

膳食营养与抑郁症的关系*

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摘 要 近十几年, 膳食营养与抑郁症的关系受到了研究者越来越多的重视。早期的研究主要考察单一营养元素或食物对于抑郁症的影响, 其中研究最多的是 n-3 多不饱和脂肪酸和叶酸, 近期的研究开始关注整体膳食模式与抑郁症的联系。膳食营养与抑郁症关联的内在机制涉及炎症反应、氧化应激和脑源性神经营养因子等。以流行病学为主的研究现状限制了膳食营养影响抑郁症的因果解释, 未来的研究应强化对两者关联的内在机制以及现实价值的考察。

关键词 抑郁症; 膳食; 营养; 膳食模式

分类号 B845

1 引言

抑郁症是一种常见的精神障碍, 其发病率在全世界范围内迅速攀升。据世界卫生组织(WHO)统计, 抑郁症已经成为目前世界的第四大疾病, 预计到 2020 年将上升为仅次于冠心病的人类第二大负担疾病(WHO, 2008)。一项截止 2010 年的调查结果显示, 全世界约有 2.98 亿人(世界人口的 4.3%)受到抑郁症的影响(Vos et al., 2012)。在中国, 包含抑郁症在内的心境障碍的发病率为 6.1%(Phillips et al., 2009)。

由于高发生率和破坏性后果, 抑郁症已经成为一个威胁公共健康的严重问题。如何找到有效途径来降低整体人群的抑郁症发病风险, 防止初期的抑郁症状最终演化为抑郁症, 已成为当前公共精神卫生领域一个亟待解决的问题。最近的十几年间, 膳食营养与抑郁症的关系受到了该领域研究者越来越多的关注。这种关注源于两个原因: 首先, 从机制上讲, 中枢单胺类神经递质系统功能紊乱是抑郁症的主要生理病理基础(Maletic et al., 2007), 膳食营养作为大脑的首要能量来源直接参

与了相关神经递质的合成和代谢, 势必会对心理和情绪产生重要影响(Parletta, Milte, & Meyer, 2013)。其次, 从流行病学角度讲, 膳食营养与代谢综合征 (metabolic syndrome, MetS) 和心血管疾病 (cardiovascular disease, CVD) 等常见的慢性疾病之间的关系已经得到研究确认, 而这些疾病与抑郁症也有着非常密切的联系(Luppino et al., 2010)。膳食营养会对抑郁症产生何种影响自然也就成为研究者关注的一个问题。本文将首先介绍单一营养元素(或食物)和膳食模式与抑郁症关联的研究进展, 然后探讨这种关联的内在机制, 最后将分析已有研究的不足并展望未来的研究重点。

2 膳食营养与抑郁症的关系

2.1 单一营养元素或食物与抑郁症的关系

单一营养元素与抑郁症的关联中, 研究者关注最多的是 n-3 多不饱和脂肪酸(n-3 polyunsaturated fatty acids, n-3PUFAs)和叶酸(folate)。

n-3PUFAs 是指第一个不饱和双键出现在碳链甲基端第三位上的脂肪酸, 以二十碳五烯酸(eicosapentaenoic acid, EPA)和二十二碳六烯酸(docosahexaenoic acid, DHA)为代表。越来越多的证据显示, 抑郁症患者大都存在 n-3PUFAs 的缺乏, 补充 EPA 和 DHA 能够明显改善抑郁症状(Lin, Huang, & Su, 2010; 郭小月, 任俊, 郭建友, 2013)。

收稿日期: 2015-02-09

* 教育部人文社会科学研究青年基金项目(12YJC190036)资助。

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由于人体无法自身合成EPA和DHA,所以只能通过饮食摄入,主要食物来源是鱼类。跨国家比较研究发现,地区的抑郁症发病率与该地区的人均鱼类消耗之间显著负相关(Hibbeln, 1998)。人群调查也表明,低频率鱼类摄入人群的抑郁症状明显高于高频率鱼类摄入人群(Silvers & Scott, 2002; Tanskanen et al., 2001)。但并不是所有研究都发现了鱼类与抑郁症的关联, Hakkarainen 等(2004)针对芬兰人群的横断研究就发现鱼类摄入与抑郁症无关。Strom, Mortensen, Halldorsson, Thorsdottir 和 Olsen (2009)针对孕妇的前瞻性队列研究也没有发现鱼类的摄入与产后抑郁症的发病有关。此外,鱼类摄入与抑郁症的关系似乎存在性别差异,两项人群研究都发现只有女性的鱼类摄入与抑郁症负相关(Smith et al., 2014; Timonen et al., 2004)。n-3PUFAs 补充剂已经初步应用于临床抑郁症的治疗。一项针对随机对照实验(random-control trials, RCTs)的元分析显示, n-3PUFAs 对临床诊断的抑郁症患者有治疗效果(Appleton, Rogers, & Ness, 2010)。不过该分析也表明, n-3PUFAs 对没有诊断为抑郁症的人群并没有明显益处,提示 n-3PUFAs 对抑郁症的治疗意义可能大于预防。

叶酸是维生素 B 复合体之一,与维生素 B₁₂ 和同型半胱氨酸(homocysteine)同属于一碳单位。叶酸进入人体后会先转化为 5-甲基四氢叶酸(5-methyltetrahydrofolate), 5-甲基四氢叶酸参与了脑内 5-HT 和多巴胺等单胺类神经递质的合成和代谢,叶酸也因此被认为与情绪和心境障碍有关。叶酸与抑郁症的关系很早就被发现(Reynolds, Preece, Bailey, & Coppen, 1970), 2007 年的一篇元分析文献总结之前的研究后指出,体内叶酸水平过低与较高的抑郁症发病率相关(Gilbody, Lightfoot, & Sheldon, 2007)。更新的研究表明,不只是叶酸,血浆内的维生素 B₁₂ 偏低或同型半胱氨酸水平偏高(通常由叶酸、维生素 B₆ 或 B₁₂ 缺乏导致)都与抑郁风险升高有关(Beydoun, Shroff, Beydoun, & Zonderman, 2010; Forti et al., 2010; Sánchez-Villegas, Doreste, et al., 2009),摄入富含叶酸和维生素 B₁₂ 的膳食则会显著降低抑郁症的发病风险(Murakami et al., 2008; Payne et al., 2009; Skarupski et al., 2010)。叶酸补充剂很早就被用于抑郁症的治疗,最近的一项研究发现, 5-甲基四氢叶酸的治疗效果要好于叶酸本身(Papakostas et al., 2012)。

除了 n-3PUFAs 和叶酸外,其他微量元素与抑郁症的联系也不断被发现。流行病学研究显示,锌(Cope & Levenson, 2010; Ranjbar et al., 2014)、铁(Stewart & Hirani, 2012; Yi et al., 2011)和硒(Gao et al., 2012; Pasco et al., 2012)等微量元素的缺乏均与抑郁症的发病有关。近年来,单一食品与抑郁症的关系开始受到关注。仅以饮料为例,研究者已经发现了几种常见饮料与抑郁症的关联。对欧美人群的研究发现,咖啡的摄入频率与抑郁症的发病风险负相关(Guo et al., 2014; Lucas et al., 2011; Ruusunen et al., 2010)。对亚洲人群的研究则表明,较高的饮茶频率能够降低抑郁症的发病风险(Feng et al., 2012; Feng et al., 2013; Niu et al., 2009)。碳酸饮料是含糖比例最高的单一食品,对西方人群的几项研究都发现了碳酸饮料的高饮用频率与抑郁症相关(Guo et al., 2014; Shi, Taylor, Wittert, Goldney, & Gill, 2010),最近一项针对中国人群的横断研究也发现了类似的关系(Yu et al., 2015)。

2.2 膳食模式与抑郁症的关系

从单一元素或食物的角度研究膳食营养与抑郁症的关联有一定局限。首先,人们吃的不是独立的营养素,而是含有多种营养素的多种食物,不同营养素和食物通常会对健康产生交互影响。其次,一些营养元素的摄入往往依附于某种特定的膳食模式,而这些膳食模式又与特定的人口学特征和生活习惯相关联,这就使得在考察单一营养或食物与抑郁症关系时的混淆因素大大增加。基于此,研究者开始关注膳食模式与抑郁症的关系。所谓膳食模式(dietary pattern),是指以多种形式结合的、人们实际生活所食用的各种食物的组合(Hu, 2002)。一般来说,研究者确定膳食模式的方法有两种:先验法(priori approach)以现有的膳食指南或其他科学饮食建议为基础,将个体的饮食与之比较,以此衡量其遵循某种膳食模式的程度;后验法(posteriori approach)以膳食调查数据为基础,运用因子分析和聚类分析等统计方法确定膳食模式种类。营养流行病学研究中最常见三种膳食模式分别是地中海膳食模式、西方膳食模式和东方膳食模式,其中前两种膳食模式与抑郁症的关联最受研究者关注。

地中海膳食模式(Mediterranean dietary pattern)是一种现代营养学所推崇的健康膳食模式,这种

模式强调多食橄榄油、豆类、非精制谷物、水果、蔬菜和鱼类, 适当食用奶制品(以奶酪和酸奶为主), 适度饮酒, 少食肉类和肉制品(Trichopoulou, Costacou, Bamia, & Trichopoulos, 2003)。先前研究表明, 地中海膳食模式对于心脑血管健康有着明确的积极影响(Mitrou et al., 2007), 近年来的研究也发现了它与抑郁症之间的关联。一项针对西班牙健康人群的前瞻性队列研究发现, 受调查者的膳食模式与地中海膳食模式的符合程度越高, 其在 4.4 年后的抑郁症发病风险就越低(Sánchez-Villegas, Delgado-Rodriguez, et al., 2009)。Rienks, Dobson 和 Mishra (2013)在一项针对澳大利亚女性的队列研究中确定了烹饪蔬菜、水果、地中海、肉类和加工肉类、奶制品和高脂高糖六种膳食模式, 结果发现其中只有地中海膳食模式能够降低 3 年后的抑郁症发病率。Skarupski, Tangney, Li, Evans 和 Morris (2013)一项针对美国 65 岁以上老年人, 追踪时间达 7.2 年的研究也发现了地中海膳食模式与较低的新发抑郁症状相关。此外, 一项针对地中海东部地区老年人的研究发现, 对鱼类、蔬菜、橄榄油和谷物的消耗与抑郁症状的严重程度负相关(Mamplakou et al., 2010)。

与地中海膳食模式相反, 西方膳食模式(Western dietary pattern)是一种典型的不健康膳食模式, 该模式包括较高比例的红肉、甜食、高脂肪食物和精制谷物以及奶制品、高糖饮料和加工肉类食品。迄今为止的大部分研究都表明, 西方膳食模式与抑郁症的高风险有关。一项针对澳大利亚女性的横断面研究发现, 以蔬菜、水果、肉类、鱼类和全麦为特征的传统膳食模式(traditional dietary pattern)与较低的抑郁症发病相关, 而典型的西方膳食模式则会增加抑郁症的发病风险(Jacka et al., 2010)。另一项针对芬兰老年人的横断研究发现, 以蔬菜、水果、全麦面包、禽类、浆果、低脂奶酪和鱼类为主的精明膳食模式(prudent dietary pattern)能够降低 25%的抑郁症发病率, 西方膳食模式则会使发病率上升 41%(Ruusunen et al., 2014)。更有力的证据来自于前瞻性队列研究。Akbaraly 等(2009)在一项对英国中年人的前瞻队列研究中区分了全食食品(whole foods)和加工食品(processed foods)两种膳食模式, 全食食品模式以水果、蔬菜和鱼类为主要特征, 加工食品模式则是典型的西方膳食模式。他们在调整了混淆因

素后发现, 加工食品模式会使 5 年后的抑郁症发病风险升高近 60%。Sánchez-Villegas 和 Verberne 等(2011)对西班牙 12,000 余名大学毕业生, 平均追踪时间为 6 年的动态前瞻性队列研究发现, 反式脂肪酸、快餐和加工糕点与较高的抑郁风险相关。另一项针对 12,400 名法国雇员, 追踪时间长达 10 年的大规模队列研究发现, 对于男性而言, 低脂肪、零食、高脂高糖和西方膳食这四种膳食模式均与抑郁症状的高发生率有关, 对于女性而言, 只有零食膳食模式与抑郁症状的高发生率有关(Le Port et al., 2012)。

虽然针对亚洲人群膳食模式与抑郁症关联的研究数据不多, 但已有的研究一定程度上体现了东方膳食的特点。在一项针对日本人群的研究中, Nanri 等(2010)发现日本膳食模式(Japanese dietary pattern)与抑郁症状的严重程度负相关。这种健康膳食模式除了包含较高比例的蔬菜和水果外, 还有蘑菇、豆制品和绿茶等具有东方特色的食品。另一项针对中国青少年人群的研究显示, 甜食模式和肉类模式与抑郁症状正相关, 以稀饭、燕麦、全麦、黄色或红色蔬菜、水果和豆浆为特点的传统中国膳食模式则与抑郁症状负相关(Weng et al., 2012)。

总的来看, 虽然不同国家和地区对于健康膳食的定义并不完全一致, 但研究结果基本上都符合类似的规律, 即富含多元和单一不饱和脂肪酸的健康膳食模式能够降低抑郁症的发病风险, 而饱和脂肪和反式不饱和脂肪含量较高的不健康膳食模式则会促进抑郁症的发生。最近的一篇元分析文献在总结了 21 项考察膳食模式与抑郁症关系的研究后发现: 以水果、蔬菜、鱼类和全麦为特征的健康膳食模式能降低 16%的抑郁症发病风险(Lai et al., 2014)。需要引起重视的是, 已有一些针对儿童和青少年(Jacka et al., 2011; Kohlboeck et al., 2012; Weng et al., 2012)的研究发现了不健康的膳食模式与抑郁症的联系。这提示该领域有必要开展起点更早和跨度更长的前瞻性队列研究, 为抑郁症的早期膳食预防提供参考。

3 膳食营养与抑郁症关联的内在机制

抑郁症的发病受遗传、生理、心理和社会等多重因素的影响, 机制非常复杂。对于膳食营养与抑郁症关联的机制, 早期较为笼统的观点认为主要是因为膳食中一些营养元素直接参与了单胺

类神经递质尤其是 5-HT 和多巴胺的合成和代谢,或影响到相关受体或转运体的活性。譬如,那些富含色氨酸(5-HT 合成前体)的食物就被发现具有很好的抗抑郁效应(Markus, 2008),而锌和铁等微量元素的缺乏会使 5-HT 合成受阻,进而增加抑郁症的发病风险(Baumgartner et al., 2012; Szeuwczyk et al., 2009)。随着研究的不断深入,一些新的假说被提出,其中主要涉及炎症反应、氧化应激和脑源性神经营养因子等机制。

3.1 炎症反应机制

炎症(inflammation)是 CVD、肥胖、糖尿病和癌症等慢性疾病的共同病理机制,也是抑郁症的一个重要风险因素。大量研究证据表明,抑郁症患者血液中的 C 反应蛋白(CRP)、前炎性细胞因子(如 IL-1、IL-6 和 TNF- α)以及可溶性白介素 2 受体等可以反映炎症程度的标志物水平均高于非抑郁个体(Howren, Lamkin, & Suls, 2009; Liu, Ho, & Mak, 2012)。学界现已普遍认同抑郁症是一种炎症性疾病(inflammatory disease),外周免疫激活通过释放前炎性细胞因子导致与抑郁症相关的各种行为以及神经内分泌和神经生化的改变(Berk et al., 2013)。

研究发现,膳食营养与机体炎症反应有密切联系。以膳食模式为例,几项研究都表明,健康的地中海膳食模式与体内较低的炎症标志物水平相关(Luciano et al., 2012; Richard, Couture, Desroches, & Lamarche, 2013; Urpi-Sarda et al., 2012),不健康的西方膳食模式则与较高的炎症标志物水平相关(Fung et al., 2001)。一项针对代谢综合征人群的研究发现,持续 5 周的地中海饮食能够显著降低血浆的 CRP 水平(Richard et al., 2013)。另一项持续 1 年的干预实验发现,采用地中海膳食模式的被试血浆内的 IL-6 和 TNF 受体的浓度水平均低于采用低脂肪膳食模式的被试(Urpi-Sarda et al., 2012)。营养元素方面,膳食纤维(Jacobs, Andersen, & Blomhoff, 2007)和 n-3PUFA (Rangel-Huerta, Aguilera, Mesa, & Gil, 2012)都被发现具有较好的抗炎症作用。

从现有的研究数据来看,那些能够促进炎症反应的膳食模式或营养元素大都会增加抑郁症的发病风险,由此可以推断炎症反应可能是膳食营养与抑郁症关联的重要内在机制。最近的美国护士健康队列研究结果为此提供了更为直接的证据

(Lucas et al., 2014)。该研究通过降秩回归(reduced-rank regression)的方法确定了一种与 CRP, IL-6 和 TNF 受体等标志物相关的炎症膳食模式(Inflammatory dietary pattern),该模式包含较高比例的碳酸饮料、精细谷物、红肉以及人造黄油和较低比例的酒精、咖啡、橄榄油以及绿色和黄色蔬菜。研究者分析 12 年的追踪数据后发现,炎症膳食模式与较高的抑郁发病风险相关,该模式得分最高组的抑郁症发病率比最低组高 40%。

虽然人群研究数据表明膳食营养与抑郁症之间存在炎症关联,但由于缺少足够的机制方面的深入研究,所以目前还无法回答的一个问题是:究竟是膳食营养因素促进了抑郁症的发生,从而导致炎症反应;还是膳食营养因素诱发了炎症反应,从而导致了抑郁症的产生?一种观点认为,某些膳食营养的炎症效应会影响脑内单胺类神经递质的浓度,进而对个体的情绪和认知产生影响(Kiecolt-Glaser, 2010)。但这仅是一种推测,目前尚缺少直接的证据支持该观点。

3.2 氧化应激机制

氧化应激(Oxidative Stress)是指体内氧化与抗氧化作用失衡,倾向于氧化,导致大量氧化中间产物产生的过程。一系列证据显示抑郁症与氧化应激有关:抑郁症患者会出现氧化应激上升和抗氧化能力下降的现象,主要表现为血浆中的抗氧化物浓度明显下降,抗氧化酶活性下降等(Maes, Galecki, Chang, & Berk, 2011; Moylan et al., 2014)。

食物是人体最为重要的抗氧化剂来源,直接影响机体的内在抗氧化能力。植物类食物如水果、蔬菜、橄榄油和坚果等富含维生素 A、C 和 E 等抗氧化剂,来自肉类、蔬菜、全麦、蛋类和酸奶等膳食的氨基酸则是人体内源性抗氧化物谷胱甘肽过氧化物酶(GpX)的重要前体。人群研究发现,以上述食物为主的地中海膳食模式与血浆抗氧化水平升高和氧化应激反应降低密切相关(Espósito et al., 2011)。番茄红素(lycopene)是自然界存在的最强抗氧化剂,Niu 等(2013)针对日本老年人群的研究发现,摄入富含番茄红素的番茄类食物(包括番茄、番茄酱等)能够明显降低抑郁症的发病风险。绿茶中含量丰富的茶多酚(tea polyphenol)是另一种较强的天然抗氧化剂,人群研究发现,绿茶的摄入与抑郁症状负相关(Niu et al., 2009)。动物研究更为直接的表明,绿茶的这种抗抑郁作用与

茶多酚的抗氧化效应有关(Zhu et al., 2012)。

由于脑组织本身能量代谢旺盛, 不饱和脂肪酸含量丰富, 因此较其他组织更易受到自由基攻击, 发生氧化应激损伤。动物研究发现, 长期给予维生素 E 能显著改善前额叶皮层和海马的抗氧化能力, 从而降低动物的抑郁样行为(Lobato et al., 2010)。预处理抗氧化剂能够阻止急性应激导致的皮层细胞损失(Lee, Choi, Lee, Choi, & Sohn, 2006)。相反的, 以西方膳食模式饲养老年小鼠 16 周, 会导致其海马内的氧化应激反应升高并产生认知损伤(Morrison et al., 2010)。这些研究证据提示, 膳食营养中的抗氧化成分能够降低抑郁风险可能主要是源于对脑组织的保护作用。

3.3 脑源性神经营养因子机制

脑源性神经营养因子(brain-derived neurotrophic factor, BDNF)是人体内含量最丰富的神经营养因子, 在神经结构和功能的可塑性中都发挥了重要作用。越来越多的证据表明 BDNF 参与了抑郁症的病理生理过程, 如抑郁症患者血浆内的 BDNF 水平偏低(Lee & Kim, 2010), 各类抗抑郁药物如 5-HT 重摄取抑制剂、NE 选择性重摄取抑制剂和单胺氧化酶抑制剂都能显著升高血浆的 BDNF 水平(Sen, Duman, & Sanacora, 2008)。

研究表明, 某些膳食营养对血浆的 BDNF 水平有明确影响。一项对意外伤害患者的开放性试验发现, 服用 3 个月的 n-3PUFAs 补充剂能够显著增加血浆的 BDNF 水平, 同时降低创伤后应激的发生率(Matsuoka et al., 2011)。另一项对健康成年人的研究发现, 单次摄入高脂膳食就会使血浆中的 BDNF 水平下降近 30% (Karczewska-Kupczewska et al., 2012)。Sánchez-Villegas 和 Galbete 等(2011)在一项研究中对健康人群开展了为期 3 年的饮食干预, 结果发现, 与对照组相比, 采用地中海膳食模式能够升高血浆的 BDNF 水平, 且这种升高作用在有抑郁倾向的个体身上表现得最为明显。膳食营养对中枢神经系统内的 BDNF 产生影响的研究数据主要来自于动物实验。研究发现, 高碳水化合物饮食(Maioli et al., 2012)或高脂肪饮食(Yamada-Goto et al., 2012)会显著降低小鼠脑内 BDNF 的水平, 富含 n-3PUFAs 的食物(鱼油)则能通过升高大鼠海马内的 BDNF 水平产生抗抑郁作用(Vines et al., 2012)。

4 研究局限和展望

迄今为止, 膳食营养与抑郁症关联的证据主要来自人群流行病学调查, 研究方法本身的局限限制了结果的解释力。

首先, 人群调查样本量大的特点导致研究者在收集相关信息时倾向于采用操作相对简便的问卷法。譬如抑郁症的测量, 这类研究通常依赖自我报告性的抑郁症状量表如抑郁自评量表(Self-rating Depression Scale, SDS)和流调用抑郁自评量表(Center for Epidemiological Survey, Depression Scale, CES-D)等, 只有少量研究采用临床诊断作为抑郁症的判别标准(Sánchez-Villegas, Doreste, et al., 2009; Sánchez-Villegas, Verberne, et al., 2011)。量表的测量结果虽然能够反映抑郁症状的严重程度, 但是与临床诊断相比, 其校标效度偏低, 因而有可能导致比实际情况更强的相关关系(Lorant et al., 2003)。此外, 研究者在确定抑郁量表的临界值(cut-off point)时缺少固定的标准, 往往根据样本特征自行选择, 存在随意性。临床诊断的鉴别方法虽然工作量较大, 但准确性更高, 应该在未来的研究中更多采用。

其次, 以横断性为主的人群研究限制了因果关系的推断。实际上, 对这类研究一直存在一种质疑的声音, 即究竟是膳食习惯诱发了抑郁, 还是抑郁导致了某种膳食习惯? 这种质疑是有一定道理的, 因为有研究发现, 抑郁症患者在食物的选择上本就有别于非抑郁患者, 他们的饮食习惯似乎更不健康, 例如更偏好高脂和高糖类食品(Whitaker, Sharpe, Wilcox, & Hutto, 2014), 对水果和蔬菜的摄入较少(Payne, Steck, George, & Steffens, 2012)。虽然在最近的一项人群研究中, Jacka, Cherbuin, Anstey 和 Butterworth (2015)没有发现膳食与抑郁症之间存在反向因果关系(reverse causality)。但要想更好的回应这一质疑, 该领域应进一步增加前瞻性队列研究的比例。除此之外, 那些与膳食营养同时发生的, 与抑郁症有关联的其他因素也会增加研究结论的不确定性, 比如吸烟、饮酒、活动量等生活习惯以及人际关系、经济地位等社会特征。这些因素同时与饮食习惯和抑郁水平都有着密切的联系。虽然采用适当的统计方法可以排除其中一些因素的影响, 但研究者很难在一项研究考察到所有可能的混淆因素。克

服这一问题的有效途径是采用预先设计(priori design)的方法,在研究开始之前就将那些可能会有重要影响的混淆变量明确下来并加以考察。

未来的研究应在人群研究发现的基础上,更加深入的探讨膳食营养与抑郁症关联的内在机制及现实价值。现有的研究在探讨内在机制时往往遵循较为粗浅的逻辑,即已有研究证明某些营养或膳食模式对炎症、氧化应激和 BDNF 等生化指标有影响,而这些膳食营养又被发现与抑郁症存在关联,由此推断膳食营养是通过其中的某种机制发挥作用的(Lopresti, Hood, & Drummond, 2013)。这种推断虽有道理但大都是间接性的,未来的研究中应适当增加对相关生化指标如 CRP、IL-1、IL-6 和 TNF- α 等炎症指标和 SOD、GpX 和 8-OHdG 等氧化应激指标的测量,这将有助于更直接的考察膳食营养与抑郁症关联的内在机制。另外需要指出的是,在探讨抑郁症的发病机制时,遗传是一个不能忽略的重要因素,早期定量行为遗传学研究表明,遗传因素可解释抑郁 24%~55% 的变异(Rice, Harold, & Thapar, 2002)。研究者在对肥胖和 CVD 等慢性疾病的研究中已经发现了膳食对于遗传因素的效应修饰(effect modification)(Lairon et al., 2009),抑郁症尚缺少这类研究数据。

现实价值方面,现有的少量干预性研究考察的大都是一些特殊人群。如 Beezhold 和 Johnston (2012)发现,肉食个体在食用两周的素食后情绪明显改善。Ciarambino 等(2011)发现,6 天的低蛋白质饮食能够显著降低糖尿病患者的抑郁症状。还有一项对超重和肥胖人群的研究发现,低脂肪饮食改善心境的效果要好于低碳水化合物饮食(Brinkworth, Buckley, Noakes, Clifton, & Wilson, 2009)。未来要想使干预性的研究结果更具现实价值和推广意义,还应该着眼于更大规模的人群单位如公司、学校乃至社区层面,在一个更为动态的社会环境中考察膳食营养对抑郁症的预防和治疗效果。

总之,如果膳食营养和抑郁症之间的因果关系确实存在,只不过由于方法学等方面的原因还没有被充分发现,那么这种关系的确定对于临床和公共精神卫生都有着非常重要的意义。一方面,作为一种可控的风险因素,膳食营养为整体人群的初级预防提供了重要的途径;另一方面,作为一种相对安全的干预策略,膳食营养也为那些对

药物和心理治疗缺少应答的抑郁症患者提供了一个新的治疗选择。

参考文献

- 郭小月, 任俊, 郭建友. (2013). n-3 系多元不饱和脂肪酸对抑郁症的影响及其机制. *心理科学进展*, 21(3), 458-467.
- Akbaraly, T. N., Brunner, E. J., Ferrie, J. E., Marmot, M. G., Kivimaki, M., & Singh-Manoux, A. (2009). Dietary pattern and depressive symptoms in middle age. *The British Journal of Psychiatry*, 195(5), 408-413.
- Appleton, K. M., Rogers, P. J., & Ness, A. R. (2010). Updated systematic review and meta-analysis of the effects of n-3 long-chain polyunsaturated fatty acids on depressed mood. *The American Journal of Clinical Nutrition*, 91(3), 757-770.
- Baumgartner, J., Smuts, C. M., Malan, L., Arnold, M., Yee, B. K., Bianco, L. E., ..., Zimmermann, M. B. (2012). In male rats with concurrent iron and (n-3) fatty acid deficiency, provision of either iron or (n-3) fatty acids alone alters monoamine metabolism and exacerbates the cognitive deficits associated with combined deficiency. *The Journal of Nutrition*, 142(8), 1472-1478.
- Beezhold, B. L., & Johnston, C. S. (2012). Restriction of meat, fish, and poultry in omnivores improves mood: A pilot randomized controlled trial. *Nutrition Journal*, 11, 9. doi: 10.1186/1475-2891-11-9
- Berk, M., Williams, L. J., Jacka, F. N., O'Neil, A., Pasco, J. A., Moylan, S., ..., Maes, M. (2013). So depression is an inflammatory disease, but where does the inflammation come from? *BMC Medicine*, 11, 200. doi: 10.1186/1741-7015-11-200
- Beydoun, M. A., Shroff, M. R., Beydoun, H. A., & Zonderman, A. B. (2010). Serum folate, vitamin B-12, and homocysteine and their association with depressive symptoms among U.S. adults. *Psychosomatic Medicine*, 72(9), 862-873.
- Brinkworth, G. D., Buckley, J. D., Noakes, M., Clifton, P. M., & Wilson, C. J. (2009). Long-term effects of a very low-carbohydrate diet and a low-fat diet on mood and cognitive function. *Archives of Internal Medicine*, 169(20), 1873-1880.
- Ciarambino, T., Ferrara, N., Castellino, P., Paolisso, G., Coppola, L., & Giordano, M. (2011). Effects of a 6-days-a-week low protein diet regimen on depressive symptoms in young-old type 2 diabetic patients. *Nutrition*, 27(1), 46-49.
- Cope, E. C., & Levenson, C. W. (2010). Role of zinc in the development and treatment of mood disorders. *Current Opinion in Clinical Nutrition and Metabolic Care*, 13(6), 685-689.

- Esposito, K., Di Palo, C., Maiorino, M. I., Petrizzo, M., Bellastella, G., Siniscalchi, I., & Giugliano, D. (2011). Long-term effect of mediterranean-style diet and calorie restriction on biomarkers of longevity and oxidative stress in overweight men. *Cardiology Research and Practice*, 2011, 293916. doi: 10.4061/2011/293916
- Feng, L., Li, J. L., Kua, E. H., Lee, T. S., Yap, K. B., John Rush, A., & Ng, T. P. (2012). Association between tea consumption and depressive symptoms in older Chinese adults. *Journal of the American Geriatrics Society*, 60(12), 2358–2360.
- Feng, L., Yan, Z. R., Sun, B. L., Cai, C. Z., Jiang, H., Kua, E. H.,..... Qiu, C. X. (2013). Tea consumption and depressive symptoms in older people in rural China. *Journal of the American Geriatrics Society*, 61(11), 1943–1947.
- Forti, P., Rietti, E., Pisacane, N., Olivelli, V., Dalmonte, E., Mecocci, P., & Ravaglia, G. (2010). Blood homocysteine and risk of depression in the elderly. *Archives of Gerontology and Geriatrics*, 51(1), 21–25.
- Fung, T. T., Rimm, E. B., Spiegelman, D., Rifai, N., Tofler, G. H., Willett, W. C., & Hu, F. B. (2001). Association between dietary patterns and plasma biomarkers of obesity and cardiovascular disease risk. *The American Journal of Clinical Nutrition*, 73(1), 61–67.
- Gao, S. J., Jin, Y. L., Unverzagt, F. W., Liang, C. K., Hall, K. S., Cao, J. X.,..... Hendrie, H. C. (2012). Selenium level and depressive symptoms in a rural elderly Chinese cohort. *BMC Psychiatry*, 12, 72. doi: 10.1186/1471-244X-12-72
- Gilbody, S., Lightfoot, T., & Sheldon, T. (2007). Is low folate a risk factor for depression? A meta-analysis and exploration of heterogeneity. *Journal of Epidemiology and Community Health*, 61(7), 631–637.
- Guo, X. G., Park, Y., Freedman, N. D., Sinha, R., Hollenbeck, A. R., Blair, A., & Chen, H. L. (2014). Sweetened beverages, coffee, and tea and depression risk among older US adults. *PLoS One*, 9(4), e94715.
- Hakkarainen, R., Partonen, T., Haukka, J., Virtamo, J., Albanes, D., & Lönngqvist, J. (2004). Is low dietary intake of omega-3 fatty acids associated with depression? *The American Journal of Psychiatry*, 161(3), 567–569.
- Hibbeln, J. R. (1998). Fish consumption and major depression. *Lancet*, 351(9110), 1213.
- Howren, M. B., Lamkin, D. M., & Suls, J. (2009). Associations of depression with C-reactive protein, IL-1, and IL-6: A meta-analysis. *Psychosomatic Medicine*, 71(2), 171–186.
- Hu, F. B. (2002). Dietary pattern analysis: A new direction in nutritional epidemiology. *Current Opinion in Lipidology*, 13(1), 3–9.
- Jacka, F. N., Cherbuin, N., Anstey, K. J., & Butterworth, P. (2015). Does reverse causality explain the relationship between diet and depression? *Journal of Affective Disorders*, 175, 248–250.
- Jacka, F. N., Kremer, P. J., Berk, M., de Silva-Sanigorski, A. M., Moodie, M., Leslie, E. R.,..... Swinburn, B. A. (2011). A prospective study of diet quality and mental health in adolescents. *PLoS One*, 6(9), e24805.
- Jacka, F. N., Pasco, J. A., Mykletun, A., Williams, L. J., Hodge, A. M., O'Reilly, S. L.,..... Berk, M. (2010). Association of Western and traditional diets with depression and anxiety in women. *The American Journal of Psychiatry*, 167(3), 305–311.
- Jacobs, D. R., Jr., Andersen, L. F., & Blomhoff, R. (2007). Whole-grain consumption is associated with a reduced risk of noncardiovascular, noncancer death attributed to inflammatory diseases in the Iowa Women's Health Study. *The American Journal of Clinical Nutrition*, 85(6), 1606–1614.
- Karczewska-Kupczewska, M., Kowalska, I., Nikolajuk, A., Adamska, A., Zielinska, M., Kaminska, N.,..... Straczkowski, M. (2012). Circulating brain-derived neurotrophic factor concentration is downregulated by intralipid/heparin infusion or high-fat meal in young healthy male subjects. *Diabetes Care*, 35(2), 358–362.
- Kiecolt-Glaser, J. K. (2010). Stress, food, and inflammation: Psychoneuroimmunology and nutrition at the cutting edge. *Psychosomatic Medicine*, 72(4), 365–369.
- Kohlboeck, G., Sausenthaler, S., Standl, M., Koletzko, S., Bauer, C. P., von Berg, A.,..... Heinrich, J. I. (2012). Food intake, diet quality and behavioral problems in children: Results from the GINI-plus/LISA-plus studies. *Annals of Nutrition & Metabolism*, 60(4), 247–256.
- Lai, J. S., Hiles, S., Bisquera, A., Hure, A. J., McEvoy, M., & Attia, J. (2014). A systematic review and meta-analysis of dietary patterns and depression in community-dwelling adults. *The American Journal of Clinical Nutrition*, 99(1), 181–197.
- Lairon, D., Defoort, C., Martin, J. C., Amiot-Carlin, M. J., Gastaldi, M., & Planells, R. (2009). Nutrigenetics: Links between genetic background and response to Mediterranean-type diets. *Public Health Nutrition*, 12(9A), 1601–1606.
- Le Port, A., Gueguen, A., Kesse-Guyot, E., Melchior, M., Lemogne, C., Nabi, H.,..... Czernichow, S. (2012). Association between dietary patterns and depressive symptoms over time: A 10-year follow-up study of the GAZEL cohort. *PLoS One*, 7(12), e51593.
- Lee, B. H., & Kim, Y. K. (2010). The roles of BDNF in the pathophysiology of major depression and in antidepressant treatment. *Psychiatry Investigation*, 7(4), 231–235.
- Lee, Y. J., Choi, B., Lee, E. H., Choi, K. S., & Sohn, S. (2006). Immobilization stress induces cell death through

- production of reactive oxygen species in the mouse cerebral cortex. *Neuroscience Letters*, 392(1-2), 27–31.
- Lin, P. Y., Huang, S. Y., & Su, K. P. (2010). A meta-analytic review of polyunsaturated fatty acid compositions in patients with depression. *Biological Psychiatry*, 68(2), 140–147.
- Liu, Y., Ho, R. C., & Mak, A. (2012). Interleukin (IL)-6, tumour necrosis factor alpha (TNF- α) and soluble interleukin-2 receptors (sIL-2R) are elevated in patients with major depressive disorder: A meta-analysis and meta-regression. *Journal of Affective Disorders*, 139(3), 230–239.
- Lobato, K. R., Cardoso, C. C., Binfare, R. W., Budni, J., Wagner, C. L., Brocardo, P. S.,..... Rodrigues, A. L. (2010). α -Tocopherol administration produces an antidepressant-like effect in predictive animal models of depression. *Behavioural Brain Research*, 209(2), 249–259.
- Lopresti, A. L., Hood, S. D., & Drummond, P. D. (2013). A review of lifestyle factors that contribute to important pathways associated with major depression: Diet, sleep and exercise. *Journal of Affective Disorders*, 148(1), 12–27.
- Lorant, V., Deliege, D., Eaton, W., Robert, A., Philippot, P., & Anseau, M. (2003). Socioeconomic inequalities in depression: A meta-analysis. *American Journal of Epidemiology*, 157(2), 98–112.
- Lucas, M., Chocano-Bedoya, P., Shulze, M. B., Mirzaei, F., O'Reilly, É. J., Okereke, O. I.,..... Ascherio, A. (2014). Inflammatory dietary pattern and risk of depression among women. *Brain, Behavior, and Immunity*, 36, 46–53.
- Lucas, M., Mirzaei, F., Pan, A., Okereke, O. I., Willett, W. C., O'Reilly, É. J.,..... Ascherio, A. (2011). Coffee, caffeine, and risk of depression among women. *Archives of Internal Medicine*, 171(17), 1571–1578.
- Luciano, M., Möttus, R., Starr, J. M., McNeill, G., Jia, X. L., Craig, L. C., & Deary, I. J. (2012). Depressive symptoms and diet: Their effects on prospective inflammation levels in the elderly. *Brain, Behavior, and Immunity*, 26(5), 717–720.
- Luppino, F. S., de Wit, L. M., Bouvy, P. F., Stijnen, T., Cuijpers, P., Penninx, B. W., & Zitman, F. G. (2010). Overweight, obesity, and depression: A systematic review and meta-analysis of longitudinal studies. *Archives of General Psychiatry*, 67(3), 220–229.
- Maes, M., Galecki, P., Chang, Y. S., & Berk, M. (2011). A review on the oxidative and nitrosative stress (O&NS) pathways in major depression and their possible contribution to the (neuro)degenerative processes in that illness. *Progress in Neuro-psychopharmacology & Biological Psychiatry*, 35(3), 676–692.
- Maioli, S., Puerta, E., Merino-Serrais, P., Fusari, L., Gil-Bea, F., Rimondini, R., & Cedazo-Minguez, A. (2012). Combination of apolipoprotein E4 and high carbohydrate diet reduces hippocampal BDNF and arc levels and impairs memory in young mice. *Journal of Alzheimer's Disease*, 32(2), 341–355.
- Maletic, V., Robinson, M., Oakes, T., Iyengar, S., Ball, S. G., & Russell, J. (2007). Neurobiology of depression: An integrated view of key findings. *International Journal of Clinical Practice*, 61(12), 2030–2040.
- Mamplakou, E., Bountziouka, V., Psaltopoulou, T., Zeimbekis, A., Tsakoundakis, N., Papaerakleous, N.,..... Panagiotakos, D. (2010). Urban environment, physical inactivity and unhealthy dietary habits correlate to depression among elderly living in eastern Mediterranean islands: The MEDIS (MEDiterranean ISlands Elderly) study. *The Journal of Nutrition, Health & Aging*, 14(6), 449–455.
- Markus, C. R. (2008). Dietary amino acids and brain serotonin function; implications for stress-related affective changes. *Neuromolecular Medicine*, 10(4), 247–258.
- Matsuoka, Y., Nishi, D., Yonemoto, N., Hamazaki, K., Hamazaki, T., & Hashimoto, K. (2011). Potential role of brain-derived neurotrophic factor in omega-3 Fatty Acid supplementation to prevent posttraumatic distress after accidental injury: An open-label pilot study. *Psychotherapy and Psychosomatics*, 80(5), 310–312.
- Mitrou, P. N., Kipnis, V., Thiébaud, A. C., Reedy, J., Subar, A. F., Wirfält, E.,..... Schatzkin, A. (2007). Mediterranean dietary pattern and prediction of all-cause mortality in a US population: Results from the NIH-AARP Diet and Health Study. *Archives of Internal Medicine*, 167(22), 2461–2468.
- Morrison, C. D., Pistell, P. J., Ingram, D. K., Johnson, W. D., Liu, Y., Fernandez-Kim, S. O.,..... Keller, J. N. (2010). High fat diet increases hippocampal oxidative stress and cognitive impairment in aged mice: Implications for decreased Nrf2 signaling. *Journal of Neurochemistry*, 114(6), 1581–1589.
- Moylan, S., Berk, M., Dean, O. M., Samuni, Y., Williams, L. J., O'Neil, A.,..... Maes, M. (2014). Oxidative & nitrosative stress in depression: Why so much stress? *Neuroscience and Biobehavioral Reviews*, 45, 46–62.
- Murakami, K., Mizoue, T., Sasaki, S., Ohta, M., Sato, M., Matsushita, Y., & Mishima, N. (2008). Dietary intake of folate, other B vitamins, and ω -3 polyunsaturated fatty acids in relation to depressive symptoms in Japanese adults. *Nutrition*, 24(2), 140–147.
- Nanri, A., Kimura, Y., Matsushita, Y., Ohta, M., Sato, M., Mishima, N.,..... Mizoue, T. (2010). Dietary patterns and depressive symptoms among Japanese men and women. *European Journal of Clinical Nutrition*, 64(8), 832–839.
- Niu, K., Guo, H., Kakizaki, M., Cui, Y., Ohmori-Matsuda, K., Guan, L.,..... Nagatomi, R. (2013). A tomato-rich diet is related to depressive symptoms among an elderly population aged 70 years and over: A population-based,

- cross-sectional analysis. *Journal of Affective Disorders*, 144(1-2), 165–170.
- Niu, K., Hozawa, A., Kuriyama, S., Ebihara, S., Guo, H., Nakaya, N.,..... Tsuji, I. (2009). Green tea consumption is associated with depressive symptoms in the elderly. *The American Journal of Clinical Nutrition*, 90(6), 1615–1622.
- Papakostas, G. I., Shelton, R. C., Zajecka, J. M., Etemad, B., Rickels, K., Clain, A.,..... Fava, M. (2012). L-methylfolate as adjunctive therapy for SSRI-resistant major depression: Results of two randomized, double-blind, parallel-sequential trials. *The American Journal of Psychiatry*, 169(12), 1267–1274.
- Parletta, N., Milte, C. M., & Meyer, B. J. (2013). Nutritional modulation of cognitive function and mental health. *The Journal of Nutritional Biochemistry*, 24(5), 725–743.
- Pasco, J. A., Jacka, F. N., Williams, L. J., Evans-Cleverdon, M., Brennan, S. L., Kotowicz, M. A.,..... Berk, M. (2012). Dietary selenium and major depression: A nested case-control study. *Complementary Therapies in Medicine*, 20(3), 119–123.
- Payne, M. E., Jamerson, B. D., Potocky, C. F., Ashley-Koch, A. E., Speer, M. C., & Steffens, D. C. (2009). Natural food folate and late-life depression. *Journal of Nutrition for the Elderly*, 28(4), 348–358.
- Payne, M. E., Steck, S. E., George, R. R., & Steffens, D. C. (2012). Fruit, vegetable, and antioxidant intakes are lower in older adults with depression. *Journal of the Academy of Nutrition and Dietetics*, 112(12), 2022–2027.
- Phillips, M. R., Zhang, J. X., Shi, Q. C., Song, Z. Q., Ding, Z. J., Pang, S. T.,..... Wang, Z. Q. (2009). Prevalence, treatment, and associated disability of mental disorders in four provinces in China during 2001-05: An epidemiological survey. *The Lancet*, 373(9680), 2041–2053.
- Rangel-Huerta, O. D., Aguilera, C. M., Mesa, M. D., & Gil, A. (2012). Omega-3 long-chain polyunsaturated fatty acids supplementation on inflammatory biomarkers: A systematic review of randomised clinical trials. *The British Journal of Nutrition*, 107(S2), S159–S170.
- Ranjbar, E., Shams, J., Sabetkasaei, M., M, M. S., Rashidkhani, B., Mostafavi, A.,..... Nasrollahzadeh, J. (2014). Effects of zinc supplementation on efficacy of antidepressant therapy, inflammatory cytokines, and brain-derived neurotrophic factor in patients with major depression. *Nutritional Neuroscience*, 17(2), 65–71.
- Reynolds, E. H., Preece, J. M., Bailey, J., & Coppen, A. (1970). Folate deficiency in depressive illness. *The British Journal of Psychiatry : The Journal of Mental Science*, 117(538), 287–292.
- Rice, F., Harold, G. T., & Thapar, A. (2002). Assessing the effects of age, sex and shared environment on the genetic aetiology of depression in childhood and adolescence. *Journal of Child Psychology and Psychiatry*, 43(8), 1039–1051.
- Richard, C., Couture, P., Desroches, S., & Lamarche, B. (2013). Effect of the Mediterranean diet with and without weight loss on markers of inflammation in men with metabolic syndrome. *Obesity*, 21(1), 51–57.
- Rienks, J., Dobson, A. J., & Mishra, G. D. (2013). Mediterranean dietary pattern and prevalence and incidence of depressive symptoms in mid-aged women: Results from a large community-based prospective study. *European Journal of Clinical Nutrition*, 67(1), 75–82.
- Ruusunen, A., Lehto, S. M., Mursu, J., Tolmunen, T., Tuomainen, T. P., Kauhanen, J., & Voutilainen, S. (2014). Dietary patterns are associated with the prevalence of elevated depressive symptoms and the risk of getting a hospital discharge diagnosis of depression in middle-aged or older Finnish men. *Journal of Affective Disorders*, 159, 1–6.
- Ruusunen, A., Lehto, S. M., Tolmunen, T., Mursu, J., Kaplan, G. A., & Voutilainen, S. (2010). Coffee, tea and caffeine intake and the risk of severe depression in middle-aged Finnish men: The Kuopio Ischaemic Heart Disease Risk Factor Study. *Public Health Nutrition*, 13(8), 1215–1220.
- Sánchez-Villegas, A., Delgado-Rodríguez, M., Alonso, A., Schlatter, J., Lahortiga, F., Serra Majem, L., & Martínez-González, M. A. (2009). Association of the Mediterranean dietary pattern with the incidence of depression: The Seguimiento Universidad de Navarra/ University of Navarra follow-up (SUN) cohort. *Archives of General Psychiatry*, 66(10), 1090–1098.
- Sánchez-Villegas, A., Doreste, J., Schlatter, J., Pla, J., Bes-Rastrollo, M., & Martínez-González, M. A. (2009). Association between folate, vitamin B₆ and vitamin B₁₂ intake and depression in the SUN cohort study. *Journal of Human Nutrition and Dietetics*, 22(2), 122–133.
- Sánchez-Villegas, A., Galbete, C., Martínez-González, M. Á., Martínez, J. A., Razquin, C., Salas-Salvadó, J.,..... Martí, A. (2011). The effect of the Mediterranean diet on plasma brain-derived neurotrophic factor (BDNF) levels: The PREDIMED-NAVARRA randomized trial. *Nutritional Neuroscience*, 14(5), 195–201.
- Sánchez-Villegas, A., Verberne, L., De Irala, J., Ruiz-Canela, M., Toledo, E., Serra-Majem, L., & Martínez-González, M. A. (2011). Dietary fat intake and the risk of depression: The SUN Project. *PloS One*, 6(1), e16268.
- Sen, S., Duman, R., & Sanacora, G. (2008). Serum brain-derived neurotrophic factor, depression, and antidepressant medications: Meta-analyses and implications. *Biological psychiatry*, 64(6), 527–532.

- Shi, Z., Taylor, A. W., Wittert, G., Goldney, R., & Gill, T. K. (2010). Soft drink consumption and mental health problems among adults in Australia. *Public Health Nutrition*, 13(7), 1073–1079.
- Silvers, K. M., & Scott, K. M. (2002). Fish consumption and self-reported physical and mental health status. *Public Health Nutrition*, 5(3), 427–431.
- Skarupski, K. A., Tangney, C., Li, H., Ouyang, B., Evans, D. A., & Morris, M. C. (2010). Longitudinal association of vitamin B-6, folate, and vitamin B-12 with depressive symptoms among older adults over time. *The American Journal of Clinical Nutrition*, 92(2), 330–335.
- Skarupski, K. A., Tangney, C. C., Li, H., Evans, D. A., & Morris, M. C. (2013). Mediterranean diet and depressive symptoms among older adults over time. *The Journal of Nutrition, Health & Aging*, 17(5), 441–445.
- Smith, K. J., Sanderson, K., McNaughton, S. A., Gall, S. L., Dwyer, T., & Venn, A. J. (2014). Longitudinal associations between fish consumption and depression in young adults. *American Journal of Epidemiology*, 179(10), 1228–1235.
- Stewart, R., & Hirani, V. (2012). Relationship between depressive symptoms, anemia, and iron status in older residents from a national survey population. *Psychosomatic Medicine*, 74(2), 208–213.
- Strom, M., Mortensen, E. L., Halldorsson, T. I., Thorsdottir, I., & Olsen, S. F. (2009). Fish and long-chain n-3 polyunsaturated fatty acid intakes during pregnancy and risk of postpartum depression: A prospective study based on a large national birth cohort. *The American Journal of Clinical Nutrition*, 90(1), 149–155.
- Szewczyk, B., Poleszak, E., Wlaz, P., Wróbel, A., Blicharska, E., Cichy, A.,.... Nowak, G. (2009). The involvement of serotonergic system in the antidepressant effect of zinc in the forced swim test. *Progress in Neuro-psychopharmacology & Biological Psychiatry*, 33(2), 323–329.
- Tanskanen, A., Hibbeln, J. R., Tuomilehto, J., Uutela, A., Haukkala, A., Viinamäki, H.,.... Vartiainen, E. (2001). Fish consumption and depressive symptoms in the general population in Finland. *Psychiatric Services*, 52(4), 529–531.
- Timonen, M., Horrobin, D., Jokelainen, J., Laitinen, J., Herva, A., & Räsänen, P. (2004). Fish consumption and depression: The Northern Finland 1966 birth cohort study. *Journal of Affective Disorders*, 82(3), 447–452.
- Trichopoulou, A., Costacou, T., Bamia, C., & Trichopoulos, D. (2003). Adherence to a Mediterranean diet and survival in a Greek population. *The New England Journal of Medicine*, 348(26), 2599–2608.
- Urpi-Sarda, M., Casas, R., Chiva-Blanch, G., Romero-Mamani, E. S., Valderas-Martinez, P., Salas-Salvado, J.,.... Estruch, R. (2012). The Mediterranean diet pattern and its main components are associated with lower plasma concentrations of tumor necrosis factor receptor 60 in patients at high risk for cardiovascular disease. *The Journal of Nutrition*, 142(6), 1019–1025.
- Vines, A., Delattre, A. M., Lima, M. M., Rodrigues, L. S., Suchecki, D., Machado, R. B.,.... Ferraz, A. C. (2012). The role of 5-HT_{1A} receptors in fish oil-mediated increased BDNF expression in the rat hippocampus and cortex: A possible antidepressant mechanism. *Neuropharmacology*, 62(1), 184–191.
- Vos, T., Flaxman, A. D., Naghavi, M., Lozano, R., Michaud, C., Ezzati, M.,.... Memish, Z. A. (2012). Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet*, 380(9859), 2163–2196.
- Weng, T. T., Hao, J. H., Qian, Q. W., Cao, H., Fu, J. L., Sun, Y.,.... Tao, F. B. (2012). Is there any relationship between dietary patterns and depression and anxiety in Chinese adolescents? *Public Health Nutrition*, 15(4), 673–682.
- Whitaker, K. M., Sharpe, P. A., Wilcox, S., & Hutto, B. E. (2014). Depressive symptoms are associated with dietary intake but not physical activity among overweight and obese women from disadvantaged neighborhoods. *Nutrition Research*, 34(4), 294–301.
- World Health Organization. (2008). Burden of disease: DALYs. *The global burden of disease: 2004 update* (pp. 40–49). Geneva: WHO.
- Yamada-Goto, N., Katsuura, G., Ochi, Y., Ebihara, K., Kusakabe, T., Hosoda, K., & Nakao, K. (2012). Impairment of fear-conditioning responses and changes of brain neurotrophic factors in diet-induced obese mice. *Journal of Neuroendocrinology*, 24(8), 1120–1125.
- Yi, S., Nanri, A., Poudel-Tandukar, K., Nonaka, D., Matsushita, Y., Hori, A., & Mizoue, T. (2011). Association between serum ferritin concentrations and depressive symptoms in Japanese municipal employees. *Psychiatry Research*, 189(3), 368–372.
- Yu, B., He, H. Y., Zhang, Q., Wu, H. M., Du, H. M., Liu, L.,.... Niu, K. J. (2015). Soft drink consumption is associated with depressive symptoms among adults in China. *Journal of Affective Disorders*, 172C, 422–427.
- Zhu, W. L., Shi, H. S., Wei, Y. M., Wang, S. J., Sun, C. Y., Ding, Z. B., & Lu, L. (2012). Green tea polyphenols produce antidepressant-like effects in adult mice. *Pharmacological Research*, 65(1), 74–80.

Diet, Nutrition, and Depression

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Abstract: The association between diet, nutrition and depression has become of increasing interest in recent decades. In the past, most studies have focused on the association of depression with specific nutrients or foods, within which n-3 polyunsaturated fatty acids (n-3PUFAs) and folate have received significant attention. There has been a shift in focus from the study of single nutrient or food toward total diet and dietary patterns in recent years. Mechanisms of action proposed to explain these consistent relationships include inflammatory processes, oxidative stress and brain-derived neurotrophic factor (BDNF). A limitation associated with many of the studies reviewed is that significant portions were correlational and/or epidemiological, thereby limiting conclusions about causation. Further studies with emphasis on the investigation of the underlying mechanism and applying values are necessary to confirm the findings obtained in these initial studies.

Key words: depression; diet; nutrition; dietary patterns