al., 2008; Ihnen et al., 2009; Swink and Stuart, 2012; Allendorfer et al., 2012). Apart from passive listening, the selected studies involved a variety of language tasks (counting, picture naming, gender judgment, rhyme judgment, anagram judgment, lexical judgment, semantic judgment, sentence comprehension, free narration, word generation, verb generation, past-tense generation), with the word/verb generation task one of the most studied (n = 6). The verbal material consisted of vocal sounds, vowels, syllables, words/pseudowords, sentences and/or stories, with words the most represented in these studies (n = 19). Finally, the presentation of the verbal material included visual logographs (n = 1), faces (n = 1), pictures (n = 3) but mostly sounds (n = 15) and/or texts (n = 14).

Regarding fMRI/PET studies, seventeen studies reported significant BOLD or cerebral blood flow differences between men and women. No sex differences were observed during passive listening or reading in all three selected studies. For active perception, covert production and overt production, however, the results are less clear. For active perception, two studies did not find any differences between female and male participants, two reported higher BOLD activity for female compared to male participants, while three reported lower BOLD activity. Moreover, the reported brain areas are inconsistent across studies. Even with similar gender judgment tasks used in two studies, no agreement can be observed on brain areas showing sex-related BOLD activity difference. Similar mixed results are found for covert and overt production. For overt production, one study reported higher BOLD activity for female compared to male participants, four reported lower BOLD activity, and three reported both lower and higher activity in distinct brain areas. Here again, the reported brain areas were not consistent and no agreement was observed despite similar verb/word generation tasks used in four studies. For overt production, one study reported higher BOLD activity for female compared to male participants, four reported lower BOLD activity, and one reported both lower and higher activity in distinct brain areas. The reported brain areas were not consistent and no agreement was observed despite similar verb/word generation tasks used in two studies.

Regarding EEG studies, all studies did find sex-related differences in auditory evoked potentials (AEP). For passive perception, three of five studies reported earlier latency of auditory evoked responses for female compared to male participants in the first four hundred milliseconds from the onset of the acoustic stimulus (N1, P2, MMN, P400). One study did not find any sex differences on MMN latency and one did not reported latency. A higher amplitude of AEP (MMN, P300, N400) was reported in three of five studies. Higher amplitude of AEP for female compared to male participants were also found in the two studies involving active perception (no latency differences between the sexes were computed). Similarly, earlier latency of P1/N1/P2 AEP for female participants were found in all three studies involving overt production with pitch-shifted feedback. Regarding amplitude, one study reported a higher N1 amplitude for female compared to male participants, the other two did not find any amplitude differences.

In sum, apart from fMRI studies involving passive perception that all reported null findings, the observed sex differences in the BOLD signal or cerebral blood flow from fMRI and PET studies are inconclusive, irrespective of the modality and task. By contrast, EEG studies consistently reported earlier latency of AEP for female compared to male participants in the first four hundred milliseconds.

Table 1
Neurobiological studies selected in the systematic review on sex differences in language processing (*study including two distinct tasks; Mod: modality, PP: passive perception, AP: active perception, CP: covert production, OP: overt production, L: logograph, A: auditory, T: text, F: face, P°: stimulus presentation, [mr]: mean range; SFG: superior frontal gyrus, MTG: middle temporal gyrus, AG: angular gyrus, RO: rolandic operculum, STG: superior temporal gyrus, OG: occipital gyrus, ITG: inferotemporal gyrus, DLPFC: dorsolateral prefrontal cortex, PrCG: precentral gyrus, PoCG: postcentral gyrus, IFG: inferior frontal gyrus, SMA: supplementary motor area, FG: fusiform gyrus, IPL: inferior parietal lobule, SPL: superior parietal lobule, CG: cingulate gyrus).

Type	First Author	Year	Mod	Task(s)	Stimuli	P°	n f/m	Mean age	Results female compared to male participants f > m
fMRI	Chen	2007	PP	reading	artificial words	L	11/13	22[mr]	ns
fMRI	Harrington*	2008	PP	listening	sentences	A	18/19	36	ns
fMRI	Ahrens	2014	PP	listening	vocal sounds, syllables, words, sentences	A	149/123	24	ns
EEG	Swink*	2012	PP	listening	vowel	A	15/15	24	earlier N1, earlier P2
EEG	van den Brink	2012	PP	listening	sentences	A	18/18	22	higher N400
EEG	Schirmer	2007	PP	listening - mmn paradigm	syllables	A	20/20	20	earlier and higher MMN, higher P300
EEG	Ikezawa	2008	PP	listening - dichotic mmn paradigm	syllables	A	21/23	28	higher MMN
EEG	Daltrozzo	2007	PP	listening - semantic priming paradigm	words/sentences	A	10/10	42	earlier N400 (word priming), lower LPC (priming)
fMRI	Junger	2013	AP	gender judgment	words	A	19/20	33	↘ right SFG, left medial orbitofrontal cortex/MTG/AG
fMRI	Smith	2019	AP	gender judgment	words	A	20/17	31	↘ right RO/STG/MTG/MFG, left SFG, cuneus/precuneus
fMRI	Clements	2006	AP	rhyme judgment	non-words	T	15/15	27[mr]	ns
fMRI	Rossel	2002	AP	lexical judgment divided visual field paradigm	words/non-words	T	6/6	32	↘ left OG/ITG, right primary visual cortex ↗ right DLPFC/IFG/MTG
fMRI	Frost	1999	AP	semantic judgment	words	A	50/50	24	ns
fMRI	Kana	2012	AP	sentence comprehension	sentences	T	19/17	21	↗ right PrCG/superior occipital lobe, left MFG/SFG, precuneus
EEG	Hill	2006	AP	lexical judgment	words/non-words	T	15/16	24	higher P100 and N170
EEG	Skrandies	1999	AP	anagram judgment	words	T	10/10	24	higher GFP (70–1200 ms)
fMRI	Ruytjtens	2006	CP	lipreading	numbers	F	9/10	21	↗ left MTG/AG/SPL/IPL, right AG/IFG/middle OG
fMRI	Sveljo	2010	CP	counting	numbers	A	6/6	35	↘ right PFC, SMA
fMRI	Garn	2009	CP	picture naming	words	P	13/13	27	↘ right STG/MTG, left MTG - ↗ left MTG/FG, CG
fMRI	Gizewski	2006	CP	verb generation	words	T	14/12	55	↘ left MTG/PrCG - ↗left IPL
fMRI	Gauthier	2009	CP	word generation	words	T	22/22	20	↘ left ITG/cerebellum/CG, right SFG/DLPFC, CG
fMRI	Allendorfer*	2012	CP	verb generation	words	A	20/20	40	↘ PrCG/PoCG/paracentral lobule
fMRI	Harrington*	2008	CP	verb generation, semantic judgment sentence comprehension	words/sentences	A/T	18/19	36	↘ left MTG/IFG (only semantic judgment)
fMRI	Kaiser	2007	CP	free narration	sentences	P	22/22	28[mr]	↘ right IFG - ↗left IFG
fMRI	Ihnen*	2009	OP	aloud reading	words/non-words	T	10/10	25	↘ left MTG/posterior insula, right STG/posterior insula ↗ left OG/PoCG, right OG/MTG, CG
PET	Grabowski	2003	OP	picture naming	words	P	31/31	33	↘ left ITG/frontal pole, right frontal pole - ↗ right IFG/PrCG
fMRI	Ihnen*	2009	OP	verb, opposite and rhyme generation	word	A/T	13/13	25	↘ left STG/IFG/PrCG/PoCG, right STG/MTG/PrCG/PoCG/insula /MFG/claustrum/parahippocampla gyrus, CG
fMRI	Allendorfer *	2012	OP	verb generation, noun repetition	words	A	20/20	40	↘ right STG/insula/putamen, left STG/IPL, precuneus (nr > vg) ↘ left IPL/SPL, precuneus (vg > nr)
PET	Jaeger	1998	OP	past tense generation	words	T	8/9	26	↗ occipital gyri, cerebellum
EEG	Swink*	2012	OP	pitch-shift feedback paradigm	vowel	T	15/15	24	earlier N1, earlier P2
EEG	Scheerer	2013	OP	pitch-shift feedback paradigm	vowel	T	10/10	23	earlier P1, higher and earlier N1, earlier P2
EEG	Li	2018	OP	pitch-shift feedback paradigm	vowel	T	24	22	earlier and lower N1, lower P2

3. Neurobiology of sex differences in language processing: a meta-analysis

To further assess whether the brain regions showing sex differences in BOLD or cerebral blood flow during language processing were (un) consistent across the fMRI and PET studies, an activation likelihood estimation (ALE) analysis was conducted. To this aim, whenever reported, coordinates of activation peaks showing either higher or lower BOLD activity or cerebral blood flow for female compared to male participants (i.e., female > male and male > female contrasts) were extracted from the selected studies (see Fig. 2). Of the 19 selected fMRI/PET studies (including 22 tasks; see Table 1), 5 studies did not find significant sex differences, 9 reported higher BOLD activity or cerebral blood flow for female compared to male participants in specific brain regions (but two did not report activation peak coordinates; Gizewski et al., 2006; Kana et al., 2012), and 14 reported lower BOLD activity or cerebral blood flow for female compared to male participants in specific brain regions (but three did not reported activation peak coordinates; Gizewski et al., 2006; Harrington and Farias, 2008; Sveljo et al., 2010). Two distinct ALE analyses were conducted based on the female > male (7 studies, 52 foci, 1 study involved an active perception task, 3 involved a covert production task and 3 involved an overt production task) and male > female contrasts (11 studies, 53 foci, 3 studies involved an active perception task, 4 involved a covert production task and 4 involved an

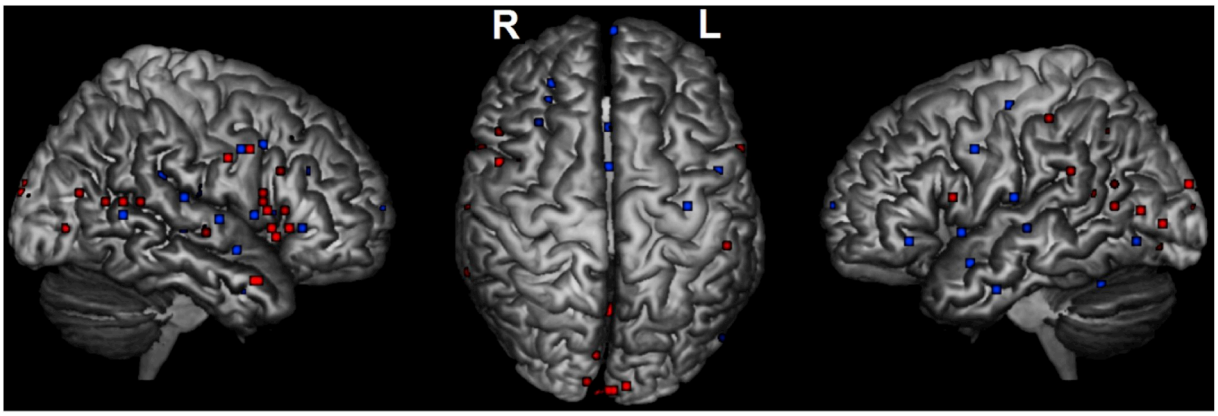


Fig. 2. Surface rendering of the maximum activation peaks reported in the literature and used in the ALE meta-analysis. Red: reported activation peaks showing higher BOLD activity for female compared to male participants (7 studies, 52 foci). Blue: reported activation peaks showing lower BOLD activity for female compared to male participants (11 studies, 53 foci). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

overt production task).

3.1. Method

The ALE meta-analyses were conducted using the GingerAle software (version 2.3.6; Eickhoff et al., 2009, 2012; Turkeltaub et al., 2012). Coordinates of interest were selected by hand and then processed by GingerAle. Throughout the meta-analysis, coordinates are reported in Talairach space. When coordinates had been reported in MNI in reviewed articles, they were converted in Talairach space by using icbm2tal coordinate-based tool transformation developed by Lancaster et al. (2007) included in GingerAle. For the computation of single maps, significant clusters were identified at a Family-Wise Error (FWE) corrected p-value threshold of 0.05 with a minimum volume of 120 mm3 (Hétu et al., 2013) and a p-value permutation of 1000 (in order to differentiate true convergence of foci from random clustering, see Eickhoff et al., 2009, 2012). When no results emerged, a less conservative False Discovery Rate (FDR) correction method was used with a p-value threshold of 0.05 a minimum volume of 120 mm3.

3.2. Results

No significant spatial coherence of the activation peaks reported in the selected studies was observed in the two ALE analyses based on the female > male and male > female contrasts.

4. Discussion

Overall, the present review and meta-analysis support the theoretical assumption that there are much more neurobiological similarities than differences between men and women during language processing. Regarding fMRI and PET studies, the reported sex differences in the BOLD signal or cerebral blood flow was highly inconsistent across modality and task. This lack of coherence was confirmed by ALE meta-analyses that failed to demonstrate any significant spatial coherence of the activation peaks reported in the selected studies. Similarly, no coherent sex differences were observed in the amplitude of auditory evoked responses in EEG studies. The disparate findings observed in the present review appear in line with previous reviews and meta-analyses that provided no evidence of sex-related differences in language proficiency and lateralization, nor in underlying brain structures and functions (Kansaku and Kitazawa, 2001; Sommer et al., 2004, 2008; Kaiser et al., 2009; Wallentin, 2009). As previously mentioned, methodological and statistical issues (including the limited sample size of some studies, the task and stimulus heterogeneity across studies) might partly explain the observed mixed findings. It is however to note that although a number of studies involved a limited sample size, overall the selected studies included a rather consequent median number of 31 female and male participants. Further, no agreement was observed even with similar gender judgment or verb/word generation tasks used in some studies. Importantly, it is also argued that, contrary to the consistent categorization of an individual as female or male through genetic, gonadal and genital phenotype, sex differences in behavioral, social and neurobiological domains do not appear consistent (Joel, 2012). Also challenging the assumption of distinctive female vs. male brain circuitry, Rippon et al. (2014) proposed four principles - overlap, mosaicism, contingency and entanglement - in sex/gender research that might indirectly explain the absence of reliable sex-related differences in the selected studies. The authors indeed argued that any individual has a mosaic of feminine and masculine characteristics, with their distribution largely overlapping at the group level. Moreover, any observed sex-related difference is thought to be contingent upon historical and social contexts that might preclude generalization. From a sociological perspective, the biological categorization of any individual is thought to affect his/her psychological, physical and material experience, making the biological sex and the social phenomenon of gender entangled. From that perspective, sex differences are also conceptualized as transient and context-dependent, through the life span, experience, and environment (Joel and McCarthy, 2017).

Despite the observed inconclusive findings in the BOLD signal, cerebral blood flow and amplitude of auditory evoked responses, it is noteworthy that a rather good agreement for N1/P2 latency differences observed between the sexes in EEG studies involving passive listening and speaking. Indeed, all these studies consistently reported earlier latency of N1/P2 auditory evoked responses for female compared to male participants. N1 and P2 auditory evoked components are known to reflect synchronous neural activation in the thalamic-cortical segment of the central nervous system, with their sources mainly originating from the supratemporal plane of the auditory cortex, in response to spectral and temporal cues of an auditory stimulation (e.g., Näätänen and Picton, 1987; Woods, 1995). During speaking, N1 and P2 are hypothesized to also reflect auditory feedback control mechanisms, through the comparison of actual auditory feedback with an internal auditory-sensory prediction (e.g., Houde et al., 2002; Heinks-Maldonado et al., 2006; Behroozmand and Larson, 2011; Chang et al., 2013; Niziolek et al., 2013; Sitek et al., 2013; Sato and Shiller, 2018). From these acknowledged and hypothesized roles of N1 and P2 components, the observed modulation of N1/P2 latency during listening and speaking suggest sex-differences in the early auditory processing of spectral and temporal phonetic cues and, possibly, in the auditory feedback control of speech production. Based on this later hypothesis, it is noteworthy that sex differences during speech production under altered or delayed auditory

feedback have also been demonstrated in previous behavioral studies, with male speakers experiencing more disruptions in speech (including decreased speech rate, increased dysfluencies, decreased articulation accuracy, slower vocal responses; Sutton et al., 1963; Bachrach, 1964; Timmons, 1971; Fukawa et al., 1988; Corey and Cuddapah, 2008; Chen et al., 2010). Although it is unclear why women produce faster N1/P2 auditory evoked responses, several possible factors might contribute to some extent to these observed sex differences, including differences in phonemic articulatory and acoustic spaces (due to the well-known differences between men and women in the anatomy of the vocal apparatus and its consequences on speech behaviors; Klatt and Klatt, 1990; Ladefoged, 2006; Simpson, 2009), in anatomical connectivity (with greater within-hemispheric connectivity observed in men and greater between-hemispheric connectivity in women, see Ingalhalikar et al., 2014), in grey matter volume and tissue density (Ruigrok et al., 2014) and in hormonal influences (although there is no convincing evidence that sex hormones plays a role in neurobiological language processing, see Wallentin, 2009). Finally, it is also noteworthy that, at the subcortical level, non-speech specific sex differences were previously observed in the evoked auditory brainstem responses during acoustic stimulation, with earlier latencies for females compared to males. These differences in the evoked auditory brainstem responses were linked to the those observed in the female and male peripheral hearing system, with larger head and cochlear sizes for males compared to females (see Krizman et al., 2012).

In conclusion, while no agreement between reported cortical activity differences between men and women was found in neurobiological studies of higher order language processing, a few EEG studies demonstrated subtle but consistent temporal differences between men and women in the auditory processing of phonetic cues during both speech perception and production. Future brain imaging studies are therefore required to investigate sex differences in the sensorimotor and phonetic neural mechanisms and brain areas that support speech perception and production.

Conflicts of interest

The author declares no competing financial interests.

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Appendix

Reference list of the 59 studies used in the review that met the following criteria: (i) sex-related neurobiological differences were assessed using either fMRI, PET, MEG or EEG (ii) in healthy female and male participants (iii) during the perception and/or the covert/overt performance of a language task involving (iv) the processing of vocal sounds, vowels, syllables, words/pseudwords, sentences or stories, presented visually or auditorily.

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