脑电磁成像进展及展望

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摘要 无创脑电磁成像技术以其高时间分辨率, 且可通过源成像技术有效提高空间分辨率的优势, 在推进大脑认知原理和脑疾病机制研究中起着不可或缺的作用. 本文从脑电/磁信号处理、脑电/磁逆问题、脑电/磁设备、脑电/磁应用等几个主要方面, 综述了相关研究的主要进展, 探讨了脑电/磁领域的若干前沿问题, 展望了今后需要重点关注的方向.

关键词 脑电, 脑磁, 逆问题, 信号处理, 多模态融合

大脑的结构和功能涉及微观、介观到宏观的不同尺度, 且每个尺度负责的主要功能不同, 相应的研究手段也有所不同, 由此注定了脑科学是21世纪最具挑战性的前沿科学^[1,2], 而基于不同原理的脑功能与结构成像技术, 是在不同尺度上获取脑信息、解码脑机制、挑战脑疾病的切入点. 就宏观尺度而言, 脑电图(electroencephalogram, EEG)、脑磁图(magnetoencephalography, MEG)、核磁共振(magnetic resonance imaging, MRI)和近红外光谱(near-infrared spectroscopy, NIRS)等可在无创情况下开展大脑的研究, 尤其脑电和近红外光谱可在移动环境下使用, 可直接针对现实人群, 更具生态性.

脑电反映的是大脑细胞群的生物电活动, 是大量神经元同步活动的突触后电位经总和后形成的, 它是

脑神经细胞的电生理活动在大脑皮层或头皮表面的总体表征. 脑磁记录的是神经细胞相关的带电离子的迁移产生的局部微弱电流所形成的颅外磁场总和. 就头表面脑电磁信号而言, 脑电对径向电流活动更敏感, 而脑磁对切向电流活动更敏感; 脑电设备价廉, 应用广泛; 脑磁受大脑结构非均匀性影响小, 空间分辨率较高, 但设备及维护昂贵. 总体上, 脑电与脑磁之间不存在简单的优劣之分, 而是具有互补性的两项重要技术. 基于Web of Science网站, 本文对2004~2018年EEG, MEG, fNIRS(functional near-infrared spectroscopy)和功能磁共振(functional magnetic resonance imaging, fMRI)的期刊论文数量进行了统计, 结果如图1所示. 总体来看, 相关技术的应用呈逐年增多的情形, 其中脑电在被fMRI短暂超越后, 再次处于主导地位, 因

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图1 2004~2018年无创脑成像技术的期刊论文数量趋势。EEG: 脑电图, MEG: 脑磁图, fNIRS: 功能性近红外光谱, fMRI: 功能磁共振成像

Figure 1 Trends of journal article number of the main non-invasive brain imaging technologies from 2004 to 2018. EEG: electroencephalogram, MEG: magnetoencephalography, fNIRS: functional near-infrared spectroscopy, fMRI: functional magnetic resonance imaging

此系统了解的脑电磁研究进展, 具有重要的学术意义和现实价值。

1 脑电/磁信号预处理方法进展

脑电/磁设备获取的信号通常是多通道的时间序列, 具有非线性、非平稳、高维度等特点, 同时可能包含各种噪声。这些因素使得脑电/磁信号的分析处理具有挑战性。

脑电/磁信号中可能存在的噪声信号包括: 眼电、肌电、心电等生理信号, 环境噪声、设备工频噪声等外部干扰信号。因而, 通常需要对脑电/磁信号进行降噪处理, 常见的降噪方法包括^[3-7]: 回归分析(regression analysis)、小波变换(wavelet transform)、主成分分析(principal component analysis)、独立成分分析(independent component analysis)、独立向量分析(independent vector analysis)、典型相关分析(canonical correlation Analysis)、经验模式分解(empirical mode decomposition)、自适应滤波(adaptive filtering)、维纳滤波(wiener filtering)等, 以及相关的组合方法, 如经验模式分解与盲源分离结合的方法^[8], 独立成分分析与源成像结合的方法^[9]。

对于脑电信号, 另一个基本而重要的预处理步骤

是重参考操作, 这是因为脑电采集的是电位差, 即活动电极(active electrode)与参考电极(reference electrode)的电位之差, 其隐含假设是参考电极处的电位为零或常数。但是, 在人体表面不存在零电位点, 导致多种参考并存于现行脑电实践的情况, 影响不同实验室结果的交流和对比^[10]。2001年, 尧德中^[11]根据电磁场理论发展了无穷远参考技术(reference electrode standardization technique, REST), 该方法认识到参考电极问题是电场问题, 即由于脑电源产生的电场同时传导到活动电极和参考电极位置而导致的问题, 由此发展的REST可将实际记录的脑电信号直接转换成理想零参考信号, 从而可标准化各种脑电记录(图2)。REST已被大量研究证实为最佳的单极参考, 现已获得广泛使用^[10,12], 最近更有研究发现, 由REST找回的原平均参考所丢失的信号有明显的生理意义^[13]。

2 脑电/磁信号特征提取与分类方法进展

特征提取及模式分类是脑电/磁信号分析处理中更为关键的步骤。当前已有丰富的方法从时域、频域和网络等不同层面对脑电/磁信号进行分析处理。

在时域上, 比较常见的有空间滤波的方法, 如共空间模式(common spatial pattern)^[14]、判别空间模式(discriminative spatial pattern)^[15]、相关成分分析方法^[16,17]; 信号分解的方法, 如张量分解(tensor decomposition)^[18]、非负矩阵分解(nonnegative matrix factorization, NMF)^[19]、奇异值谱分解(singular spectrum analysis)^[20]; 以及其他方法, 如稀疏表示(sparse representation)^[21]、字典学习(dictionary learning)^[22]、压缩感知(compressed sensing)^[23]和黎曼几何(Riemannian geometry)分析方法^[24]等。值得一提的是, 前面降噪中提到的很多方法同样可用于成分分析和特征提取, 如独立成分分析^[25]、经验模式分解^[26]、典型相关分析^[27]、非线性典型相关分析^[28]等。

在频域上, 除了传统的傅里叶变换、小波分析等方法, 出现了一些新的分析方法, 如基于谱分解的时频分析方法(spectral decomposition)^[29]、状态空间多窗谱分析(state-space multitaper time-frequency analysis)^[30]、高阶谱分析(higher order spectral)^[31,32]、拓扑时频分析(topographic time-frequency decomposition)^[33]、基于 L_p 范数的自回归模型功率谱^[34,35]等。

图2 不同参考电极技术处理后的仿真脑电信号对比示意图^[10]. AR: 平均参考, LM: 连接耳参考, Cz: 头顶单点参考, REST: 无穷远零参考. 图上AR, LM, Cz, REST所对应的信号即为不同参考电极引入的干扰信号或者说是所丢失的信号

Figure 2 Illustration of a simulated EEG data with different reference electrodes^[10]. AR: average reference, LM: linked mastoids, Cz: head vertex reference, REST: zero reference at infinity. The signals corresponding to AR, LM, Cz, REST channels in red are the interference signals or the lost signals of the reference electrodes

在网络层面, 处理方法主要包括网络构建和网络分析两个部分. 网络构建的方法包括: 基于相干(coherence)^[36,37]、相位同步(phase synchronization)^[38]、同步似然(synchronization likelihood)^[39,40]、Granger因果^[41,42]、自适应直接传递函数(adaptive directed transfer function, ADTF)^[43]、跨频耦合(cross-frequency coupling)^[44]以及一些其他方法^[45-47]. 网络分析方法, 主要

有基于图论的分析方法^[48,49]、时变脑网络分析^[50,51]、网络动态分析^[52-54]、网络重组^[55,56]、多层网络^[57,58]、高阶网络^[59]等. 最近出现的网络分析处理算法则有Lp范数Granger因果有向网络分析方法和Lp($p \leq 1$)范数偏有向相干(partial directed coherence)网络分析方法, 这些方法能在噪声情况下比较准确地估计出网络连接模式^[60,61]. 在网络层面上的共空间模式分解算法, 可用于

提取不同状态下的脑网络空间特征^[62], 在区分精神分裂人和正常人的分类上取得了很好的效果^[63]; 基于脑电的大尺度脑网络分析方法, 在运动想象和P300的脑机制研究中显示了好的效果^[55,64].

对于分类方法, 除了传统的机器学习方法, 如线性判别分析(linear discriminant analysis)^[65,66]、支持向量机(support vector machines)^[67]. 近些年来一些新的机器学习方法, 如超限学习机(extreme learning machine)^[68]、深度学习(deep learning)^[69~71]等也越来越多用于脑电信号. 此外, 贝叶斯机器学习(Bayesian machine learning, BML)也被用于脑电信号的特征提取和分类^[72].

3 脑电/磁逆问题研究进展

脑电/磁逆问题是脑电/磁研究领域中具有挑战性的研究方向之一, 其中涉及复杂的数学建模与仿真问题以及神经科学和医学的理论知识^[73]. 由于逆问题的病态性和非唯一性, 脑电/磁逆问题仍是当前研究的难点和热点. 通过逆问题求解, 可以实现大脑活动的源定位和获取源信号, 然后基于源信号进行脑网络构建与分析等^[74~77].

对于脑电逆问题, 其源模型通常有两种^[77]: 等效偶极子和分布源模型. 基于偶极子的方法先假定等效产生头皮信号的偶极子数, 然后通过非线性优化等方法估计出偶极子的位置和大小. 而分布源模型则假设大量的点源均匀分布在大脑容积中的灰质网格上, 然后通过求解线性逆问题估计出每个源的活动强度. 其中的分布源可以是点电荷分布源, 也可以是偶极子分布源^[78~80].

在分布源方法方面, 已经出现了多种逆问题求解算法, 如最小模估计(minimum norm estimate, MNE)^[81]、多信号分类(multiple signal classification, MUSIC)^[82]、线性约束最小方差(linear constrained minimum variance, LCMV)^[83]、加权最小模估计(weighted minimum norm estimate, wMNE)^[84]、欠定系统聚焦算法(focal underdetermined system solver, FOCUSS)^[85]、低分辨率电磁层析成像(low resolution electromagnetic tomography, LORETA)^[86]、标准化低分辨率电磁层析成像(standardized low resolution electromagnetic tomography, sLORETA)^[87]、精准低分辨率

层析成像(exact low resolution brain electromagnetic tomography, eLORETA)^[88]、自相关增强算法(self-coherence enhancement algorithm, SCEA)^[89]、可变分辨率电磁层析成像分析(variable resolution electromagnetic tomographic analysis, VARETA)^[90]等.

事实上, 在大脑的高级认知过程中, 脑功能区响应表现出稀疏性, 为此结合 L_p 模稀疏约束和贝叶斯框架等方法的脑电逆问题受到了越来越多的关注^[91~100], 在这方面, 已出现了从 L_0 模到 $L_p(p \leq 1)$ 的系列成像算法(图3)^[93~95], 以及结合 L_p 范数稀疏约束和 L_p 范数残差测度能在低信噪比下稳健成像的方法^[101]. 发展稀疏分解的理论和方法, 用稀疏性约束来替换常用的加权最小模形式的约束, 不仅能获得具有稀疏性的源定位结果, 还可以消除由于加权最小模约束而引起的源向表面飘移的现象.

在脑电逆成像技术中, 准确重构信号源尺寸是另一个具有挑战性的问题, 稀疏约束(L_1 范数为代表)和光滑约束(L_2 范数为代表)的方法容易造成信号源的大小估计出现偏差^[92,102,103]. 对此, 可在时域-空域先验约束下, 利用贝叶斯推断和凸优化技术^[91,92,104,105], 或先行假定分布源的模糊程度^[73,89], 实现对弥散性分布源的恰当重构.

需要说明的是, 脑磁逆问题与脑电逆问题是相似的, 在此不再专门重复叙述.

4 脑电/磁设备的研发进展

4.1 脑电设备

目前国内市场上的高端脑电采集系统大部分都是欧美国家研制的, 其性能指标较高且稳定性好, 已广泛应用于对脑电信号精度要求较高的脑科学研究领域. 近十几年来, 电子科技大学等高校和科研院所也陆续推出了高性能的脑电采集系统, 正在推动脑电设备从过去单纯依赖进口到国内自主创新研发的新阶段.

传统的脑电设备采用湿电极技术, 需要在电极和头皮之间注入导电膏或导电液, 给使用者带来不便, 同时也增加了实验的准备时间. 为了克服这些问题, 近些年来, 国内外科科研院所和公司开始研发干电极技术或半干电极技术. 同时, 可穿戴的脑电信号采集设备也已在试验性的应用中, 如耳后电极脑电采集设备^[106]、耳内干电极脑电采集设备^[107]等. 总体上脑电

图3 不同脑电源成像算法源定位结果示意图^[95]. L1模方法, MNS: 最小模方法, 3SCO: 源空间稀疏编码优化方法(L0模), LORETA: 低分辨率层析方法

Figure 3 Illustrations of the source imaging results by different EEG source imaging methods^[95]. L1 norm estimate, MNS: minimum norm solution, 3SCO: solution space sparse coding optimization (L0 norm), LORETA: low resolution electromagnetic tomography

设备正朝着便携可穿戴、无线和多模化方向发展, 将为实验室外真实自然场景下的研究和应用提供基础。

4.2 脑磁设备

脑磁场非常微弱, 其幅度在 10^{-12} T, 而人类活动的环境磁场在 10^{-7} T, 地磁场则在 10^{-4} T, 因此需要非常灵敏的传感器和降噪技术。现行脑磁设备都是基于超导量子干涉装置(super-conducting quantum interfere device, SQUID)。近年来, 欧美相关公司已推出了300多个通道的全头型脑磁系统。然而, 这类超导脑磁设备造价昂贵, 且需要在高性能屏蔽室和超低温下运行, 因此维护运行成本也高; 其探头位置固定且距头皮较远, 使得检出的信号较弱。总体上, 该类系统适应性较差, 阻碍了其大规模使用。

近些年来, 基于原子磁力计的脑磁图系统逐步兴起, 已被学界公认为下一代脑磁图的发展方向^[108,109]。2006年, 无自旋交换弛豫(spin-exchange relaxation free, SERF)原子磁力计被用于开展脑磁研究^[110]。2010和2013年, 紧凑型和多通道的SERF磁力计分别被用于测量脑磁信号^[111,112]。2017年, 光泵磁力计(optically pumped magnetometers, OPM)测量到了脑磁信号^[113]。OPM是基于光学射频双共振现象的超灵敏原子磁力计, 可插入3D打印的头盔内探测脑磁, 探头更接近于头表, 有利于更好地检出脑磁信号。同年, 基于碱金属Cs原子的SERF磁力计, 研究人员获得了由听觉刺激诱发的大脑初级听觉皮层活动的磁信号^[114]。2018年, 可

穿戴的移动脑磁设备开始出现^[115], 穿戴这种新型设备的被试可以自由运动, 这项发明被认为是神经成像的又一次重要技术革新。国内, 北京大学和中国科学院生物物理研究所等单位也分别研制出了OPM脑磁图原理样机。

与基于SQUID的传统脑磁设备相比, 基于OPM的脑磁设备可在常温下工作, 探头可紧贴头皮, 使其信号幅度比SQUID大, 且建设/运行成本低(室温探头, 无需液氮)、可做成穿戴式等, 但目前的传感器还没有SQUID那么稳健, 探头尺寸与灵敏度的矛盾有待突破, 信号的稳定性尚需改善。因此, 学界认为, OPM脑磁短期内还难以全面替代SQUID脑磁系统。

5 脑电/磁的应用

脑电/磁信号具有高的时间分辨率, 可通过源成像技术有效提高空间分辨力, 在认知神经学科、神经工程、脑疾病临床等领域中有着广泛的应用^[116,117]。

5.1 认知领域中的应用

在认知神经科学领域, 可以脑电/磁信号为载体, 探索大脑功能活动区域、信息整合与分离、脑网络拓扑结构等方面的信息^[118]。当前的热点包括静息条件下的大脑功能活动模式^[54,119]和任务条件下的时-空-频模式等^[120~124]。在认知神经科学的基础研究中, 基于脑电/磁成像的研究方法已用于听觉、视觉、语言、运动、记忆、意识、情感、智力、学习等众多领域^[125~131]。

5.2 临床问题中的应用

脑电的优势是它便于进行长时间的记录, 可连续检查睡眠和清醒期的脑电活动, 因而被广泛用于睡眠监测及相关问题的研究中^[132~134]。在临床上, 脑电既可用于功能性疾病, 如癫痫、精神分裂症、帕金森综合征、阿尔茨海默病等疾病的诊断^[135~137]; 也可用于协助诊断器质性疾病, 如脑肿瘤、多发性硬化等^[138~141]以及视觉疾病的诊断^[142,143], 同时也可用于评价疗效和判断预后等。

脑磁的临床应用包括^[144,145]: 术前评估、颅内手术靶点定位、癫痫病灶定位、脑功能损害评估、精神和神经疾病诊断、胎儿脑磁分析、听觉功能异常诊断等。

5.3 脑-机接口领域中的应用

最近20年来, 脑电由于其非侵入性和高时间分辨率以及脑电设备的便携性等优点, 在脑-机接口(brain-computer interface, BCI)领域获得了广泛的应用. 利用脑电可解码用户的意愿, 实现单向或者闭环控制. BCI的应用领域范围十分广泛, 包括^[146~153]设备控制、神经反馈、神经康复、精神和神经疾病治疗、状态监测、认知训练、航空航天、教学评估、游戏娱乐等.

相比于脑电, 脑磁在神经工程领域的应用较少^[154,155], 主要原因是现行基于SQUID的脑磁设备昂贵、不便携、必须安装在特定的磁屏蔽室. 随着基于OPM的脑磁设备的发展, 脑磁在神经工程领域的应用研究将有望逐步增多.

6 脑电/磁的若干前沿问题

6.1 脑电/磁信号的来源及意义

自人类脑电被发现90年来(1929~), 脑认知功能和脑疾病等领域取得了丰富的研究成果, 但人们对脑电信号的来源及其意义仍知之甚少^[156]. 什么样的神经微回路(neural microcircuit)产生了与认知过程相关的时间、频谱和空间特征? 脑电信号中的一些特定模式如相位扰动(phase perturbations), 基于相位或能量的连接、跨频耦合等, 如何与认知功能相关? 神经振荡(neural oscillations)是脑电最显著的特征, 过去几十年的大量研究表明, 知觉、认知、运动和情绪加工等都与特定的振荡模式相关, 但其背后的神经机制仍然不清楚. 脑电被认为是大量神经元的突触后电位的总和, 但这种说法在理解脑电的空间、频谱和时间特征上缺乏足够的解释力.

当前, 研究人员正从3个方面推进对有关脑电各种特征的来源及意义的认识: (i) 脑电特征与记忆、知觉、情绪、语言、行动以及其他认知过程关系的研究; (ii) 神经微回路的组织和操作的神经生理研究; (iii) 发展和利用操纵大脑的新技术来深化对相关机制的认识.

以上这些有关脑电的基础性问题也同样适用于脑磁^[156].

6.2 神经活动能否被MRI所直接检测?

功能磁共振技术是利用神经活动引起的血氧饱和

水平的变化(blood oxygenation level-dependent, BOLD), 因此它不是神经活动的直接表达. 自功能磁共振技术得到应用以来, 研究人员就一直在考虑能否利用MRI直接检测神经电活动^[157~159]. 从理论上讲, 神经电流(neuronal current, nc)的存在就伴随着相应的神经磁场(neuronal magnetic field)的存在. 磁共振技术能否实现对该弱磁场的检测成为回答该问题的焦点. 当前探讨的情况包括水模、离体脑片、人脑神经活动实验、模型仿真计算等.

2010年的一项磁共振监测alpha波的研究中发现, alpha频段的磁共振信号在不同条件下有明显的改变, 初步证明了在特定的条件下应用磁共振检测神经电流活动信号是可能的^[160]. 在另一项工作中, 借助计算理论仿真对nc-MRI的可行性进行了探讨^[157]. 结果表明, 相向树突分支的存在可以提高神经磁场的可检测性. 近期, 国内开展的一项新的研究表明, 跨膜水交换(active transmembrane water exchange)可能是功能磁共振能检测神经元活动的机制^[161]. 此外, 麻省理工学院的研究人员设计出了一种基于磁共振成像的钙活性成像方法^[162], 该方法可以跟踪活体动物神经元内的信号传导过程, 能够将神经活动与特定行为联系起来.

6.3 同步多模态信息获取与融合技术

近半个世纪来, 人们发展了多种时-空分辨率不同的脑功能成像技术(图4). 其中脑电和脑磁具有很好的时间分辨率, 但空间分辨率明显不足, 为此对同步脑电-磁共振技术给予了很高的期待. 在硬件方面, 需要克服两套系统的兼容性问题, 尤其是磁共振的强磁场环境对脑电系统的影响, 在这方面, 国际上已有比较成熟的方案, 现在的关注焦点在于信号的处理方面: (i) 脑电信号中的心冲击干扰问题, 目前仍缺乏有效的去除方法; (ii) 脑电与磁共振信息的融合问题, 其难度在于两种信息分别来自于不同的时间和空间尺度, 因此是一种跨尺度的融合. 在这方面已先后推出了多种方案: 非对称融合, 如基于fMRI约束的EEG成像^[163]; 对称融合, 如基于正演生成同步EEG-fMRI的模型方法^[164]、网络空间的EEG/fMRI融合^[165]、EEG-fMRI的分层级可信度融合^[166]等.

6.4 脑电/磁的计算模型

当前脑科学研究正在从传统的“实验科学”向“实

图4 不同成像技术的时-空分辨率示意图。SEEG: 立体定向脑电图技术, ECoG: 皮层脑电图, EEG: 脑电图, MEG: 脑磁图, NIRS: 近红外光谱, fMRI: 功能磁共振, PET: 正电子断层成像, SPECT: 单光子发射计算机断层成像术

Figure 4 The temporal and spatial resolutions of different imaging technologies. SEEG: stereoencephalography, ECoG: electrocorticographic, EEG: electroencephalogram, MEG: magnetoencephalography, NIRS: near-infrared spectroscopy, fMRI: functional magnetic resonance imaging, PET: positron emission tomography, SPECT: single photon emission computed tomography

验与计算并重”的范式转变, 强调将实验神经科学和侧重于理论与模型的计算神经科学进行有力地交叉融合。这是因为, 基于人或动物电生理的实验不可能穷尽考查参数的所有可能情况, 由此决定了所得到的结论具有局限性。基于计算模型, 则可以遍历拟考查参数的所有可能情况, 为大脑机制研究提供新的窗口。近10年来, 越来越多的研究人员借助大尺度的全脑皮层网络模型来研究大脑的结构与功能间的映射关系, 阐明大脑的工作机制^[167~169]以及脑功能异常的回路基础^[170,171], 如失神癫痫的皮层丘脑基底节回路模型等^[172]。脑电/磁信号具有丰富的时间信息, 借助大尺度模型将其与脑内机制联系起来, 可望大大拓展脑电/磁信号的解释空间。

6.5 脑器交互研究

脑器交互(brain-apparatus communication, BAC)指脑与器械如外骨骼或计算机(脑-机接口), 以及脑与身体器官如肠胃、免疫系统、手、脚等的交互^[173]。它包括借助各种技术活化大脑(activating brain), 如借助BCI重新打开闭锁的大脑(locked-in病人); 干预、修复大脑(modulating brain), 如深部脑刺激(deep brain stimulation, DBS)^[174]、经颅磁刺激(transcranial magnetic

stimulation, TMS)^[175]、经颅直流电刺激(transcranial direct-current stimulation, tDCS)^[176]、功能电刺激(functional electrical stimulation, FES)^[177]、经颅超声神经调控(transcranial ultrasound stimulation, TUS)^[178]等; 以及借助舞蹈、音乐、游戏等途径增强大脑(en-hancing brain)与其他器官的协同关系等^[179,180]。BAC概念的提出, 为脑电的开拓应用展示了一个广阔的空间, 包括受损大脑功能替代、修复与增强, 如四肢瘫痪病人借助运动想象和功能电刺激, 实现对圆柱物体的抓握动作^[181]; 与此同时, 也有利于对应用过程中所引起的大脑可塑性机制的理解。

6.6 高频振荡研究

高频振荡(high-frequency oscillations, HFOs)指80 Hz以上的电生理信号。在正常人的慢波睡眠或安静闭目状态, HFOs出现频率增高。通常认为正常的HFOs参与了大脑信息编码、感觉整合和记忆形成等^[182~184]。研究表明, 高频振荡与癫痫发作有着密切关系, 在癫痫发作前、发作期以及发作间期, 患者的大脑皮层、海马和内嗅皮层中均可检测到病理性的HFOs^[185]。HFOs可能是癫痫的有效生物学特征, 已用于癫痫病灶的定位和癫痫发作的预测^[186]。

当前, 高频振荡的脑电和脑磁研究以及相关应用还远未达到成熟的程度。高频振荡的产生机制目前还不清楚^[187,188], 癫痫脑电信号中高频振荡的识别、生理性和病理性高频振荡的区分等仍存在很多问题^[189,190], 高频振荡特征提取与病灶定位算法还需进一步发展^[191,192]。这些方面的研究进展将有助于高频振荡在临床上更广泛地应用。

6.7 定量脑电图技术

根据人们对脑电图的解释方式, 脑电图被分为定性脑电图和定量脑电图(quantitative electroencephalography, qEEG), 前者是指脑电图专家通过观看脑电图波形来进行解释, 这种方式在目前的临床实践中仍然占据主导地位, 原因在于脑电图的复杂性, 后者则是指基于计算机处理结果进行解释的方式。定量脑电图中的分析包括头表空间分布特征、时域波形、频谱特征、相位信息、信号复杂度、脑功能网络特征、源定位、源空间的信号分析等。近30年来, 定量脑电图技术在认知研究和临床实践中得到了越来越广泛的应

用^[193~196].

显然, qEEG是伴随信息处理技术的进步而不断发展演进的, 其中一个很基础的因素就是所分析脑电的真实性, 理论上的脑电采集应该基于零参考, 否则非零的参考信号会作为一个挥之不去的假信号隐藏在记录之中(图2), 影响定量分析的结果. 新近发展的脑电零参考技术较好地解决了这一历史性的问题. 已有文献研究证实, 零参考电极技术会在时域波形、频谱、脑网络、潜伏期等方面获得更加客观合理的结果^[197~200], 因此qEEG领域的一个重要的工作就是推动基于REST的定量化分析研究, 从而促进不同实验室结果的直接对比和历史上大量研究结果的规范化统一. 显然, 该工作有可能对脑电的应用产生重要而系统性的影响, 包括确认和更新人们对脑认知和部分脑疾病的脑电现象的认识.

7 总结与展望

信号处理、人工智能、计算机等领域的快速发展, 推动了脑电/磁成像技术的不断进步. 近年来, 我国在脑电/磁的理论、算法、软件、硬件和应用系统等方面均取得了一些重要的成果, 基本达到了与国际并跑的水平. 除了前面列举的几个前沿问题, 以下方向也是今后需要继续重点关注的.

7.1 脑电逆问题

脑电逆问题是一个欠定的数学问题, 一个重要的方向是发展带约束和先验的有效反演算法, 以获得更加精确的脑区定位和源信号反演, 包括合理利用 $L_0/L_1(L_p)$ 模稀疏约束、多模态信息的融合反演, 以推进高时空分辨率的逆问题求解.

7.2 脑电/磁设备

目前的脑电研究还主要集中在0.5~45 Hz的传统频段, 忽略了较高和较低频段所携带的独特信息, 其中低频可能和血氧代谢等密切相关, 高频信息可能与特定的核团功能有关, 因而有特殊的定位价值. 为此, 需要发展宽频段(直流到几千Hz)的脑电采集设备, 同时推进新一代基于OPM的脑磁设备的发展和完善. 此外, 同步采集脑电、血氧消耗水平、肌电、心电、脑磁等多生理信号的多模态成像技术, 多脑同步采集(hypers-

canning)技术^[201], 小型、集成、无线、可穿戴式脑电磁设备等, 都将是今后的重要研究方向.

7.3 人工智能与脑电/磁信号处理

新近已有研究人员尝试将深度学习引入情绪识别、睡眠等相关脑电数据的分析中, 并取得了比传统机器学习更好的效果. 事实上, 脑电/磁数据的已有量和增长量都是巨大的, 为利用深度学习构建各种精神性和神经性疾病的早期预防、监测、诊断模型提供了基础. 同时, 脑电/磁逆问题的求解应该也会从深度学习找到新的突破口. 此外, 在基于脑电的脑-机接口研究中, 深度学习方法也逐步增多, 但性能相比于深度学习在其他领域的应用还有待进一步提升, 如何根据不同实验范式得到的脑信号构建有效的深度学习算法框架值得深入研究. 尤其值得长期关注的是, 在当前的深度学习向未来的类脑智能过渡的过程中, 将会发现和利用更多的脑机制模型, 也自然会大大促进脑电/磁信号处理技术的发展.

7.4 脑电/磁大数据平台建设

当今的脑科学研究已经步入大数据时代, 面对体量大、多样化、非结构化的数据集, 传统单个研究中心的作坊式的分析处理方式, 以及传统的数据库工具可能无法对其内容进行抓取、处理和管理. 将大数据与人工智能引入脑电和脑磁领域, 有可能为患者提供更精准的诊断与治疗方法, 也为健康人群提供健康风险警示, 这是今后相当一段时间内的重要研究方向. 联合多单位和多成像中心建立数据的共享和处理平台, 并进行分析工具的开发, 已成为学界的共识. 这类平台将制定出完善的数据采集、存储、处理、使用和管理规范, 以实现数据的有效共享和利用. 事实上, 国内外均已有了相应的平台出现, 如电子科技大学的webbrain平台. 基于互联网+、智能+等技术和理念, 这类系统将实现对不同单位的多样、异构数据的统一管理、高效处理和分析; 使研究人员能利用机器学习、大数据分析以及计算建模等方法对脑电/磁数据以及处理方法进行有效地整合和规范, 进而获取高时空分辨率的一定尺度的神经活动的“全景电影”. 这将为各种认知活动的神经机理和各种重大神经精神疾病的研究提供重要的支持. 当前, 相应的平台还需进一步发展, 需开发出高运算效率且稳定易用的数据处

理、分析和可视化工具, 将脑电/磁等多个模态的数据在空间和时间上融合; 开发规范、通用性高且使用方便的数据分享工具等。整个平台要做到能用、可用、有用而且好用。

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Progresses and prospects of brain electromagnetic imaging

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Non-invasive electroencephalogram (EEG) and magnetoencephalography (MEG) imaging technologies have high temporal resolution, and the potential to enhance its spatial resolution by electric source imaging (ESI), thus they play an indispensable role in promoting the researches of cognition principles and mechanisms of brain diseases. In this paper, a comprehensive review is presented to the main progresses in such as EEG/MEG signal processing, EEG/MEG inverse problem, EEG/MEG equipment development and EEG/MEG applications, etc. Additionally, some frontier topics and potentially valuable directions are specially explored.

EEG, MEG, inverse problem, signal processing, multimodal fusion

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