

语言功能偏侧化及其与利手、功能连接的关系*

王 潇 吴国榕 吴欣然 邱 江 陈 红

(西南大学心理学部, 认知与人格教育部重点实验室, 重庆 400715)

摘 要 对大脑语言功能偏侧化的探索起始于早期对脑损伤病人的研究。现代脑影像学研究发现, 语言功能偏侧化涉及额叶、颞叶、扣带回、梭状回和辅助运动区等脑区。语言偏侧化与利手和静息态功能连接之间的关系表现为: 右利手的语言优势位于左半球, 而左利手的则分布在左半球、右半球或两个半球; 语言功能偏侧化与利手系数、静息态半球内功能连接之间具有正相关关系, 与半球间功能连接呈负相关, 并且语言功能偏侧化与静息态功能连接之间的关系在左右利手个体之间存在差异。总之, 大脑语言功能偏侧化、利手和静息态功能连接三者之间存在相互影响, 基于脑连接和遗传机制的研究将有望揭示出其底层的神经生理机制。

关键词 语言功能偏侧化; 利手; 静息态功能连接

分类号 B842

1 引言

大脑语言功能的偏侧化是最明显的脑功能偏侧化特征, 一直是神经科学研究的焦点。在 19 世纪, Marc Dax 和 Paul Broca 就提出言语障碍与脑半球额叶损伤有关联。现在大量使用功能性磁共振成像(functional Magnetic Resonance Imaging, fMRI)的研究通过对语言任务的分析发现语言功能偏侧化所涉及的脑区主要有额叶和颞叶, 而且它们的解剖形态也表现出与功能偏侧化相对应的特征(Gao et al., 2017; Liu, Stufflebeam, Sepulcre, Hedden, & Buckner, 2009; Mazoyer et al., 2014; Zago et al., 2017)。有研究表明, 语言功能偏侧化和利手有关。左利手大约占全世界人口数量的 10%, 其 70%~80% 的语言优势半球是左半球, 其余的则表现为右半球优势和双侧半球优势; 而 90% 以上的右利手都是左半球优势(Willems, van der Haegen, Fisher, & Francks, 2014)。多数研究发现利手与语言功能偏侧化之间存在显著的正相关关系, 即利手系数越高(越趋于右利手), 其语言功能左半球偏侧化的程度越高(Groen, Whitehouse, Badcock, & Bishop, 2013; Haberling, Corballis, &

Corballis, 2016; Kondyli, Stathopoulou, Badcock, & Papadatou-Pastou, 2017)。此外, 一项关于利手与静息态功能连接(Functional Connectivity, FC)的研究表明, 利手是唯一与 FC 的不对称性有关的行为变量(Raemaekers, Schellekens, Petridou, & Ramsey, 2018)。静息态 FC 作为反映区域间信息传递的一个重要指标(Roland et al., 2017), 它与语言功能偏侧化也密切相关(Joliot, Tzourio-Mazoyer, & Mazoyer, 2016; N. Tzourio-Mazoyer, Joliot, Marie, & Mazoyer, 2016)。鉴于语言功能偏侧化、利手和静息态 FC 三者之间的紧密联系, 将它们统一起来进行研究, 有望为今后的研究提供更多新的洞见。本文的主要目的是综述大脑语言偏侧化的科学研究, 总结该领域研究的最新进展, 为今后的科学研究提供参考。由于语言功能偏侧化的实验任务相对较多, 其中语言产生任务, 尤其是词汇产生任务(Word Generation/ Production Task), 是最常用的也是最能揭示语言产生过程的一种任务范式(Knecht et al., 2000)。因此, 本文将重点总结语言产生任务引起的大脑功能偏侧化特征, 以及它们与利手、静息态 FC 的关系。

2 语言功能的偏侧化

2.1 语言功能偏侧化的大脑功能基础

语言功能涉及的脑区主要集中在左半球额下

收稿日期: 2019-04-12

*国家自然科学基金项目(61876156)。

通信作者: 吴国榕, E-mail: gronwu@gmail.com

回和颞叶区域。左侧额下回也被称为布洛卡区(Broca's Area), 是语言处理的关键脑区, 其中岛盖部(pars opercularis)主要与语言产生和语音处理有关, 三角部(pars triangularis)主要与语义加工有关(Price, 2012)。另外, 在2004年的一篇研究综述中, 作者认为除了额叶与语言处理有关之外, 左侧的颞中回和颞上回在词汇产生和图片命名任务中也具有重要作用(Indefrey & Levelt, 2004)。颞中回和颞上回, 其中包含威尔尼克区(Wernicke's Area), 主要负责在阅读中处理词汇意义(Acheson & Hagoort, 2013; Bigler et al., 2007)。

早期的研究发现左侧额叶在语言产生中具有重要作用。比如, 基于正电子成像术(Positron Emission Tomography, PET)的研究发现左侧的背侧和腹侧额下回(BA44、45、47区)、内侧额回等脑区与语言产生有关(Price, 2012)。McCarthy, Blamire, Rothman, Gruetter 和 Shulman (1993)基于fMRI获得了与PET研究几乎一致的结论, 即左侧额下回在词汇产生任务中激活了。近年来, 随着研究技术的不断提高, 研究者在不同的任务条件中发现语言产生过程不仅引起了左侧额叶的激活, 还引起了颞叶血氧水平依赖(Blood Oxygenation Level Dependent, BOLD)信号的变化(Price, 2012; Vigneau et al., 2011)。比如, 在句子和词表产生任务(Sentence and word list production tasks)下, 激活的脑区主要分布在左侧的额下回、额中回和颞上回后部(Mazoyer et al., 2014; Zago et al., 2017)。类似地, 词汇语义分类任务和汉语语义任务所激活的脑区也主要集中在左侧额下回和颞叶(Gao et al., 2017; Liu et al., 2009)。一项基于128篇fMRI研究的元分析表明, 在音韵、词汇语义和句子产生任务中, 大脑激活的区域在左半球中占据的比率比右半球更高, 这些脑区主要集中在额叶和颞叶区域(Vigneau et al., 2006; Vigneau et al., 2011)。综上, 左侧额叶和颞叶与语言功能的偏侧化具有密不可分的关系。

除了额叶和颞叶区域与语言处理有关外, 不少研究显示前扣带、梭状回以及辅助运动区也在语言产生任务中发挥了重要作用。当被试在动词产生任务中生成不常用的动词词汇时, 前扣带区域的脑活动出现了显著增强(Barch, Braver, Sabb, & Noll, 2000)。梭状回不仅在面孔识别中发挥重要作用(Frassle et al., 2016; Kanwisher, McDermott, &

Chun, 1997), 而且在阅读和词汇识别中也同样不可或缺(Dehaene & Cohen, 2011; Weiner & Zilles, 2016)。比如, 左侧梭状回在句子和词表产生任务下会激活(Mazoyer et al., 2014; Zago et al., 2017), 它与其周围皮质也被称为视觉词形区(Visual Word Form Area)。有研究表明左侧梭状回和额下回在语言任务中具有相同的偏侧化特征(Haegen, Cai, & Brysbaert, 2012)。此外, 在默读词汇(Zago et al., 2017)或区分语义(Gao et al., 2017)的任务中有辅助运动区的参与, 其作用可能是通过加大抑制熟悉词汇的力度对陌生词汇做出正确反应(Tremblay & Gracco, 2010)。除了大脑皮层上的区域参与语言产生过程外, 右侧小脑也是一个能揭示语言功能偏侧化特征的关键脑区(Gao, Wang, Yu, & Chen, 2015)。这些研究表明语言与脑内很多区域都有关系, 这些区域间的相互作用使语言的识别、学习和运用变得更加流畅。

2.2 语言功能偏侧化的大脑解剖形态基础

研究表明大脑的解剖形态特征与语言功能偏侧化有关联, 但这种关系是微弱的, 且无法得到很好的重复验证(Nathalie Tzourio-Mazoyer, Perrone-Bertolotti, Jobard, Mazoyer, & Baciou, 2017)。一项研究表明, 语言功能左半球偏侧化的程度越高则脑体积越大(Nathalie Tzourio-Mazoyer, Petit, et al., 2010)。对特定脑区的研究发现, 颞平面(Planum Temporale)的左侧皮层面积与语言功能的偏侧化呈正相关(Tzourio, Nkanga-Ngila, & Mazoyer, 1998); 颞横回(Heschl's Gyrus)的左侧体积大小与处理语音刺激时的激活范围大小呈正相关(Warrier et al., 2009); 前脑岛皮层表面面积的左侧不对称性与词汇识别的功能偏侧化呈正相关(Chiarello, Vazquez, Felton, & Leonard, 2013); Wada测试表明额下回三角部的皮层面积不对称性与语言功能的偏侧化有关, 但近期的研究并没有证实这一发现(Nathalie Tzourio-Mazoyer et al., 2017)。基于大脑纤维束的研究表明, 胼胝体(Corpus Callosum)中部的面积越大, 则语言功能的偏侧化程度越高(Josse, Seghier, Kherif, & Price, 2008); 弓形束(Arcuate Fasciculus)的部分各向异性(Fractional Anisotropy, FA)的不对称性与语言功能偏侧化之间有很强的正相关关系(Haeblerling, Badzakova-Trajkov, & Corballis, 2013)。此外, 基于大脑白质结构网络的图论研究表明, 左半球具有更多枢纽

(hub)区域,在语言和运动等高度特异性的活动中左半球具有更重要的作用;而右半球具有更强的区域间连通性,所以它在处理整合信息时更具有优势(Iturria-Medina et al., 2011; Li et al., 2014)。以上研究表明,大脑的语言系统不仅具有功能偏侧化的特征,还在灰质和白质的解剖形态上表现出相应的不对称性特征。

2.3 语言功能偏侧化的大脑神经化学基础

大脑中多巴胺能和谷氨酸能神经递质的传递也为语言功能的偏侧化提供了神经化学基础。左半球的多巴胺系统可能通过对复杂序列运动的控制从而对语言功能的偏侧化产生了影响(Toga & Thompson, 2003; Tucker & Williamson, 1984)。脑影像研究表明,多巴胺能神经递质的传输与词汇产生任务的表现呈显著的正相关(Cervenka, Backman, Cselenyi, Halldin, & Farde, 2008),谷氨酸能神经递质传递水平的降低与语言功能偏侧化的降低有关系(Hugdahl et al., 2008)。此外,与其他编码突触传导受体的基因相比,编码多巴胺和谷氨酸突触传导受体的mRNA是最具左侧不对称特征的受体基因(Karlebach & Francks, 2015),同时,与这两者传递系统有关的基因也会影响语言功能的偏侧化(S. Ocklenburg et al., 2013; Sebastian Ocklenburg et al., 2011; Sebastian Ocklenburg, Beste, Arning, Peterburs, & Guentuerkuen, 2014)。因此,语言功能的偏侧化也表现在神经递质这种微观水平上。

2.4 语言功能的偏侧化与脑损伤

对大脑单侧半球损伤病例的研究,为解释功能偏侧化的神经机制提供了强有力的证据。一些研究发现早期脑半球损伤病人的语言功能会通过对侧半球来获得代偿性发展,这一现象在儿童和青少年人群中尤为明显(Liegeois et al., 2004; Staudt, 2007)。在词汇产生任务中,相比于健康组被试,左侧脑室周(periventricular)损伤病人的脑活动在与左侧语言区相对应的右侧同伦脑区更为强烈(Chang, Lin, Meng, & Fan, 2018; Staudt et al., 2002)。不少研究还显示,左半球切除(Liegeois, Connelly, Baldeweg, & Vargha-Khadem, 2008; Molinaro, Dunabeitia, Marin-Gutierrez, & Carreiras, 2010)以及左半球大面积损伤(Muter, Taylor, & Vargha-khadem, 1997)的儿童会通过右半球语言同伦脑区的活动来补偿左半球的语言功能,助其恢复正常的语言能力。研究表明,脑肿瘤(Tumor)的位置也会影响

病人的语言功能偏侧化。比如,左侧额叶区域存在肿瘤的病人,其语言功能的偏侧化水平较低(Gohel et al., 2019; Partovi et al., 2012)。脑肿瘤病人在执行词汇产生任务时,布洛卡区激活的偏侧化程度显著降低;而在执行句子产生任务时,威尔尼克区激活的偏侧化程度显著降低(Partovi et al., 2012)。一项对中风(Stroke)儿童和青少年病人的研究表明,在左侧语言功能区的右侧同伦区域出现了显著激活,并表现出双侧或右侧语言功能的偏侧化特征,而且右侧同伦脑区的激活还与较差的语言能力有关(Bartha-Doering et al., 2018)。

脑损伤是造成癫痫的主要外在因素,其中局灶性癫痫(Focal Epilepsy)为语言功能偏侧化及功能可塑性的研究提供了独特的视角。53%的癫痫病人存在语言网络的异常功能表征,其中以左侧半球的颞叶癫痫最常见(Nathalie Tzourio-Mazoyer et al., 2017)。一些研究表明,术前颞叶激活的不对称性程度越高,术后的语言功能损伤越严重(Bonelli et al., 2012; Sabsevitz et al., 2003);术前内侧颞叶语言功能表现为双侧化的病人,在术后呈现出左侧语言功能的偏侧化(Helmstaedter, Fritz, Gonzalez Perez, Elger, & Weber, 2006)。在与行为表现的关系中,语言功能偏侧化模式的改变也与语言任务的行为量表得分有关系,比如术前音韵任务中双侧颞叶的激活强度与量表得分的降低有关,而术后颞叶功能的完全左侧化与量表分数的升高有关(Perrone-Bertolotti, Zoubrinetzky, Yvert, Le Bas, & Baciú, 2012)。在先天局灶性脑损伤的癫痫病人中,左半球损伤的病人具有右半球语言功能优势,其优势程度与左半球皮层损伤的程度呈显著正相关(Chilosi et al., 2017)。但是,并非所有的左半球损伤都会造成语言功能向右半球转移,甚至左侧布洛卡区的损伤也不会导致右半球成为语言优势半球(Liegeois et al., 2004; Raja Beharelle et al., 2010)。一项对早期左半球局灶性脑损伤青少年病人的研究也显示,并非所有病人都会发展出右半球代偿性的语言功能(Raja Beharelle et al., 2010)。

3 语言功能的偏侧化与利手的关系

3.1 语言功能偏侧化的大脑功能基础与利手的关系

语言功能偏侧化和利手的关系最早通过Wada测试来确定,研究发现98%的右利手和70%

的左利手的语言优势位于左半球(Rasmussen & Milner, 1977)。基于功能性经颅多普勒超声(functional Transcranial Doppler ultrasonography, fTCD)的研究发现 27%的左利手语言优势位于右半球, 这与 Wada 测试的结果相似(Knecht et al., 2000)。而基于 fMRI 的研究也大都重复出类似的结论(Knecht et al., 2000; Perlaki et al., 2013; Zago et al., 2017)。一般来说, 几乎所有的右利手和超过半数的左利手的语言功能优势半球为左半球, 即典型的语言功能偏侧化; 还有一部分左利手是右半球优势, 或者不存在明显的优势半球, 即非典型的语言功能偏侧化(Knecht et al., 2000; Perlaki et al., 2013; Zago et al., 2017)。但是, 如果排除大脑右半球语言优势的个体, 利手对语言功能偏侧化几乎没有影响(Jerzy P. Szaflarski et al., 2012)。此外, 右利手的右侧小脑在语言任务中表现出显著激活, 而左利手在大脑和小脑上的语言功能偏侧化程度都更低(Gao et al., 2017)。

大脑功能的偏侧化一般用偏侧化系数(Lateralization Index, LI)来表示, 其计算公式为 $(L-R)/(L+R)$, 其中 L 和 R 分别表示左半球和右半球的激活强度或激活的体素数目。LI 为正值表示该任务引起的左半球偏侧化程度较高, 反之, 则右半球偏侧化程度较高。对利手的测量最常使用爱丁堡利手调查表(Edinburgh Handedness Inventory, EHI) (Oldfield, 1971), 该问卷通过对使用者日常生活中的用手习惯来判断其优势手(利手)和非优势手。一般来说, 问卷得分在 30 分以上为右利手, -30 分以下则为左利手, 分数处于两者之间的评定为双利手。在脑影像研究中, 如果只是将利手

作为分类变量, 会因为左右利手人数的悬殊而难以探索出两者在大脑功能偏侧化和解剖形态特征上的差异。比如, Mazoyer 团队的研究发现利手与语言功能优势半球之间的关系并不显著(Mazoyer et al., 2014); ENIGMA (Enhancing Imaging Genetics through Meta-Analysis) 组织的研究显示利手对全脑皮层厚度和灰质体积的不对称性没有显著影响(Guadalupe et al., 2017; Kong et al., 2018)。因此, 有些研究者进一步探究了语言功能偏侧化系数和利手系数之间的线性关系。大多数使用词汇产生任务的研究表明, 语言功能偏侧化系数和利手系数之间普遍呈正相关关系(Badzakova-Trajkov, Haberling, Roberts, & Corballis, 2010; Groen et al., 2013; Haberling et al., 2016; Kondyli et al., 2017; Somers et al., 2015; J.P. Szaflarski et al., 2002), 也就是说语言功能左半球偏侧化的程度越大, 其利手性可能偏右的程度越大。进一步比较这些研究发现, 额叶功能偏侧化与利手系数的相关关系比颞叶功能偏侧化更强(Haberling et al., 2016; J.P. Szaflarski et al., 2002), 而且小脑功能偏侧化与利手系数呈现显著的负相关(Haberling et al., 2016)。此外, 随着年龄的增长, 右利手在颞顶区域的语言功能偏侧化程度逐渐降低, 而左利手的偏侧化模式并没有出现显著变化(Nenert et al., 2017)。为了清晰呈现出语言功能的偏侧化系数与利手系数之间的相关关系, 我们将这些文献整理在表 1 中。

3.2 语言功能偏侧化的大脑结构基础与利手的关系

左右利手个体不仅在执行语言任务时的脑区激活上存在差异, 而且在这些区域的大脑解剖形

表 1 语言功能偏侧化系数与利手系数的相关

研究文献	LH/N	r	p	实验任务
Kondyli et al. (2017)	30/60	0.095	>0.05	无声词汇产生任务
		0.643	<0.01	书面词汇产生任务
Haberling & Corballis (2016)	46/92	0.316	<0.01	词汇产生任务
		0.267	>0.05	同义词任务
Somers et al. (2015)	154/310	0.285	<0.001	词汇产生任务
Groen et al. (2013)	12/57	0.29	<0.05	语音产生任务
Badzakova-Trajkov et al. (2010)	48/155	0.357	0.001	词汇产生任务
Szaflarski et al. (2002)	20/50	0.28	0.046	语义决定任务

注: LH 为左利手被试数目。N 为被试总数。 r 为语言功能偏侧化系数与利手系数的相关系数, p 为该相关系数的显著性。

态上也有所不同。比如,右利手左侧布洛卡区岛盖部的体积比左利手大,而左利手的右侧同伦区域的体积显著大于右利手(Powell, Kemp, Roberts, & Garcia-Finana, 2012)。从脑结构不对称性上来讲,颞平面是全脑不对称性最强的脑区,右利手颞平面面积的左侧不对称性程度较高(Shapleske, Rossell, Woodruff, & David, 1999),而左利手的不对称性程度则较低,这种差异与左利手的语言优势半球有关(Herve, Crivello, Perchey, Mazoyer, & Tzourio-Mazoyer, 2006);但也有研究发现用手偏好对左侧颞平面的皮层面积及其不对称性没有影响(Nathalie Tzourio-Mazoyer, Simon, et al., 2010)。除了个体的利手性本身对颞平面的体积有影响之外,家族左利性(Familial Sinistrality)也与其体积有关系,它表现为家族史上有左利手个体的被试具有更小的左侧颞平面体积,其中母亲为左利手个体的被试体积最小(Nathalie Tzourio-Mazoyer, Simon, et al., 2010)。基于扩散张量成像(Diffusion Tensor Imaging, DTI)的研究表明,在右利手和双利手中,弓形束的不对称性方向与语言功能的偏侧化方向相同(Silva & Citterio, 2017);在左利手中,左侧上纵束白质微结构完整性的降低与右半球语言优势的形成有关系(Perlaki et al., 2013)。以上研究表明,在语言功能偏侧化这个特征上,左右利手不仅在功能特异性区域上有差异,而且在这些区域的解剖形态特性上也有所不同。

4 语言功能偏侧化与静息态功能连接的关系

人脑活动不仅在任务状态下具有偏侧化特征,在静息状态下也表现出不对称的模式。大脑静息态下 FC 的不对称性并不是由某个网络的偏侧化造成的,而是由多个网络共同作用导致的,其中视觉网络、语言网络以及默认网络等都对其有较大影响(Liu et al., 2009)。大脑静息态 FC 的不对称性并非一出生就形成了。以左侧的额下回和后颞上沟为种子点的 FC 为例,成年人的半球内 FC 较强,而刚出生两周的婴儿则表现为半球间的 FC 较强(Perani et al., 2011)。已有研究发现语言功能偏侧化与静息态半球间连接之间存在显著的负相关,但和半球内连接的关系是正相关(Joliot et al., 2016; N. Tzourio-Mazoyer et al., 2016)。基于上文的描述,左利手和右利手在语言功能偏侧化的方

向和程度上具有差异,在功能偏侧化程度和静息态 FC 之间的关系上也不一致。

4.1 利手对语言功能偏侧化与功能连接之间关系的影响

近年来,不少研究开始探讨利手对语言功能偏侧化和静息态半球间、半球内 FC 之间关系的影响。Mazoyer 等使用 BIL&GIN (Brain Imaging of Lateralization by the Groupe d'Imagerie Fonctionnelle) 数据库(Mazoyer et al., 2016)中的 297 名被试(157 名左利手)分析了左右利手的静息态半球间、半球内 FC 与语言功能偏侧化的关系(Joliot et al., 2016; N. Tzourio-Mazoyer et al., 2016)。他们在 AICHA (Atlas of Intrinsic Connectivity of Homotopic Areas) (Joliot et al., 2015)中选取了在不同语言功能偏侧化中存在显著 BOLD 信号差异的 36 对同伦感兴趣区域(Region of Interest, ROI),发现这些 ROI 的静息态半球间同伦连接与语言功能的偏侧化呈负相关(N. Tzourio-Mazoyer et al., 2016),也就是说,静息态下大脑两半球的自发活动越一致,由实验任务所引起的大脑激活偏侧化程度越小。因此,在语言功能上呈现出双侧半球优势的左利手中出现了较强的 FC (即大脑的自发活动较一致)。对两半球语言网络的 FC 研究也表明左利手的半球间连接强度较强(Wiberg et al., 2019)。在对右利手群体的研究中发现,语义判断任务的偏侧化和语言网络的半球间 FC 不对称性之间存在显著的正相关关系(半球间 FC 的不对称性定义为大脑两半球同伦种子区域(seed region)与目标区域(target region)之间 FC 的相对强度),而且语言区 FC 的不对称性可以解释任务激活变异的 48% (Liu et al., 2009)。一项基于条件格兰杰因果分析的研究探索了左右利手在语言任务中有效连接(Effective Connectivity, EC)的差异,结果表明左利手比右利手具有更多的半球间连接(Gao et al., 2017)。此外,关于静息态半球内 FC 不对称性的研究发现,半球内 FC 的不对称性和语言功能偏侧化之间存在显著的正相关(半球内 FC 的不对称性定义为左半球内部的 FC 强度与右半球内部 FC 强度的差异),虽然这种关系在左右利手中不存在显著的差异,但在右利手个体中这种关系更强(Joliot et al., 2016; D. Wang, Buckner, & Liu, 2014)。通过这些研究,我们发现静息状态和语言任务状态下的脑连接模式之间的关系表现为:静息态半球间连接越强,语

言功能偏侧化程度越弱,而半球内连接强度与语言功能偏侧化的关系则是正相关关系;具体而言,左利手个体的语言功能偏侧化程度较低,其静息态半球间FC较强;而右利手个体的语言功能偏侧化程度较强,半球内FC的不对称性较为明显。

4.2 不同语言优势半球和大脑解剖形态特征对功能连接的影响

语言功能偏侧化与静息态FC的关系还表现在不同语言优势半球的FC以及FC不对称性的差异上。从不同语言优势半球上来看,语言优势的半球差异主要与左侧额下回的静息态FC模式有关系,表现为语言优势位于右半球的个体与典型的左半球语言优势个体相比,在左侧额下回与其他语言功能相关脑区(比如双侧角回、双侧楔前叶)之间的FC存在减弱的现象(S. Wang, van der Haegen, Tao, & Cai, 2018),并且语言功能的偏侧化程度与FC强度之间存在显著的相关(Gao et al., 2017; N. Tzourio-Mazoyer et al., 2016; S. Wang et al., 2018)。右半球语言优势个体的右侧额下回在语言功能上并不等同于典型语言优势个体的左侧额下回所具有的语言功能(S. Wang et al., 2018)。同样,也有研究表明静息态FC的不对称性不仅与语言功能的偏侧化之间存在显著的正相关(Liu et al., 2009; Raemaekers et al., 2018),而且与利手的关系也表现为正相关(Raemaekers et al., 2018)。此外,由于视觉词形区与额下回具有相同的偏侧化方向,所以在右半球语言优势模式中,右侧梭状回的静息态全局功能连接密度(global Functional Connectivity Density, gFCD)也较高(S. Wang et al., 2018)。

左右利手在大脑解剖形态上的差异可能会导致脑连接模式存在差异。比如,左利手比右利手具有更大的胼胝体(Cowell & Gurd, 2018; Westerhausen et al., 2003; Witelson, 1985),而胼胝体主要负责传递两半球之间的信息(Roland et al., 2017),所以较大的胼胝体使左利手两半球间具有更强的静息态FC,从而降低了语言功能偏侧化的程度。另外,失语症病人在语言任务中的表现与左侧额下回和颞中回的活动强度呈正相关(Tyler et al., 2011),并且与弓形束的完整性也呈现出正相关(Papoutsis, Stamatakis, Griffiths, Marslen-Wilson, & Tyler, 2011)。从语言功能优势半球来说,虽然左侧与右侧半球优势的个体都存在脑岛体积的左侧不对称,但左侧语言优势半球的个体其左侧脑岛的体积更

大(Greve et al., 2013),而且当语言功能优势位于右半球时,右侧额下回与左侧脑岛的FC越弱,语言功能右半球偏侧化的程度越强(S. Wang et al., 2018)。虽然研究表明大脑解剖形态特征与语言功能偏侧化之间存在微弱的关系,但还没有明显的证据可以证实二者之间的关系,未来对大脑解剖形态与脑连接的研究有助于进一步明确大脑结构、脑连接和语言功能偏侧化之间的关系。

5 小结与展望

现有文献已对语言功能的偏侧化进行了较为全面和深入地研究,我们在此综述了语言功能偏侧化所涉及的脑区,以及其与利手和静息态功能连接的关系。综合已有研究,我们发现,语言功能主要涉及的脑区是左半球额叶和颞叶的大部分区域,同时还包括前扣带、梭状回以及辅助运动区等;语言功能偏侧化系数与利手系数之间存在正相关关系;语言功能偏侧化与静息态功能连接之间的紧密关系表现为半球间静息态功能连接越强,语言功能偏侧化程度越弱,而半球内连接强度与语言功能偏侧化之间则呈现出正相关关系,而且这些关联也会受到利手性差异的影响。总之,语言功能偏侧化、利手和静息态功能连接三者之间存在复杂的关系,这些关系可能与遗传、大脑解剖形态的不对称性、环境、后天经验以及疾病等都有联系。我们总结了以下几点内容,它们值得在今后研究中进一步地探索。

首先,关于语言功能偏侧化的解剖形态基础仍然需要进一步研究。除了大脑灰质的解剖形态与语言功能的偏侧化有关系之外,大脑的白质纤维连接着数以万计的神经细胞,其表面包裹的髓磷脂会加速信号的传递,那么双侧半球是否存在白质纤维结构上的不对称性和信息传递效率上的差异,这些不对称性和差异性又与语言功能的偏侧化有什么关系?此外,大脑结构协变的研究,例如灰质体积、皮层厚度,可以揭示出大脑脑区的解剖形态发展变化的规律,这些形态学上的共变可能与功能的偏侧化存在某种关系,所以未来的研究也可以从对大脑结构协变的研究上更加清晰地描绘语言功能偏侧化的本质。

其次,关于语言功能偏侧化的基因和遗传研究可能会揭示出这种功能偏侧化的微观机制。现有研究表明,基因会在一定程度上影响大脑语言

功能的偏侧化以及相应的大脑解剖形态特性,但现有的很多研究都是从脑形态层面探讨基因对大脑不对称性的影响,针对脑功能偏侧化与基因的大型实验研究还很欠缺(Bishop, 2013)。近期一项针对右侧语言功能优势的全基因组关联(Genome-Wide Association Study, GWAS)的研究结果表明没有单个的基因与右侧功能优势有关系(Carrion-Castillo et al., 2019)。鉴于语言功能偏侧化和利手的紧密关系,基因层面的研究也可能会对其与利手的关系做出进一步解释。对利手的 GWAS 研究发现,利手是具有高度多基因性的性状特征,与利手相关的基因位点与大脑微管结构的形成和调节以及精神疾病的发生有关(Partida et al., 2019; Wiberg et al., 2019)。未来的研究可以在基因层面探究语言功能偏侧化和利手的微观机制,从而对两者的形成与发展获得更深层次的理解,以推动左利手和右利手在语言功能偏侧化上的差异研究,进一步解释两者之间的交互关系。

第三,利手与大脑语言功能偏侧化的共同神经基础也需进一步挖掘。虽然前人研究已经表明,利手与语言功能偏侧化之间并不是绝对的关系,排除语言功能位于右半球的左利手,两者之间似乎并没有值得关注的联系,但左利手出现语言功能偏侧化多样性的背后是否存在某种神经机制的作用?另外,利手作为一种外显的行为层面的现象,有研究表明,后天强行纠正左利手个体使用右手会使这些个体的双侧壳核体积明显小于左利手和右利手个体,这可能与运动功能的发展和突触剪除有关系(Kloppel, Mangin, Vongerichten, Frackowiak, & Siebner, 2010)。那么,被强行纠正使用右手的左利手个体是不是也在大脑语言功能的偏侧化上与正常成长的左利手和右利手个体有所不同?

最后,大脑语言功能偏侧化和静息态功能连接的关系还需从后天经验的角度进一步探索。不同职业的个体因后天经验的不同会使大脑网络连接有所不同,也可能在执行相同的任务时存在不同脑区的激活,因此这些个体层面的后天经验可能也会大脑的功能偏侧化和静息态功能连接造成影响。所以,未来对大脑功能偏侧化的研究应该延伸到更广泛的人群中,探索不同后天经验的影响。

参考文献

- Acheson, D. J., & Hagoort, P. (2013). Stimulating the brain's language network: Syntactic ambiguity resolution after TMS to the inferior frontal gyrus and middle temporal gyrus. *Journal of Cognitive Neuroscience*, 25(10), 1664–1677. doi:10.1162/jocn_a_00430
- Badzakova-Trajkov, G., Haeberling, I. S., Roberts, R. P., & Corballis, M. C. (2010). Cerebral asymmetries: Complementary and independent processes. *PLoS One*, 5(3), e9682. doi:10.1371/journal.pone.0009682
- Barch, D. M., Braver, T. S., Sabb, F. W., & Noll, D. C. (2000). Anterior cingulate and the monitoring of response conflict: Evidence from an fMRI study of overt verb generation. *Journal of Cognitive Neuroscience*, 12(2), 298–309.
- Bartha-Doering, L., Novak, A., Kollndorfer, K., Schuler, A.-L., Kasprian, G., Langs, G., ... Seidl, R. (2018). Atypical language representation is unfavorable for language abilities following childhood stroke. *European Journal of Paediatric Neurology*, 23(1), 102–116. doi:10.1016/j.ejpn.2018.09.007
- Bigler, E. D., Mortensen, S., Neeley, E. S., Ozonoff, S., Krasny, L., Johnson, M., ... Lainhart, J. E. (2007). Superior temporal gyrus, language function, and autism. *Developmental Neuropsychology*, 31(2), 217–238. doi:10.1080/87565640701190841
- Bishop, D. V. M. (2013). Cerebral asymmetry and language development: Cause, correlate, or consequence? *Science*, 340(6138), 1230531. doi:10.1126/science.1230531
- Bonelli, S. B., Thompson, P. J., Yogarajah, M., Vollmar, C., Powell, R. H., Symms, M. R., ... Duncan, J. S. (2012). Imaging language networks before and after anterior temporal lobe resection: Results of a longitudinal fMRI study. *Epilepsia*, 53(4), 639–650. doi:10.1111/j.1528-1167.2012.03433.x
- Carrion-Castillo, A., van der Haegen, L., Tzourio-Mazoyer, N., Kavaklioglu, T., Badillo, S., Chavent, M., ... Francks, C. (2019). Genome sequencing for rightward hemispheric language dominance. *Genes, Brain and Behavior*, 18(5), e12572. doi:10.1111/gbb.12572
- Cervenka, S., Backman, L., Cselenyi, Z., Halldin, C., & Farde, L. (2008). Associations between dopamine D2-receptor binding and cognitive performance indicate functional compartmentalization of the human striatum. *Neuroimage*, 40(3), 1287–1295. doi:10.1016/j.neuroimage.2007.12.063
- Chang, Y. T., Lin, S. C., Meng, L. F., & Fan, Y. T. (2018). Atypical temporal activation pattern and central-right brain compensation during semantic judgment task in children with early left brain damage. *Brain and Language*, 177–178, 37–43. doi:10.1016/j.bandl.2018.01.005

- Chiarello, C., Vazquez, D., Felton, A., & Leonard, C. M. (2013). Structural asymmetry of anterior insula: Behavioral correlates and individual differences. *Brain and Language*, 126(2), 109–122. doi:10.1016/j.bandl.2013.03.005
- Chilosi, A. M., Bulgheroni, S., Turi, M., Cristofani, P., Biagi, L., Erbetta, A., ... Cioni, G. (2017). Hemispheric language organization after congenital left brain lesions: A comparison between functional transcranial Doppler and functional MRI. *Journal of Neuropsychology*, 13(1), 46–66. doi:10.1111/jnp.12128
- Cowell, P., & Gurd, J. (2018). Handedness and the corpus callosum: A review and further analyses of discordant twins. *Neuroscience*, 388, 57–68. doi:10.1016/j.neuroscience.2018.06.017
- Dehaene, S., & Cohen, L. (2011). The unique role of the visual word form area in reading. *Trends in Cognitive Sciences*, 15(6), 254–262. doi:10.1016/j.tics.2011.04.003
- Frassle, S., Paulus, F. M., Krach, S., Schweinberger, S. R., Stephan, K. E., & Jansen, A. (2016). Mechanisms of hemispheric lateralization: Asymmetric interhemispheric recruitment in the face perception network. *Neuroimage*, 124(Pt A), 977–988. doi:10.1016/j.neuroimage.2015.09.055
- Gao, Q., Tao, Z., Cheng, L., Leng, J., Wang, J., Yu, C., & Chen, H. (2017). Language lateralization during the Chinese semantic task relates to the contralateral cerebra-cerebellar interactions at rest. *Scientific Report*, 7(1), 14056. doi:10.1038/s41598-017-14600-9
- Gao, Q., Wang, J., Yu, C., & Chen, H. (2015). Effect of handedness on brain activity patterns and effective connectivity network during the semantic task of Chinese characters. *Scientific Report*, 5, 18262. doi:10.1038/srep18262
- Gohel, S., Laino, M. E., Rajeev-Kumar, G., Jenabi, M., Peck, K., Hatzoglou, V., ... Vachha, B. (2019). Resting-state functional connectivity of the middle frontal gyrus can predict language lateralization in patients with brain tumors. *American Journal of Neuroradiology*, 40(2), 319–325. doi:10.3174/ajnr.A5932
- Greve, D. N., van der Haegen, L., Cai, Q., Stufflebeam, S., Sabuncu, M. R., Fischl, B., & Brysbaert, M. (2013). A surface-based analysis of language lateralization and cortical asymmetry. *Journal of Cognitive Neuroscience*, 25(9), 1477–1492. doi:10.1162/jocn_a_00405
- Groen, M. A., Whitehouse, A. J. O., Badcock, N. A., & Bishop, D. V. M. (2013). Associations between handedness and cerebral lateralisation for language: A comparison of three measures in children. *PLoS One*, 8(5), e64876. doi:10.1371/journal.pone.0064876
- Guadalupe, T., Mathias, S. R., Vanerp, T. G. M., Whelan, C. D., Zwiers, M. P., Abe, Y., ... Francks, C. (2017). Human subcortical brain asymmetries in 15, 847 people worldwide reveal effects of age and sex. *Brain imaging and behavior*, 11(5), 1497–1514. doi:10.1007/s11682-016-9629-z
- Haberling, I. S., Corballis, P. M., & Corballis, M. C. (2016). Language, gesture, and handedness: Evidence for independent lateralized networks. *Cortex*, 82, 72–85. doi:10.1016/j.cortex.2016.06.003
- Haeberling, I. S., Badzakova-Trajkov, G., & Corballis, M. C. (2013). Asymmetries of the arcuate fasciculus in monozygotic twins: Genetic and nongenetic influences. *PLoS One*, 8(1), e52315. doi:10.1371/journal.pone.0052315
- Haegen, L. V. d., Cai, Q., & Brysbaert, M. (2012). Colateralization of Broca's area and the visual word form area in left-handers: fMRI evidence. *Brain and Language*, 122(3), 171–178.
- Helmstaedter, C., Fritz, N. E., Gonzalez Perez, P. A., Elger, C. E., & Weber, B. (2006). Shift-back of right into left hemisphere language dominance after control of epileptic seizures: Evidence for epilepsy driven functional cerebral organization. *Epilepsy Research*, 70(2-3), 257–262. doi:10.1016/j.eplepsyres.2006.03.005
- Herve, P. Y., Crivello, F., Perchey, G., Mazoyer, B., & Tzourio-Mazoyer, N. (2006). Handedness and cerebral anatomical asymmetries in young adult males. *Neuroimage*, 29(4), 1066–1079. doi:10.1016/j.neuroimage.2005.08.031
- Hugdahl, K., Loberg, E.-M., Specht, K., Steen, V. M., van Wagneningen, H., & Jorgensen, H. A. (2008). Auditory hallucinations in schizophrenia: The role of cognitive, brain structural and genetic disturbances in the left temporal lobe. *Frontiers in Human Neuroscience*, 1, 6. doi:10.3389/neuro.09.006.2007
- Indefrey, P., & Levelt, W. J. (2004). The spatial and temporal signatures of word production components. *Cognition*, 92(1–2), 101–144. doi:10.1016/j.cognition.2002.06.001
- Iturria-Medina, Y., Perez Fernandez, A., Morris, D. M., Canales-Rodriguez, E. J., Haroon, H. A., Garcia Penton, L., ... Melie-Garcia, L. (2011). Brain hemispheric structural efficiency and interconnectivity rightward asymmetry in human and nonhuman primates. *Cerebral Cortex*, 21(1), 56–67. doi:10.1093/cercor/bhq058
- Joliot, M., Jobard, G., Naveau, M., Delcroix, N., Petit, L., Zago, L., ... Tzourio-Mazoyer, N. (2015). AICHA: An atlas of intrinsic connectivity of homotopic areas. *Journal of Neuroscience Methods*, 254, 46–59. doi:10.1016/j.jneumeth.2015.07.013
- Joliot, M., Tzourio-Mazoyer, N., & Mazoyer, B. (2016). Intra-hemispheric intrinsic connectivity asymmetry and its relationships with handedness and language lateralization. *Neuropsychologia*, 93(Pt B), 437–447. doi:10.1016/j.neuropsychologia.2016.03.013
- Josse, G., Seghier, M. L., Kherif, F., & Price, C. J. (2008).

- Explaining function with anatomy: Language lateralization and corpus callosum size. *Journal of Neuroscience*, 28(52), 14132–14139. doi:10.1523/jneurosci.4383-08.2008
- Kanwisher, N., McDermott, J., & Chun, M. M. (1997). The fusiform face area: A module in human extrastriate cortex specialized for face perception. *Journal of Neuroscience*, 17(11), 4302–4311.
- Karlbach, G., & Francks, C. (2015). Lateralization of gene expression in human language cortex. *Cortex*, 67, 30–36. doi:10.1016/j.cortex.2015.03.003
- Kloeppel, S., Mangin, J.-F., Vongerichten, A., Frackowiak, R. S. J., & Siebner, H. R. (2010). Nurture versus nature: Long-term impact of forced right-handedness on structure of pericentral cortex and basal ganglia. *Journal of Neuroscience*, 30(9), 3271–3275. doi:10.1523/jneurosci.4394-09.2010
- Knecht, S., Dräger, B., Deppe, M., Bobe, L., Lohmann, H., Floel, A., ... Henningsen, H. (2000). Handedness and hemispheric language dominance in healthy humans. *Brain*, 123(12), 2512–2518.
- Kondyli, D., Stathopoulou, D., Badcock, N. A., & Papadatou-Pastou, M. (2017). Cerebral laterality for the generation of silent and written language in male and female right- and left-handers: A functional transcranial doppler ultrasound study. *Acta Neuropsychologica*, 15(4), 407–432.
- Kong, X.-Z., Mathias, S. R., Guadalupe, T., Glahn, D. C., Franke, B., Crivello, F., ... Francks, C. (2018). Mapping cortical brain asymmetry in 17, 141 healthy individuals worldwide via the ENIGMA Consortium. *Proceedings of the National Academy of Sciences of the United States of America*, 115(22), E5154–E5163. doi:10.1073/pnas.1718418115
- Li, M., Chen, H., Wang, J., Liu, F., Long, Z., Wang, Y., ... Chen, H. (2014). Handedness- and hemisphere-related differences in small-world brain networks: A diffusion tensor imaging tractography study. *Brain connectivity*, 4(2), 145–156. doi:10.1089/brain.2013.0211
- Liegeois, F., Connelly, A., Baldeweg, T., & Vargha-Khadem, F. (2008). Speaking with a single cerebral hemisphere: fMRI language organization after hemispherectomy in childhood. *Brain & Language*, 106(3), 195–203. doi:10.1016/j.bandl.2008.01.010
- Liegeois, F., Connelly, A., Cross, J. H., Boyd, S. G., Gadian, D. G., Vargha-Khadem, F., & Baldeweg, T. (2004). Language reorganization in children with early-onset lesions of the left hemisphere: An fMRI study. *Brain*, 127(6), 1229–1236. doi:10.1093/brain/awh159
- Liu, H., Stufflebeam, S. M., Sepulcre, J., Hedden, T., & Buckner, R. L. (2009). Evidence from intrinsic activity that asymmetry of the human brain is controlled by multiple factors. *Proceedings of the National Academy of Sciences of the United States of America*, 106(48), 20499–20503.
- Mazoyer, B., Mellet, E., Perchey, G., Zago, L., Crivello, F., Jobard, G., ... Tzourio-Mazoyer, N. (2016). BIL&GIN: A neuroimaging, cognitive, behavioral, and genetic database for the study of human brain lateralization. *Neuroimage*, 124(Pt B), 1225–1231. doi:10.1016/j.neuroimage.2015.02.071
- Mazoyer, B., Zago, L., Jobard, G., Crivello, F., Joliot, M., Perchey, G., ... Tzourio-Mazoyer, N. (2014). Gaussian mixture modeling of hemispheric lateralization for language in a large sample of healthy individuals balanced for handedness. *PLoS One*, 9(6), e101165. doi:10.1371/journal.pone.0101165
- Mccarthy, G., Blamire, A. M., Rothman, D. L., Gruetter, R., & Shulman, R. G. (1993). Echo-planar magnetic resonance imaging studies of frontal cortex activation during word generation in humans. *Proceedings of the National Academy of Sciences of the United States of America*, 90(11), 4952–4956.
- Molinaro, N., Dunabeitia, J. A., Marin-Gutierrez, A., & Carreiras, M. (2010). From numbers to letters: Feedback regularization in visual word recognition. *Neuropsychologia*, 48(5), 1343–1355. doi:10.1016/j.neuropsychologia.2009.12.037
- Muter, V., Taylor, S., & Vargha-khadem, F. (1997). A longitudinal study of early intellectual development in hemiplegic children. *Neuropsychologia*, 35(3), 289–298.
- Nenert, R., Allendorfer, J. B., Martin, A. M., Banks, C., Vannest, J., Holland, S. K., & Szaflarski, J. P. (2017). Age-related language lateralization assessed by fMRI: The effects of sex and handedness. *Brain Research*, 1674, 20–35. doi:10.1016/j.brainres.2017.08.021
- Ocklenburg, S., Arning, L., Gerding, W. M., Epplen, J. T., Gunturkun, O., & Beste, C. (2013). Cholecystokinin A receptor (CCKAR) gene variation is associated with language lateralization. *PLoS One*, 8(1), e53643. doi:10.1371/journal.pone.0053643
- Ocklenburg, S., Arning, L., Hahn, C., Gerding, W. M., Epplen, J. T., Guentuerkuen, O., & Beste, C. (2011). Variation in the NMDA receptor 2B subunit gene GRIN2B is associated with differential language lateralization. *Behavioural Brain Research*, 225(1), 284–289. doi:10.1016/j.bbr.2011.07.042
- Ocklenburg, S., Beste, C., Arning, L., Peterburs, J., & Guentuerkuen, O. (2014). The ontogenesis of language lateralization and its relation to handedness. *Neuroscience and Biobehavioral Reviews*, 43, 191–198. doi:10.1016/j.neubiorev.2014.04.008
- Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh Inventory. *Neuropsychologia*, 9(1), 97–113.

- Papoutsis, M., Stamatakis, E. A., Griffiths, J., Marslen-Wilson, W. D., & Tyler, L. K. (2011). Is left fronto-temporal connectivity essential for syntax? Effective connectivity, tractography and performance in left-hemisphere damaged patients. *Neuroimage*, 58(2), 656–664. doi:10.1016/j.neuroimage.2011.06.036
- Partida, G. C., Tung, J. Y., Eriksson, N., Albrecht, E., Aliev, F., Andreassen, O. A., ... Medland, S. E. (2019). Genome-wide association study identifies 49 common genetic variants associated with handedness. *bioRxiv*, 831321
- Partovi, S., Jacobi, B., Rapps, N., Zipp, L., Karimi, S., Rengier, F., ... Stippich, C. (2012). Clinical standardized fMRI reveals altered language lateralization in patients with brain tumor. *American Journal of Neuroradiology*, 33(11), 2151–2157. doi:10.3174/ajnr.A3137
- Perani, D., Saccuman, M. C., Scifo, P., Anwander, A., Spada, D., Baldoli, C., ... Friederici, A. D. (2011). Neural language networks at birth. *Proceedings of the National Academy of Sciences of the United States of America*, 108(38), 16056–16061. doi:10.1073/pnas.1102991108
- Perlaki, G., Horvath, R., Orsi, G., Aradi, M., Auer, T., Varga, E., ... Janszky, J. (2013). White-matter microstructure and language lateralization in left-handers: A whole-brain MRI analysis. *Brain and Cognition*, 82(3), 319–328. doi:10.1016/j.bandc.2013.05.005
- Perrone-Bertolotti, M., Zoubrinetzky, R., Yvert, G., Le Bas, J. F., & Baci, M. (2012). Functional MRI and neuropsychological evidence for language plasticity before and after surgery in one patient with left temporal lobe epilepsy. *Epilepsy & Behavior*, 23(1), 81–86. doi:10.1016/j.yebeh.2011.11.011
- Powell, J. L., Kemp, G. J., Roberts, N., & Garcia-Finana, M. (2012). Sulcal morphology and volume of Broca's area linked to handedness and sex. *Brain and Language*, 121(3), 206–218. doi:10.1016/j.bandl.2012.03.003
- Price, C. J. (2012). A review and synthesis of the first 20 years of PET and fMRI studies of heard speech, spoken language and reading. *Neuroimage*, 62(2), 816–847. doi:10.1016/j.neuroimage.2012.04.062
- Raemaekers, M., Schellekens, W., Petridou, N., & Ramsey, N. F. (2018). Knowing left from right: Asymmetric functional connectivity during resting state. *Brain Structure & Function*, 223(4), 1909–1922. doi:10.1007/s00429-017-1604-y
- Raja Beharelle, A., Dick, A. S., Josse, G., Solodkin, A., Huttenlocher, P. R., Levine, S. C., & Small, S. L. (2010). Left hemisphere regions are critical for language in the face of early left focal brain injury. *Brain*, 133(6), 1707–1716. doi:10.1093/brain/awq104
- Rasmussen, T., & Milner, B. (1977). The role of early left-brain injury in determining lateralization of cerebral speech functions. *Annals New York Academy of Sciences*, 299(1), 355–369.
- Roland, J. L., Snyder, A. Z., Hacker, C. D., Mitra, A., Shimony, J. S., Limbrick, D. D., ... Leuthardt, E. C. (2017). On the role of the corpus callosum in interhemispheric functional connectivity in humans. *Proceedings of the National Academy of Sciences of the United States of America*, 114(50), 13278–13283. doi:10.1073/pnas.1707050114
- Sabsevitz, D. S., Swanson, S. J., Hammeke, T. A., Spanaki, M. V., Possing, E. T., Morris, G. L., ... Binder, J. R. (2003). Use of preoperative functional neuroimaging to predict language deficits from epilepsy surgery. *Neurology*, 60(11), 5.
- Shapleske, J., Rossell, S. L., Woodruff, P. W. R., & David, A. S. (1999). The planum temporale: A systematic, quantitative review of its structural, functional and clinical significance. *Brain Research Reviews*, 29(1), 26–49.
- Silva, G., & Citterio, A. (2017). Hemispheric asymmetries in dorsal language pathway white-matter tracts: A magnetic resonance imaging tractography and functional magnetic resonance imaging study. *Neuroradiology Journal*, 30(5), 470–476. doi:10.1177/1971400917720829
- Somers, M., Aukes, M. F., Ophoff, R. A., Boks, M. P., Fleer, W., de Visser, K. L., ... Sommer, I. E. (2015). On the relationship between degree of hand-preference and degree of language lateralization. *Brain and Language*, 144, 10–15. doi:10.1016/j.bandl.2015.03.006
- Staudt, M. (2007). (Re-)organization of the developing human brain following periventricular white matter lesions. *Neuroscience and Biobehavioral Reviews*, 31(8), 1150–1156. doi:10.1016/j.neubiorev.2007.05.005
- Staudt, M., Lidzba, K., Grodd, W., Wildgruber, D., Erb, M., & Krageloh-Mann, I. (2002). Right-hemispheric organization of language following early left-sided brain lesions: Functional MRI topography. *Neuroimage*, 16(4), 954–967. doi:10.1006/nimg.2002.1108
- Szaflarski, J. P., Binder, J. R., Possing, E. T., McKiernan, K. A., Ward, B. D., & Hammeke, T. A. (2002). Language lateralization in left-handed and ambidextrous people. *Neurology*, 59(2), 8.
- Szaflarski, J. P., Rajagopal, A., Altaye, M., Byars, A. W., Jacola, L., Schmithorst, V. J., ... Holland, S. K. (2012). Left-handedness and language lateralization in children. *Brain Research*, 1433, 85–97. doi:10.1016/j.brainres.2011.11.026
- Toga, A. W., & Thompson, P. M. (2003). Mapping brain asymmetry. *Nature Reviews Neuroscience*, 4(1), 37–48. doi:10.1038/nrn1009
- Tremblay, P., & Gracco, V. L. (2010). On the selection of words and oral motor responses: Evidence of a response-independent fronto-parietal network. *Cortex*, 46(1), 15–28. doi:10.1016/j.cortex.2009.03.003
- Tucker, D. M., & Williamson, P. A. (1984). Asymmetric neural

- control systems in human self-regulation. *Psychological Review*, 91(2), 185-215.
- Tyler, L. K., Marslen-Wilson, W. D., Randall, B., Wright, P., Devereux, B. J., Zhuang, J., ... Stamatakis, E. A. (2011). Left inferior frontal cortex and syntax: Function, structure and behaviour in patients with left hemisphere damage. *Brain*, 134(Pt 2), 415-431. doi:10.1093/brain/awq369
- Tzourio-Mazoyer, N., Joliot, M., Marie, D., & Mazoyer, B. (2016). Variation in homotopic areas' activity and inter-hemispheric intrinsic connectivity with type of language lateralization: An fMRI study of covert sentence generation in 297 healthy volunteers. *Brain Structure and Function*, 221(5), 2735-2753. doi:10.1007/s00429-015-1068-x
- Tzourio-Mazoyer, N., Perrone-Bertolotti, M., Jobard, G., Mazoyer, B., & Baci, M. (2017). Multi-factorial modulation of hemispheric specialization and plasticity for language in healthy and pathological conditions: A review. *Cortex*, 86, 314-339. doi:10.1016/j.cortex.2016.05.013
- Tzourio-Mazoyer, N., Petit, L., Razafimandimby, A., Crivello, F., Zago, L., Jobard, G., ... Mazoyer, B. (2010). Left hemisphere lateralization for language in right-handers is controlled in part by familial sinistrality, manual preference strength, and head size. *Journal of Neuroscience*, 30(40), 13314-13318. doi:10.1523/jneurosci.2593-10.2010
- Tzourio-Mazoyer, N., Simon, G., Crivello, F., Jobard, G., Zago, L., Percey, G., ... Mazoyer, B. (2010). Effect of familial sinistrality on planum temporale surface and brain tissue asymmetries. *Cerebral Cortex*, 20(6), 1476-1485. doi:10.1093/cercor/bhp209
- Tzourio, N., Nkanga-Ngila, B., & Mazoyer, B. (1998). Left planum temporale surface correlates with functional dominance during story listening. *Neuroreport*, 9(5), 829-833.
- Vigneau, M., Beaucois, V., Herve, P. Y., Duffau, H., Crivello, F., Houde, O., ... Tzourio-Mazoyer, N. (2006). Meta-analyzing left hemisphere language areas: Phonology, semantics, and sentence processing. *Neuroimage*, 30(4), 1414-1432. doi:10.1016/j.neuroimage.2005.11.002
- Vigneau, M., Beaucois, V., Herve, P. Y., Jobard, G., Petit, L., Crivello, F., ... Tzourio-Mazoyer, N. (2011). What is right-hemisphere contribution to phonological, lexico-semantic, and sentence processing? Insights from a meta-analysis. *Neuroimage*, 54(1), 577-593. doi:10.1016/j.neuroimage.2010.07.036
- Wang, D., Buckner, R. L., & Liu, H. (2014). Functional specialization in the human brain estimated by intrinsic hemispheric interaction. *Journal of Neuroscience*, 34(37), 12341-12352. doi:10.1523/JNEUROSCI.0787-14.2014
- Wang, S., van der Haegen, L., Tao, L., & Cai, Q. (2018). Brain functional organization associated with language lateralization. *Cerebral Cortex*, 29(10), 4312-4320. doi:10.1093/cercor/bhy313
- Warrier, C., Wong, P., Penhune, V., Zatorre, R., Parrish, T., Abrams, D., & Kraus, N. (2009). Relating structure to function: Heschl's gyrus and acoustic processing. *Journal of Neuroscience*, 29(1), 61-69. doi:10.1523/JNEUROSCI.3489-08.2009
- Weiner, K. S., & Zilles, K. (2016). The anatomical and functional specialization of the fusiform gyrus. *Neuropsychologia*, 83, 48-62. doi:10.1016/j.neuropsychologia.2015.06.033
- Westerhausen, R., Walter, C., Kreuder, F., Wittling, R. A., Schweiger, E., & Wittling, W. (2003). The influence of handedness and gender on the microstructure of the human corpus callosum: A diffusion-tensor magnetic resonance imaging study. *Neuroscience Letters*, 351(2), 99-102. doi:10.1016/s0304-3940(03)00946-7
- Wiberg, A., Ng, M., Al Omran, Y., Alfaro-Almagro, F., McCarthy, P., Marchini, J., ... Furniss, D. (2019). Handedness, language areas and neuropsychiatric diseases: Insights from brain imaging and genetics. *Brain*, 142(10), 2938-2947. doi:10.1093/brain/awz257
- Willems, R. M., van der Haegen, L., Fisher, S. E., & Francks, C. (2014). On the other hand: Including left-handers in cognitive neuroscience and neurogenetics. *Nature Reviews Neuroscience*, 15(3), 193-201. doi:10.1038/nrn3679
- Witelson, S. F. (1985). The brain connection: The corpus callosum is larger in left-handers. *Science*, 229(4714), 665-668.
- Zago, L., Herve, P. Y., Genuer, R., Laurent, A., Mazoyer, B., Tzourio-Mazoyer, N., & Joliot, M. (2017). Predicting hemispheric dominance for language production in healthy individuals using support vector machine. *Human Brain Mapping*, 38(12), 5871-5889. doi:10.1002/hbm.23770

Language lateralization, handedness and functional connectivity

WANG Xiao; WU Guorong; WU Xinran; QIU Jiang; CHEN Hong

*(Faculty of Psychology, Southwest University, Key Laboratory of Cognition and Personality,
Ministry of Education, Chongqing 400715, China)*

Abstract: Language lateralization is one of the most obvious characteristics of brain functional lateralization. Previous neuroimaging studies identified numerous brain regions associated with language lateralization, such as the frontal and temporal lobes, the cingulate and fusiform gyrus, the supplementary motor area, and so on. This review synthesizes current published literature relevant to language lateralization, with an emphasis on handedness and functional connectivity. Our findings show that language lateralization is positively correlated with handedness and intra-hemisphere connectivity but is negatively correlated with inter-hemispheric connectivity. Moreover, the left- and right-handers exhibit different correlation profiles between language lateralization and functional connectivity. We discuss the relationship between language lateralization, handedness, and functional connectivity, and we propose areas for further research.

Key words: language lateralization; handedness; resting state functional connectivity