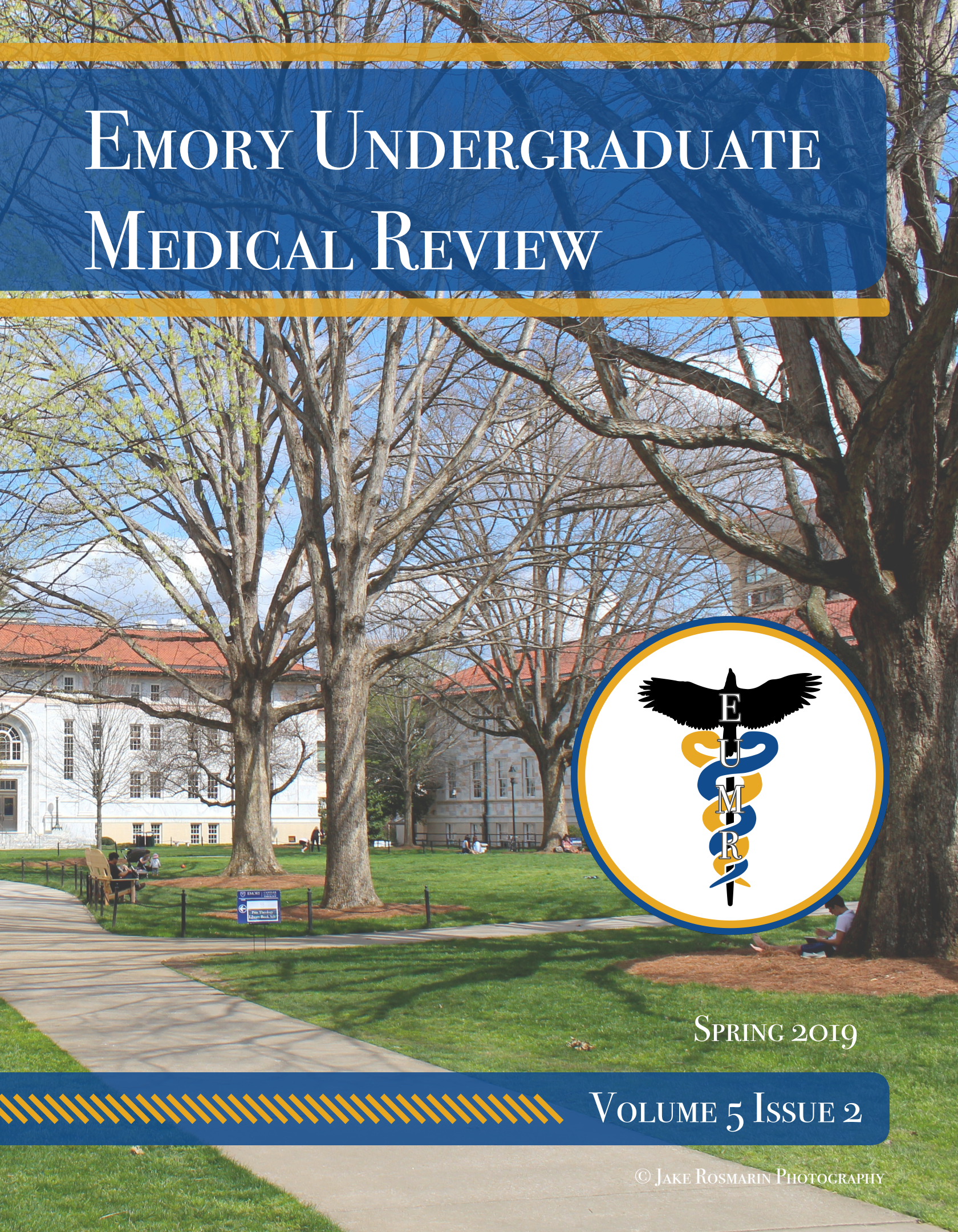
Emory Undergraduate Medical Review



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About EUMR

Mission Statement

The Emory Undergraduate Medical Review (EUMR) publishes a semesterly journal that features faculty and student-authored articles on cutting-edge medical issues. Our interdisciplinary articles span various clinical fields and are peer reviewed by medical professionals from more than a dozen leading academic institutions including Emory University, Yale University, and the Mayo Clinic.

In addition to our publication, EUMR hosts various medically-related events on campus, including collaborations with the School of Medicine. Our projects have been featured by Emory's News Center and have caught the attention of President Sterk.

Our Advisor

Dr. Michael Crutcher, PhD

Emory

Dr. Michael Crutcher is one of the many distinguished faculty members in Emory's Neuroscience and Behavioral Biology Department. Having received his PhD in Physiology from Johns Hopkins University, he joined the Department of Neurology and of the Neuroscience Ph.D. program at Emory in 1991. His research is primarily focused on the neural mechanisms of visually guided reaching movements in monkeys.

Dr. Crutcher has taught many NBB courses over the years such as: freshman seminar courses (NBB 190) on Brain Enhancement, Curiosities of Neurology and Neuroscience, and Neuroethics as well as Perspectives in Neuroscience and Behavioral Biology (NBB 401 SWR), Biology of Movement Control (NBB 370), Neuroscience Research Methods (NBB 221), Functional Neuroanatomy (NBB 470), and Topics in Neuroscience and Behavioral Biology (NBB 270).

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Is Buying Organic Truly Beneficial For Your Health?

Authored by: Emily Maccabee
Edited by: Hannah Kelly **Reviewed by: Dr. Tyler Cymet**

It is becoming increasingly confusing for people to choose which foods are best for them. Between social media and trendy diets, it is hard to know what is truly beneficial for one's health. A common confusing area is organic foods and whether they are actually healthy or not. "Organic" is defined as relating to or belonging to the class of chemical compounds with a carbon basis. Scientific opinion is divided on whether there are significant nutritional differences between organic and non-organic foods. Organic food has been thought to contain more antioxidant compounds linked to better health than non-organic food and contains lower levels of toxic metals and pesticides, according to some scientific analyses to date (Baranski, 2014). Yet, other studies have found no substantial differences or significant nutritional benefits from consuming organically-grown foods over foods and crops grown using traditional methods (Baranski, 2014). This article aims to analyze the medical benefits and potential drawbacks of eating organic foods and to offer guidance on choosing organic produce if the benefits outweigh the costs.

The US organic industry is one of the fastest-growing sectors in the food industry. At 42%, fruits and vegetables account for the largest portion of organic sales. According to the Organic Trade Association Manufacturer Survey, switching to organic fruits and vegetables could yield the same benefits as adding one or two portions of the recommended "five a day," which encompasses the five recommended portions of fruits and vegetables.

> "According to Newcastle University's Professor Carlo Leifert, 'this study demonstrates that choosing food produced according to organic standards can lead to increased intake of nutritionally-desirable antioxidants and reduced exposure to toxic heavy metals' (Baranki, 2014)."

Researchers have found a 30% lower rate of detectable contamination by pesticide residues in organically-grown produce. Two studies found that children who ate conventional produce had higher levels of pesticide residues in their urine, and that these levels fell when children switched to eating organic foods. Once ingested, phytoestrogenic and xenoestrogenic chemicals can disrupt the endocrine system by mimicking the effects of estrogen in the body. This ultimately leads to a continuous increase in estrogen levels and can cause weight gain. Additionally, herbicides and pesticides disrupt male hormones. Atrazine, for example, is one of the most common chemicals used on crops, especially corn. It mimics estrogen and also disrupts testosterone and androgen. These pesticides and herbicides are typically used on non-organically genetically modified crops to create processed foods that line the grocery shelves. These same crops are also the basis for animal feed that is fed to factory-farmed meats and fish (Holzman, 2012).

What about the food animals eat? Antibiotics and hormones are used in animal feed to prevent disease and make animals grow faster; the food animals consume comprises 70% of the total antibiotics used in America, including antibiotics utilized for treating human disease, such as penicillin, tetracycline, and erythromycin. This overuse of antibiotics has been shown to increase antibiotic-resistant bacteria in animals, and consequently, increases drug-resistant infections in people (Holzman, 2012).

Organic meat and dairy also have their pros and cons. A study finds that organic dairy and meat contain about 50% more omega-3 fatty acids (Mitchell, Hong, & Koh, 2007). These fatty acids are thought to decrease anxiety and depression, promote brain health (specifically during pregnancy and early life) and heart health, reduce symptoms of metabolic syndrome, fight inflammation and autoimmune diseases,decrease this risk of mental disorders, reduce risk of cancer, lower fat levels in the liver, promote bone and joint health, improve sleep, and many more benefits (Holzman, 2012). This increase is due to animals foraging on grasses rich in these nutrients, which consequently end up in dairy and meats. The findings are based on data

pooled from more than 200 studies, and research in the US has pointed to similar benefits (Benbrook, 2013; (Holzman, 2012).

Furthermore, Charles Benbrook, a professor of Agriculture at Washington State University and former chief scientist at the Organic Center, claims that several well-designed US studies have shown that organic crops have higher concentrations of antioxidants and vitamins than conventional crops. For crops such as apples, strawberries, grapes, tomatoes, milk, carrots, and grains, organic produce has 10-30% higher levels of several nutrients, including vitamin C, antioxidants, and phenolic acids, as reported in most studies (Holzman, 2012). Moreover, a study published in 2014 in the British Journal of Nutrition found that organic crops-- ranging from carrots and broccoli to apples and blueberries-- have higher concentrations of antioxidants and other beneficial compounds. The study claims that organic crops contain about 50% more anthocyanins and flavonols compared with conventional crops. Anthocyanins, compounds linked to anti-inflammatory effects, give fruits and vegetables such as blueberries their dark hues. Flavonols have been shown to protect against cell damage and enhance the immune system's ability to combat disease (Barański et al., 2016).

Organic crops tend to be exposed to higher levels of stress to fend off insects that would have normally been avoided due to pesticide use. In organic agriculture, the produce fends for itself by producing polyacetylenes, which reduce inflammation and cancer risk (Holzman, 2012). That being said, the amount that must be eaten to benefit human health remains unclear. Also, organic produce does not contain nitrogen from synthetic fertilizers as conventional crops do, and as a result, organic crops tend to grow more slowly and produce more secondary plant metabolites. This boils down to increasing the concentration of flavonoids even more, such as quercetin (MITCHELL, A., HONG, Y., & KOH, E. (2007). In addition to lower levels of pesticide residues and increased antioxidants, there are lower concentrations of the metal cadmium, also found in soil, which can cause neurological adverse health effects (Średnicka-Tober & Barański, 2016).

Even with all of the benefits, plenty of people are still reluctant to buy organic. Professor of nutrition Ian Givens at the University of Reading claims that organic farming only represents a marginal increase in nutritional or health benefits. He points out that dairy products would only increase omega-3 intake by small amounts (Średnicka-Tober, D., & Barański, M. (2016). An analysis by researchers at Stanford University published several years ago concluded there was no legitimate evidence that organic fruits and vegetables were more nutritious overall (Smith-Spangler, 2012). Additionally, organic crops that may have higher levels of antioxidants do not consistently have higher levels of vitamins. Vitamin E, for example, did not vary much between organic vs. non-organic farming in one study (Holzman, 2012).

The verdict? A majority of people (65%) who estimate that most or some of their diet is organic believe that food additives pose a serious risk to health over a person's lifetime, versus 41% among those who report eating little to no organic foods . More specifically, 42% of U.S. adults who say most or some of the food they eat is organic believe that eating fruits and vegetables grown with pesticides poses serious health risks for the average person over their lifetime. In comparison, just 25% of those who eat little or no organic food share that view (Benbrook, et. al., 2013).

Overall, potential nutritional benefits are supported by scientific research; however, the amount of benefit has been proven to be marginal when compared to non-organically grown foods.

Nevertheless, this area of research is just beginning to evolve and is focusing on antibiotic resistance, environmental effects of agricultural shifts to organically-grown foods, the effects of toxins in conventionally-grown foods, and more. It is difficult to predict what will happen in terms of conclusive evidence with this topic, but as for now, the general population and scientists are rather divided in their thoughts on the benefits of organic versus non-organically grown foods.

Many claims have been circulating, claiming organic, colorful fresh fruits and vegetables are necessary for optimal health, however there is less attention devoted to the published studies that counter this.

Organic farmers boast growing crops without the pesticides and toxic metals, however, studies have shown that organic agriculture only improves health by a marginal level.

References

Baranski, M. (2014). Organic vs non-organic food. British Journal of Nutrition,115, 994-1011. Retrieved February 6, 2019, from https://research.ncl.ac.uk/nefg/QOF/page.php?page=1.

Beckett, E. (2017, August 29). Challenging idea organic fruits, vegetables more nutritious, better for the environment. Retrieved March 18, 2019.

Holzman, D. C. (2012). Organic Food Conclusions Don't Tell the Whole Story. Environmental Health Perspectives, 120(12), 458A. doi:https://doi.org/10.1289/ehp.120-a458

Średnicka-Tober, D., & Barański, M. (2016). Higher PUFA and n-3 PUFA, conjugated linoleic acid, α-tocopherol and iron, but lower iodine and selenium concentrations in organic milk: A systematic literature review and meta- and redundancy analyses. British Journal of Nutrition, 115(6), 1043-1060. doi:10.1017/S0007114516000349

Benbrook, C. M., Butler, G., Latif, M. A., Leifert, C., & Davis, D. R. (2013). Organic Production Enhances Milk Nutritional Quality by Shifting Fatty Acid Composition: A United States–Wide, 18-Month Study. PLoS ONE,8(12), 1-13. doi:10.1371/journal.pone.0082429

Barański, M., Volakakis, N., & Srednicka-Tober, D. (2014). Higher antioxidant and lower cadmium concentrations and lower incidence of pesticide residues in organically grown crops: A systematic literature review and meta-analyses. British Journal of Nutrition, 112(5), 794-811. doi:10.1017/S0007114514001366

Mitchell, A., Hong, Y., Koh, E. (2007). Ten-Year Comparison of the Influence of Organic and Conventional Crop Management Practices on the Content of Flavonoids in Tomatoes. J. Agric. Food Chem, 55, 6154-6159. Retrieved February 6, 2019.

Sean, C. (2016, November 3). Department to look at possibility of reopening Organic Farming Scheme. Retrieved March 18, 2019, from https://www.agriland.ie/farming-news/department-to-look-at-possibility-of-reopening-organic-farming-scheme/

Smith-Spangler, C., Brandeau, M. L., Hunter, G. E., & Bavinger, J. C. (2012). Are Organic Foods Safer or Healthier Than Conventional Alternatives?: A Systematic Review. Annals of Internal Medicine, 157(5), 348-366. doi:10.7326/0003-4819-157-5-201209040-00007

Image Citations

Beckett, E. (2017, August 29). Challenging idea organic fruits, vegetables more nutritious, better for the environment. Retrieved March 18, 2019, from https://geneticliteracyproject.org/2017/08/29/think-organic-vegetables-fruit-offer-nutritional-environmental-benefits/

Sean, C. (2016, November 3). Department to look at possibility of reopening Organic Farming Scheme. Retrieved March 18, 2019, from https://www.agriland.ie/farming-news/department-to-look-at-possibility-of-reopening-organic-farming-scheme/

Disparities in Care: Racial and Religious Biases in Medicine

Authored by: Lucy Mangalapalli & Albert Zhang
Edited by: Preethi Reddi **Reviewed by: Dr. Lynn O'Neill**

It seems so simple, right? You call and visit your doctor when you're sick. Unfortunately, a 2015 review of 7,674 adults across the United States found otherwise. According to the study by Taber et al., 30.3% of respondents said they "avoid visiting their doctor even when they suspect they should." Of that cohort, 33.3% avoided their doctor due to unfavorable notions of the healthcare system, including physician or provider-related concerns (Taber, Leyva, & Persoskie, 2015). While the exact reasons given by respondents varied, further research has found that one contributor of healthcare underutilization by certain demographics of patients may be their historical relationships with healthcare providers which have resulted in systemic bias. The Tuskegee Syphilis Study, for example, forced Blacks to participate in medical experiments during the 19th century and provided them with the lowest-quality of care, if any (Freimuth et al., 2001). Almost 60 years after the study began in 1932, the aftermath of the Tuskegee study continues to haunt clinical research surrounding the Black community — a 1990 survey conducted by the Southern Christian Leadership Conference found that 35% of Black parishioners believed HIV/AIDS was a manufactured form of genocide against their race (Gamble, 1997). This animosity and misconception continues to haunt public health research into HIV/AIDS in Black populations today, in the face of the fact that Blacks grapple with a 2.6-fold disparity in risk of acquiring the disease compared with Whites (Morris, Kurth, Hamilton, Moody, & Wakefield, 2009; Thomas & Quinn, 1991). While the Tuskegee study is no doubt an extreme example of grossly unethical conduct which has tarnished the reputation of the medical community for an entire racial demographic, recent research suggests that more subtle transgressions continue to preclude certain groups from obtaining the medical care they need due to dislike and mistrust (Braunstein, Sherber, Schulman, Ding, & Powe, 2008; Craig & Wright, 2012). In this article, we review select examples of these disparities and propose solutions to address them.

Previous literature has found that one major source of racial disparities in healthcare access is implicit racial bias by physicians. A 2012 study on implicit racial bias among physicians towards White and Black patients found that Black patients were 8% less likely to feel confident and 10% less likely to trust a physician with "moderate implicit bias" (implicit association test (IAT) score of +0.5 on a -2.0 to +2.0 scale) compared to a physician without any implicit bias (IAT score of 0.0). In addition, the study showed that Black patients were 12% less likely to report that a physician with a higher IAT score involved them in medical decisions versus a physician with a lower score (Cooper et al., 2012). The results of the Cooper study offer insight into one possible cause of early findings in a community tracking study conducted from 1998 to 1999 by the Center for Health System Change to measure of trust of physicians by individuals across 19 cities. The study found that Black patients reported a higher distrust towards healthcare professionals than White patients, even after controlling for education level, gender, income level, age, and insurance status (Armstrong, Ravenell, McMurphy, & Putt, 2007). Although factors other than implicit bias among physicians and trust level among patients certainly contribute to racial disparities, these studies serve to highlight areas of significant interest.

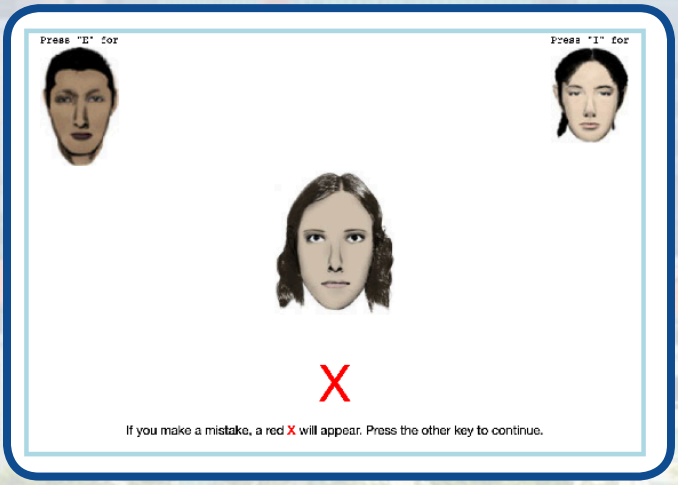
"30.3% of respondents said they "avoid visiting their doctor even when they suspect they should." Of that cohort, 33.3% avoided their doctor due to unfavorable notions of the healthcare system..."

In addition to race, research has shown that religious biases also present a prominent obstacle when obtaining healthcare. Research has shown that Muslim patients face particular difficulties in this area. According to a study published in the Journal of Muslim Mental Health which analyzed the types of discrimination reported by Muslim Americans in healthcare settings, being ignored by practitioners was reported by 55.4% of those surveyed and was the most common problem faced by respondents

(Martin, 2015). Other forms of discrimination identified by the study included issues with traditional Islamic dress (43.9%), religious holidays (25.6%), lack of knowledge about Islam (13.3%), and issues regarding a practitioner's gender (6.7%). One patient, for example, wrote that, "Going into a surgery, health care providers didn't recognize the importance of me keeping my hijab on and wanting most of my body covered," Another said that, "... the fact that our holy day is Friday was never taken into consideration even after being explained," and that the practitioners "[brought] in male [coworkers] without my consent." [I felt] uncomfortable with [the] questions asked of me in front of [a] male," the patient reported (Martin, 2015). While not statistically conclusive and limited to Muslim patients, these responses can only serve as a glimpse into the challenges in obtaining medical treatment faced by those whose religious practices are different than those of the predominant culture on the U.S.

A doctor injects a patient with a placebo as part of the Tuskegee Syphilis Study, which damaged the reputation of the medical community amongst Blacks (National Archives Atlanta, 1932).

Numerous solutions have been proposed to address these issues. One solution calls for a more diversified population of physicians available for patients. An overview of Kaiser Permanente's Northern California Diabetes Registry in 2005 showed that, of the patients on the registry, only 9.7% of African American patients and 11.2% of Hispanic patients had a race-concordant physician. Yet, these two groups were more likely than White or Asian patients to have a race-concordant physician if they chose their provider themselves, indicating a preference for race-concordant physicians (Traylor, Schmittdiel, Uratsu, Mangione, & Subramanian, 2010). This corroborates Saha et al's previous research which found that race-concordant physicians lead to higher satisfaction ratings and greater utilization of healthcare resources amongst Black patients (S. Saha, Komaromy, Koepsell, & Bindman, 1999). By increasing the diversity of physicians available by providing training and opportunity at an early level, the quality of care available may increase for all patients (American College of Physicians, 2010).



The Implicit Association Test (IAT) can measure implicit racial bias amongst physicians so that they can better provide care to all patients. Participants are asked to rapidly categorize the skin tone of pictures containing varying facial expressions (Zhang, 2019).

With regards to potential bias in the care of Muslim patients, Dr. Basem Attum and Dr. Zafar Shamoon, two Muslim physicians in the United States, have suggested that physicians should recognize and respect more aspects of the Islamic faith (Attum & Shamoon, 2019). A brochure drafted by the Islamic Council of Victoria directed at non-Muslim physicians recommends that understanding beliefs of Islam regarding illness, healthcare, and death — including practices of family members visiting sick relatives, beliefs and practices surrounding childbirth, forbiddance of pork and alcohol, and involvement of family in end-of-life and posthumous ceremonies — can help provide culturally-competent care for Muslim patients (Islamic Council of Victoria, 2010).

These are just a handful of solutions to healthcare disparities across racial and religious groups, and more work needs to be done. However,

"...race-concordant physicians lead to higher satisfaction ratings and greater utilization of healthcare resources amongst Black patients."

these solutions suggest that increased awareness and education, in conjunction with recruiting a diverse body of physicians, can lead to tangible improvements in interactions between physicians and groups who have historically faced systematic biases, ignorance, and discrimination by healthcare professionals.

References

American College of Physicians. (2010). Racial and Ethnic Disparities in Healthcare: Updated 2010. American College of Physicians. Retrieved from https://www.acponline.org/acp_policy/policies/racial_ethnic_disparities_2010.pdf

Armstrong, K., Ravenell, K. L., McMurphy, S., & Putt, M. (2007). Racial/ethnic differences in physician distrust in the United States. American Journal of Public Health, 97(7), 1283–1289. https://doi.org/10.2105/AJPH.2005.080762

Attum, B., & Shamoon, Z. (2019). Cultural Competence in the Care of Muslim Patients and Their Families. In StatPearls. Treasure Island (FL): StatPearls Publishing. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/29763108

Braunstein, J. B., Sherber, N. S., Schulman, S. P., Ding, E. L., & Powe, N. R. (2008). Race, medical researcher distrust, perceived harm, and willingness to participate in cardiovascular prevention trials. Medicine, 87(1), 1–9. https://doi.org/10.1097/MD.0b013e3181625d78

Cooper, L. A., Roter, D. L., Carson, K. A., Beach, M. C., Sabin, J. A., Greenwald, A. G., & Inui, T. S. (2012). The associations of clinicians' implicit attitudes about race with medical visit communication and patient ratings of interpersonal care. American Journal of Public Health, 102(5), 979–987. https://doi.org/10.2105/AJPH.2011.300558

Craig, H., & Wright, B. (2012). Nonadherence to prophylactic medication: Negative attitudes toward doctors a strong predictor. Australian Family Physician, 41(10), 815–818. Retrieved from https://www.racgp.org.au/afp/2012/october/nonadherence-to-prophylactic-medication/

Freimuth, V. S., Quinn, S. C., Thomas, S. B., Cole, G., Zook, E., & Duncan, T. (2001). African Americans' views on research and the Tuskegee Syphilis study. Social Science & Medicine, 52(5), 797–808. https://doi.org/10.1016/S0277-9536(00)00178-7

Gamble, V. N. (1997). Under the shadow of Tuskegee: African Americans and health care. American Journal of Public Health, 87(11), 1773–1778. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/9366634

Islamic Council of Victoria. (2010). Caring for Muslim Patients: A Guide for Health Care Professionals and Pastoral Carers. Retrieved from http://www.icv.org.au/icvdocs/caringformuslimpatients.pdf

Martin, M. B. (2015). Perceived Discrimination of Muslims in Health Care. Journal of Muslim Mental Health, 9(2). https://doi.org/10.3998/jmmh.10381607.0009.203

Morris, M., Kurth, A. E., Hamilton, D. T., Moody, J., & Wakefield, S. (2009). Concurrent partnerships and HIV prevalence disparities by race: linking science and public health practice. American Journal of Public Health, 99(6), 1023–1031. https://doi.org/10.2105/AJPH.2008.147835

Saha, S., Arbelaez, J. J., & Cooper, L. A. (2003). Patient-physician relationships and racial disparities in the quality of health care. American Journal of Public Health, 93(10), 1713–1719. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/14534227

Saha, S., Komaromy, M., Koepsell, T. D., & Bindman, A. B. (1999). Patient-physician racial concordance and the perceived quality and use of health care. Archives of Internal Medicine, 159(9), 997–1004. https://doi.org/10.1001/archinte.159.9.997

Taber, J. M., Leyva, B., & Persoskie, A. (2015). Why do people avoid medical care? A qualitative study using national data. Journal of General Internal Medicine, 30(3), 290–297. https://doi.org/10.1007/s11606-014-3089-1

Thomas, S. B., & Quinn, S. C. (1991). The Tuskegee Syphilis Study, 1932 to 1972: implications for HIV education and AIDS risk education programs in the black community. American Journal of Public Health, 81(11), 1498–1505. https://doi.org/10.2105/AJPH.81.11.1498

Traylor, A. H., Schmittdiel, J. A., Uratsu, C. S., Mangione, C. M., & Subramanian, U. (2010). The predictors of patient-physician race and ethnic concordance: a medical facility fixed-effects approach. Health Services Research, 45(3), 792–805. https://doi.org/10.1111/j.1475-6773.2010.01086.x

Image Citations

National Archives Atlanta. (1932). Doctor injecting a patient with placebo as part of the Tuskegee Syphilis Study [Digital image]. Retrieved from https://commons.wikimedia.org/wiki/File:Tuskegee-syphilis-study_doctor-injecting-subject.jpg

The Association Between Depresssion and Inflammation

Authored by: Alex Sandberg
Edited by: Chris Keyes **Reviewed by: Dr. Michael Crutcher**

Depression affects nearly 10% of adults in the United States and 300 million people around the world. If it is not treated, depression can cause serious distress in all aspects of life, from sleep and social interactions to bowel movements (Miller and Raison, 2016). Most infamously, depression has been found to be one of the leading causes of suicide in the United States (Centers for Disease Control and Prevention, 2019). While a genetic foundation for depression is being studied in research, there are a multitude of environmental factors that may contribute to its development. Alcohol abuse, sleep deprivation, and a lack of proper nutrition are among the leading environmental causes of depression (WebMD, 2019). Since the 1950's, antidepressants have been synthesized to combat the disorder through disrupting neurotransmitter pathways in the central nervous system. However, many antidepressants lack the ability to treat secondary complications of depression that can cause drastic alterations within the body. It has been found recently that depression may have a direct relationship to inflammation, similar to the body's standard repair mechanism. Studies have shown that, without exposure to any pathogens, people diagnosed as clinically depressed have higher inflammatory adrenal hormonal secretions, c-reactive proteins, platelets, and neutrophil-to-lymphocyte ratios (Miller et al., 2005). In order to understand these developments, certain topics must be investigated, such as the impact of increased inflammation in the body and the evolutionary factors behind this relationship. Many of these impacts have implications for other prominent diseases, which include cancer inflammation and diabetes.

The main mechanism that controls the relationship between depression and inflammation is the neuroendocrine system. Evidence shows that through neuroendocrine mechanisms, major inflammatory responses can promote the onset of depression. In the afferent nerve pathway, cytokines (cell signaling proteins) can activate afferent neurons that send messages to the brain to secrete norepinephrine, serotonin, and various other neurohormones and transmitters that can cause depression symptoms (Howland, 2019). In the humoral pathway, cytokines are secreted by macrophages that are stimulated as an inflammatory response. The cytokines can then diffuse into the circumventricular organs of the brain (Almond, 2013). Neural pathways can also stimulate cytokine diffusion through the blood-brain barrier into the hypothalamus through numerous transport proteins. These pathways mentioned contribute to low levels of tryptophan (a precursor to serotonin) and glutamatergic agents, all of which result in excitatory states throughout the central nervous system. Depression, along with stress, has also been reported to lead to multiple responses. Cortisol release stressors has been shown to be intertwined with depression and previous traumatic experiences. Individuals with depression may have a softened response to stressors compared to normally functioning individuals. Additionally, researchers have found that debilitating cognitive disorders can increase inflammatory responses in depressed individuals (Strawbridge, Young and Cleare, 2017). There is evidence that both variables can promote the development of the other; therefore, we can theorize that the relationship is

Figure 1: Depression has been linked to increased inflammation in the human body (Kaulitzki, 2019)

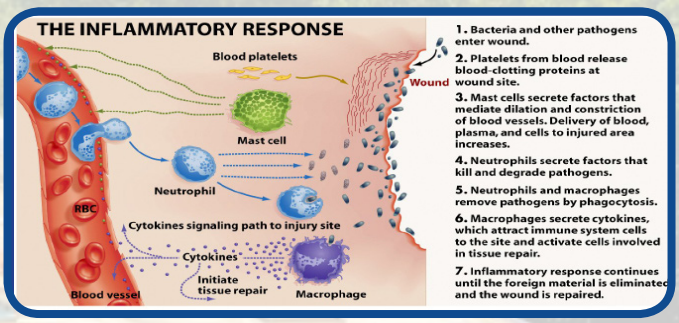
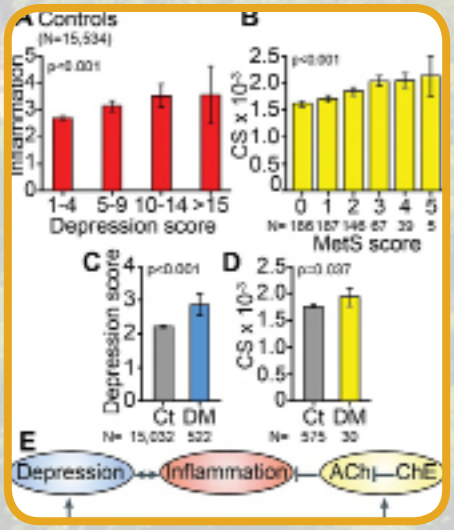


Figure 2: The multitude of inflammatory responses as a result of pathogens or a wound. The general responses show similarities to depression linked inflammation (Biological Science 2e 2005).

bidirectional.

The direct relationship between inflammation and depression has substantial implications for disease development and prognosis. Chronic inflammation, which is found in many clinically depressed individuals, can result in an increase in gene mutations and higher risk for obesity, allergies, and most importantly, disease (Dantzer et al., 2008). Type II diabetes mellitus has been linked to inflammatory biomarkers that cause depression. Many depressed individuals show inflammatory stimulation of the hypothalamus-pituitary-adrenal axis (central stress system) that produce catecholamine hormones that subsequently promote insulin resistance found in diabetic patients. In fact, in a study performed at the University Hospitals of Leicester, a cohort of women that displayed depressive symptoms also displayed increased leptin and c- reactive protein levels (CRP) found in individuals exhibiting a pro-inflammatory response. There was also found to be higher overall HOMO IR levels: a biomarker linked to diabetes found in insulin resistant individuals (Webb et al., 2017). Another study performed at the Hebrew University of Jerusalem examined levels of cholinesterase: an enzyme that break down acetylcholine and can predict inflammation and risk for disease. The figure below demonstrates the team's findings, which present an elevated ratio of metabolic rate to resting metabolic rate (MetS score), a key predictor of diabetes and cardiovascular risk (Shenhar-Tsarfaty and Toker, 2016).



The direct relationship between depression and MetS: a key predictor in diabetes (Shenhar-Tsarfaty and Toker, 2016).

Many of the biomarkers mentioned in both of these studies are not just linked to diabetes. Increased levels of inflammatory agents are an indicator for susceptibility to a variety of diseases, including cancer (Smith, 2015).

Chronic stress response is a symptom in depressed patients that promotes the release of a cascade of hormones that have been found to modulate tumor growth. For instance, hormones such as cortisol and catecholamines can trigger the activity of natural killer cells and lymphocytes. While the complete mechanism is still not understood, depressed subjects seem to have alterations in their immune cell functions that normally operate to suppress tumor growth (Smith, 2015). The differences in treatment between clinically depressed and non-clinically depressed cancer patients is currently being investigated across many cancer specialties. With the information we know about inflammatory levels and depression, the interaction between antidepressants and cancer-fighting therapies must be strongly considered.

"Many depressed individuals show inflammatory stimulation of the hypothalamus-pituitary-adrenal axis (central stress system) that produce catecholamine hormones that subsequently promote insulin resistance found in diabetic patients."

The question many of us may be pondering is: how have humans evolved this inflammatory response to depression? This response has strong similarities to the "fight or flight" response involving the release of epinephrine, commonly known as adrenaline, to avoid predation. While there is no immediate threat in the case to a depressed individual, the subject's low self-esteem acts as an activator for the release of cortisol and catecholamines (Miller and Raison, 2016). Without exposure to a pathogen, these hormones stimulate an inflammatory response, thus causing a greater probability of developing depressive symptoms and the other diseases already mentioned. In theory, the "fight or flight" response through natural selection acts as a productive mechanism. However, today we can observe the negative mismatch it has on populations around the world (Miller and Raison, 2016).

References

Almond, M. (2013). Depression and Inflammation: Examining the Link. Current Psychiatry, 12(6), pp.25-31.

Centers for Disease Control and Prevention. (2019). More than a mental health problem. [online]

Dantzer, R., O'Connor, J., Freund, G., Johnson, R. and Kelley, K. (2008). From inflammation to sickness and depression: when the immune system subjugates the brain. Nature Reviews Neuroscience, 9(1), pp.46-56.

Howland, R. (2019). Vagus Nerve Stimulation. [online] NCBI.].

Miller, A., & Raison, C. (2016). The role of inflammation in depression: from evolutionary imperative to modern treatment target. Nature Reviews Immunology, 16(1), pp.22-34.

Miller, G., Rohleder, N., Stetler, C., & Kirschbaum, C. (2005). Clinical Depression and Regulation of the Inflammatory Response During Acute Stress. Psychosomatic Medicine, 67(5), pp.679-687.

Smith, H. (2015). Depression in cancer patients: Pathogenesis, implications and treatment (Review). Oncology Letters, 9(4), pp.1509-1514.

Strawbridge, R., Young, A., & Cleare, A. (2017). Biomarkers for depression: recent insights, current challenges and future prospects. Neuropsychiatric Disease and Treatment, [online] Volume 13, pp.1245-1262. Available at:

WebMD. (2019). Untreated Depression.

Webb, M., Davies, M., Ashra, N., Bodicoat, D., Brady, E., Webb, D. Khunti, K. (2017). The association between depressive symptoms and insulin resistance, inflammation and adiposity in men and women. PLOS ONE, 12(11), p.e0187448.Referenc-es

Image Citations

Shenhar-Tsarfaty, S., & Toker, S. (2016). Weakened Cholinergic Blockade of Inflammation Associates with Diabetes-Related Depression. Molecular Medicine, 22(1), p.1.

Pharmacogenomics and Precision Medicine in Clinical Psychiatry

Authored by: Sri Ponnazhagan
Edited by: Sharvil Patel **Reviewed by: Dr. Kim Tran**

Each year, millions of Americans nationwide suffer from mental illnesses such as major depressive disorder and social anxiety disorder. The severity of these illnesses' clinical manifestations varies in degree and poses challenges to clinical psychiatrists who try to prescribe effective treatment combinations individualized to each patient. Though patient care based on genomic information in this particular field is relatively new, there have been impressive strides with recent advancements in molecular medicine. In particular, new treatment approaches based on cutting-edge genomic, transcriptomic, and proteomic tools and refinements in understanding pharmacogenomics are promising to revolutionize the way psychiatric patients will be treated in the near future. With an emphasis on more accurate and personalized treatments, pharmacogenomics

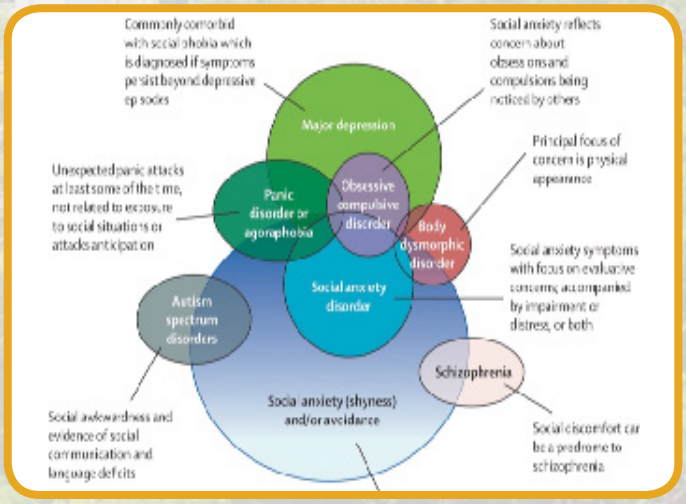


Figure 1: Unique and common conditions that overlap among social anxiety disorders. (Stein & Stein 2008)

is now a promising component of antidepressant treatments. From collectively reviewing the genomic imprint of the pathophysiological basis of psychiatric disorders, risk factor association in these illnesses, and existing limitations in current treatment options, pharmacogenomics-based treatment approaches can suit individual patients and clinical practices.

Although an exhaustive list of psychiatric disorders may impede classifying them based on a single factor, broadly, they can be grouped into schizophrenia, depression, bipolar diseases, and anxiety disorders. Among these, anxiety disorders comprise several types, including generalized anxiety disorders, panic disorders, and phobia-related disorders. A comprehensive representation of the types of behavioral disorders and symptoms associated with them was provided by Stein & Stein (Stein & Stein 2008), shown in Figure 1.

For a long time, diagnosis of depression relied on the identification of several key symptoms, including emotional, neurovegetative, and neurocognitive symptoms (Malhi & Mann 2018).

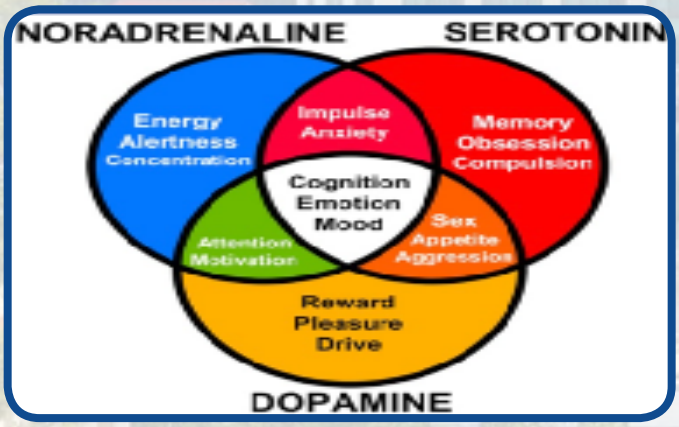


Figure 2: Association of monoamine neurotransmitters to behavioral traits in depression and anxiety. (Palkhivala (2019)

None of these diagnostic parameters represented a pathogenetic understanding of depression, therefore depression was more defined as a disorder based on symptoms forming a syndrome that cause emotional and functional impairment. However, remarkable progress in understanding the types of psychiatry disorders in the last few years identified how genetic predisposition, environmental triggers, allelic, and epigenetic risk factors in the brain manifest in differential penetrance among patients. Although the incidence of risk factors for each anxiety disorder varies, there are general risk factors that are associated with all types of anxiety, such as exposure to mental stress or negative environmental events in childhood and adulthood, familial incidence of mental illness, and as secondary complications of other health conditions such as hormonal imbalance. Based on differential diagnosis of these manifestations, treatments for anxiety disorders follow a general pattern that includes

psychotherapy, cognitive behavioral therapy, and anti-anxiety medications (e.g. antidepressants and beta blockers).

In a recent article from University Health News, Alison Palkhivala provided a comprehensive depiction of how brain chemistry and neurotransmitters link to behavioral outcome in people with depression (Palkhivala 2019). In people with depression, the levels of certain brain chemicals are thought to be out of balance, particularly the neurotransmitters serotonin, dopamine, and norepinephrine.

From existing limitations in treatments for anxiety disorders, it is apparent that choosing the right therapy and medication, dose, and treatment plan is extremely important for treating patients with anxiety disorders. Pharmacogenomics, or precision medicine efforts, provide great hope to realizing this dogma. According to the National Institutes of Health,

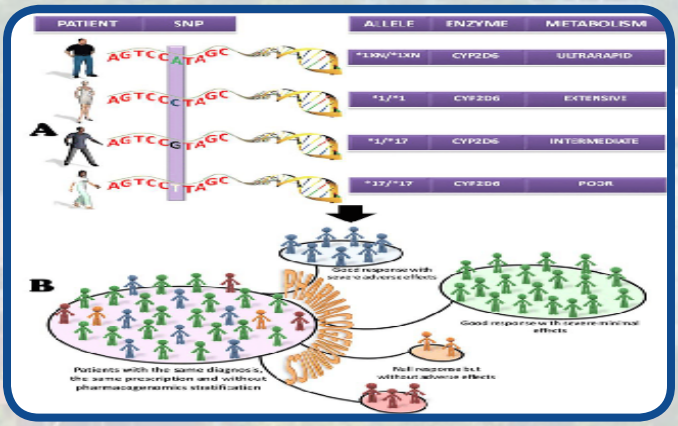


Figure 3: (A) Identification of CYP2D6 genetic variability by genome sequencing, predicted enzyme activity and (B) pharmacogenomics-based identification of patient population for precision medicine. (Leon-Cachon et. al 2012)

pharmacogenomics is the study of how genes affect a person's response to drugs (NIH 2019). As the name implies, this new field combines pharmacology and genomics to develop effective, safe medications and doses to tailor a person's genetic makeup for maximum efficiency with minimal adverse effects. This field of molecular medicine is highly promising because unlike the current standard of care's one-dose-for-all approach, pharmacogenomics allows physicians to consider the genetic makeup of each patient. By making decisions based on genome sequencing, clinicians can target specific functionalities of aberrant genes and the consequences of these aberrations' prognosis on patients' present and future treatments. Individual variability in drug responses for efficacy, tolerability and safety are commonly encountered limitations while treating psychiatric patients with generalized drugs, based on demonstrated symptoms and patient history. The above limitations get further exacerbated by patient factors such as chronic illnesses, sex, age, ethnicity, and genetic variability. Additional environmental factors including smoking, and/or diet only further complicate the outcome of drug efficacy (Crettol, De Leon, Hiemke & Eap 2014). The variability in drug response is affected by pharmacokinetics, consisting of absorption, distribution, metabolism, and excretion which cause

> "This new field combines pharmacology and genomics to develop effective, safe medications and doses to tailor a person's genetic makeup for maximum efficiency."

unstable plasma concentrations (Eap 2016). A better understanding at the molecular level through genetic imprinting is a promising way to bridge the gap between drug non-responsiveness and consequential side effects. Precisely, genomic sequencing of a patient DNA will enable identification of polymorphisms in either pharmacokinetic genes, which encode proteins that affect drug blood levels, or pharmacodynamic genes, that encode cellular receptor proteins involved

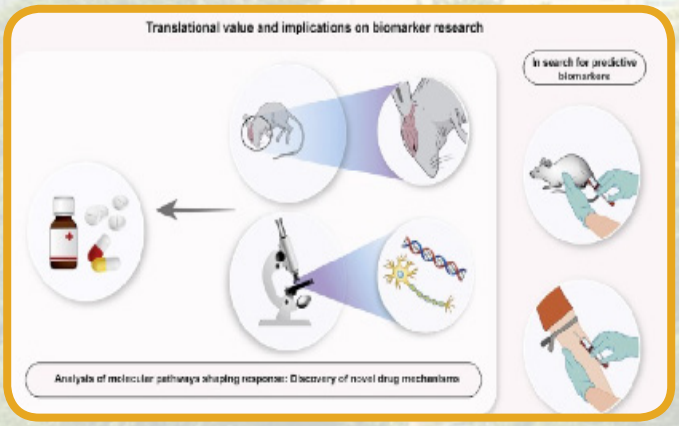


Figure 4: Laboratory animals can be used to test psychiatric drug effects based on behavioral variation, identical to human patients, and used in the identification of predictive biomarkers or treatment response.

in drug binding to target tissues.

Among pharmacokinetic proteins, the members of the cytochrome P450 (CYP) family, a group of proteins that function as major enzymes involved in drug metabolism, account for more than 90% of all drug metabolism in the body (Geundrich 2008). Although more than 50 CYP enzymes have been identified in humans, only a few of them play major role in drug metabolism (Jaquenoud Sirot, van der Velden, Rentsch, Eap & Baumann P

2006). From a psychiatric treatment perspective, metabolism of psychotropic and analgesic drugs used for symptomatic management of attention-deficit hyperactivity disorder (ADHD) are influenced by CYP2D6, CYP2C19, CYP2C9, CYP1A2, CYP2B6, and CYP3A4. Among these, the CYP2D6 has been identified to exert a strong influence on pharmacokinetics of many psychotropic drugs. Interestingly, a better understanding of molecular genetics of CYP2D6 identified phenotypic variants of the enzyme in activity, classified as poor, intermediate, extensive, and ultra-rapid metabolizers. Genetic determinants on functional heterogeneity among CYP2D6 identified the existence of no alleles for the poor version, heterozygosity with one active and one inactive allele or two alleles with reduced activity for intermediate phenotype, two wild-type alleles for the extensive enzyme activity, and 3 - 13 copies of gene amplification representing the ultra-rapid enzyme variant (Bertilsson 2002). In addition to more than 100 variants and invariants, single-nucleotide polymorphisms (SNPs) have been identified for CYP2D6 gene (Hicks, Swen & Thorn 2013). Variations in enzyme function, based on allelic heterogeneity and SNPs, result in altered pharmacokinetics of psychiatry drugs, such as a higher risk of side effects in patients with at least one nonfunctional CYP2D6 allele than in those with two nonfunctional alleles (ibid Hicks et. al 2013). Among psychotropic antidepressant drugs studied so far as being strongly influenced by CYP2D6 enzyme activity, drugs for ADHD such as atomoxetine; antidepressant drugs such as tricyclics (TCAs) or tetracyclics (TeCAs) that are serotonin and/or norepinephrine reuptake inhibitors, selective serotonin reuptake inhibitors; and antipsychotic drugs rank highly (Bertilsson 2010). These discoveries led the Clinical Pharmacogenetics Implementation Consortium (CPIC) of the National Institutes of Health's Pharmacogenomics Research Network to develop a detailed guideline for CYP2D6 and CYP2C19 genotypes and dosing of TCAs (Bartilsson 2002; Bertilsson, Dahl, Dalen, & Al Shurbaji 2010). Similar to CYP2D6, the CYP2C19 gene is also highly polymorphic with more than 30 known variants, and allele frequencies that are strongly influenced by ethnicity (Kirchheiner, Henckel & Franke 2005). A comprehensive illustration of principles in precision genomic identification and predictive outcomes in the application of pharmacogenomics of CYP2D6 genes was provided by León-Cachón et al (León-Cachón, Ascacio-Martínez, & Barrera-Saldaña 2012), as shown in Figure 3.

Similar to pharmacokinetic drug approach, the use of genetic testing and precision medicine presents more promise for preventing adverse drug reactions. The serotonin transporter system is the most studied pharmacodynamics gene system. Because of the common mechanism of many antidepressants that causes them to bind to serotonin transporters, the inhibition of the reuptake of serotonin by the serotonin transporter results in drug efficacy (Coleman & Gouaux 2016). Polymorphisms in the serotonin transporter-linked polymorphic region (5-HT-TLPR) of the serotonin transporter gene (SLC6A4) have been extensively studied. The long allele (I) of this gene is associated with a twofold higher expression than the short allele, and heterogeneity from this allelic combination determines response to selective serotonin reuptake inhibitors (SSRIs) based on race, sex, age and at onset of depression modulating the association (Porcelli, Fabbri & Serretti 2012).

Despite the hope and promise in pharmacogenomics approaches for treating clinical psychiatry patients, several challenges exist that need to be overcome, such as ethical, legal and social implications. Namely, these limitations include issues with implementing the data directly into the clinic, a lack of availability of cutting-edge molecular diagnostic tools across care providers, inefficient cost-effectiveness, limited availability of data from evidence-based research since the field is still in infancy, and inaccurate interpretation (Ma, Lee & Kuo 2012). Further, even progressions made in cutting-edge precision medicine tools, including high-efficiency whole genome sequencing platforms and powerful bioinformatics algorithms and software, have not translated easily to the clinic is because of lack of clinically accessible biological and genetic predictors for routine use in depression treatment. To address these limitations, studies involving preclinical animal models appear promising. In order to model the heterogeneity of response to antidepressant treatment in preclinical animals as in human patients, three important considerations need to be met: construct validity elements of similar depressive-like behavior (Belzung & Lemoine 2011); face validity elements in terms of anatomical, biochemical, and neuropathological features similar to humans (Nestler & Hyman 2010); and establish predictive validity, focused on the ability of a preclinical animal model to serve as a tool for pharmacological research. One such study aimed at identifying neurobiological mechanisms underlying response to antidepressant treatment identified the role of glucocorticoid receptor in shaping response to antidepressants [(Herzog, Beckman, Lieb, Ryu & Muller 2018); Figure 4].

Overall, examining the pathophysiological basis of psychiatric disorders, analyzing risk factor association in these illnesses, and noting existing limitations in present treatment options allow

pharmacogenomics-based approaches to better suit individual patients and clinical practices. Combining these analyses with ongoing advances in multi-disciplinary fields such as molecular genetics, metabolomics, proteomics, and bioinformatics, outcomes are gleaned from preclinical and clinical research that should enable advancing the field of precision psychiatry in the coming decades.

References

Stein MB, Stein DJ. Social anxiety disorder. Lancet 2008; 371: 1115-1125.

Malhi GS, Mann JJ. Depression. Lancet. 2018;392: 2299-2312.

Palkhivala A. Depression - What Causes Depression? Brain Chemistry and Neurotransmitters Play Major Roles. University Health News, January 31, 2019; https://universityhealthnews.com/daily/depression/what-causes-depression/

NIH. What is pharmacogenomics?. National Institute of Health 2019. https://ghr.nlm.nih.gov/primer/genomicresearch/pharmacogenomics

Crettol S, De Leon J, Hiemke C, Eap CB. Pharmacogenomics in psychiatry: from TDM to genomic medicine. Clin Pharmacol Ther. 2014;95: 254- 257

Jaquenoud Sirot E, van der Velden JW, Rentsch K, Eap CB, Baumann P. Therapeutic drug monitoring and pharmacogenetic tests as tools in pharmacovigilance. Drug Saf. 2006;29: 735-768.

Eap CB. Personalized prescribing: a new medical model for clinical implementation of psychotropic drugs. Dialogues in Clinical Neuroscience 2016; 18: 313-322.

Guengerich FP. Cytochrome p450 and chemical toxicology. Chem Res Toxicol. 2008;21: 70-83.

Bertilsson L, Dahl ML, Dalen P, Al Shurbaji A. Molecular genetics of CYP2D6: clinical relevance with focus on psychotropic drugs. Br J Clin Pharmacol. 2002;53: 111-122.

Hicks JK, Swen JJ, Thorn CF, et al. Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants. Clin Pharmacol Ther. 2013;93: 402-408.

Bertilsson L. CYP2D6, serotonin, and suicide--a relationship? Clin Pharmacol Ther. 2010;88: 304-305.

Kirchheiner J, Henckel HB, Franke L, et al. Impact of the CYP2D6 ultrarapid metabolizer genotype on doxepin pharmacokinetics and serotonin in platelets. Pharmacogenet Genomics. 2005;15: 579-587.

León-Cachón RB, Ascacio-Martínez JA, Barrera-Saldaña HA. Individual response to drug therapy: bases and study approaches. Rev Invest Clin. 2012;64:364-376.

Coleman J., Gouaux E. How Antidepressants Block Serotonin Transport. Berkeley Lab 2016. https://als.lbl.gov/antidepressants-block-serotonin-transport/

Porcelli S, Fabbri C, Serretti A. Meta-analysis of serotonin transporter gene promoter polymorphism (5-HTTLPR) association with antidepressant efficacy. Eur Neuropsychopharmacol. 2012;22: 239-258.

Ma JD, Lee KC, Kuo GM. Clinical application of pharmacogenomics. J Pharm Pract. 2012;25: 417–427.

Belzung C, Lemoine M. Criteria of validity for animal models of psychiatric disorders: Focus on anxiety disorders and depression. Biol Mood Anxiety Disord. 2011;1:9.

Nestler EJ, Hyman SE. Animal models of neuropsychiatric disorders. Nat Neurosci. 2010;13: 1161–1169.

Herzog DP, Beckmann H, Lieb K, Ryu S, Müller MB. Understanding and Predicting Antidepressant Response: Using Animal Models to Move Toward Precision Psychiatry. Front Psychiatry. 2018; 9:512.

Image Citations

Herzog DP, Beckmann H, Lieb K, Ryu S, Müller MB. Understanding and Predicting Antidepressant Response: Using Animal Models to Move Toward Precision Psychiatry. Front Psychiatry. 2018; 9:512.

León-Cachón RB, Ascacio-Martínez JA, Barrera-Saldaña HA. Individual response to drug therapy: bases and study approaches. Rev Invest Clin. 2012;64:364-376.

Palkhivala A. "What causes Depression? Brain Chemistry and Neurotransmitters Play Major Roles" University Health News, January 31, 2019;

Stein MB, Stein DJ. Social anxiety disorder. Lancet 2008; 371: 1115-1125. Figure 1

The Serious Effects of Obesity on Joint Degeneration

Authored by: Chris Keyes
Edited by: Jonathan Regenold **Reviewed by: Dr. Sarah Blanton**

Osteoarthritis (OA), also known as arthrosis, is the most common cause of chronic pain worldwide (Prakash, Gabdulina, Trofimov, & Livshits, 2017). OA is "a disease characterized by loss of articular cartilage, hypertrophic bony changes, and inflammatory synovitis;" the fundamental problem in OA is understood to be an imbalance of cartilage homeostasis such that cartilage catabolism exceeds cartilage anabolism (Wei, Lee, Wei, Qu, & Zhang, 2017). Due to its prevalence and symptomatic severity, healthcare costs for the treatment of OA are quite high. The prevalence of OA among adults aged 25 and older in the US is 13.9% (Plotnikoff et al., 2015). 80% of individuals with OA experience movement limitation, and 25% of people with OA are unable to perform major activities of daily living (Bliddal, Leeds, & Christensen, 2014). In the United States alone, osteoarthritis yearly treatment costs are in excess of $10 billion (Bliddal et al., 2014).

"In the United States alone, osteoarthritis yearly treatment costs are in excess of $10 billion (Bliddal et al., 2014)."

Both age and obesity contribute to the development of OA. These risk factors overlap in the obese elderly population and cause high rates of OA. A recent Korean study compared rates of obese and non-obese elderly people having OA using odds ratios. An odds ratio (OR) measures the association between an exposure and an outcome (in this case, the exposure is obesity, and the outcome is OA). An OR of 1 means that exposure does not influence outcome; ratios greater than 1 mean that exposure is associated with higher odds of outcome, and ratios less than 1 mean that exposure is associated with lower odds of outcome (Szumilas, 2010). In the Korean study, elderly obese men had an OR of 1.54, and elderly obese women had an OR of 7.64 (Jin et al., 2017). These statistics show the powerful effects of obesity in a population already predisposed to OA. Since age is not a modifiable risk factor in treatment, obesity must be addressed as much as possible, especially within the elderly population. Unfortunately, obesity rates have skyrocketed in recent years: since 1980, the number of obese individuals worldwide has roughly doubled. More than 35% of the elderly are obese in the US (Bliddal et al., 2014).

Obesity is commonly associated with cardiovascular disease and diabetes among the American public, but its impacts upon joint health cannot be ignored. Through research, obesity has been linked to numerous adverse medical conditions, including OA. If severe enough, the joint's cartilage can degrade until the cartilage fails to cover all of the joint area and results in bone-on-bone contact, causing considerable pain and lessened joint mobility (Markenson, 2012).

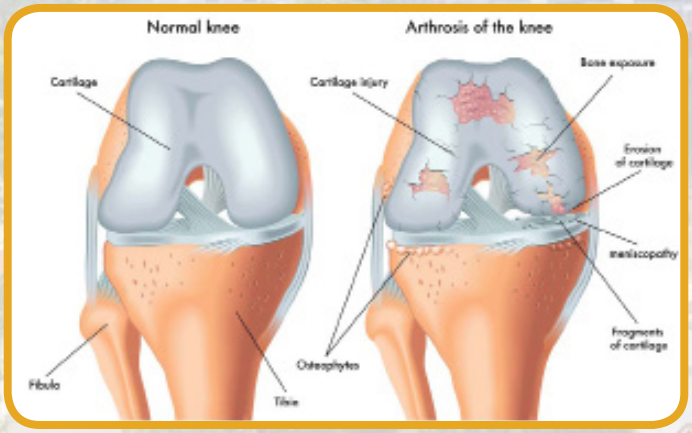


Figure 1: A normal, healthy knee compared to a knee affected by osteoarthritis.

Due to the heavy impact of obesity on both the initial development and progression of OA, researchers have been turning their attention to measuring this impact as well as to refining treatments for OA that incorporate consideration and adjustment of body weight. In the US, healthcare practitioners measure obesity with the Body Mass Index (BMI): a comparison of a person's weight over his or her height. A person is considered obese by American healthcare standards if his or her BMI is greater than or equal to 30 kg/m2 (Bliddal et al., 2014).

"The correlation between obesity and osteoarthritis is quite strong: for each unit increase in BMI a patient's risk of knee OA increases by 15%" (Duclos, 2016).

The correlation between obesity and osteoarthritis is quite strong: for each unit increase in BMI a patient's risk of knee OA increases by 15% (Duclos, 2016). However, correlation alone has limited usefulness for treatment without supporting knowledge about causation. The causative relationship is much more complex than one may at first assume. Perhaps the most intuitive link between the conditions is that increased weight adds more mechanical stress to joints, increasing the rate at which the joints' cartilage wears down. Each additional kilogram of body weight adds six kilograms of load to each of a patient's knees (Duclos, 2016).

There are also many indirect ways in which obesity affects joint deterioration, as is evident in the fact that all joints—even non-weight-bearing joints—can become arthritic (Prakash et al., 2017). There is evidence that mechanical stress causes the release of pro-inflammatory mediators from joints. These mediators include cytokines such as IL-6 and C-reactive protein. Such mediators likely cause in-joint inflammatory reactions that lead to further tissue stress. Obesity is also linked to other medical problems such as hyperinsulinemia. Excessive insulin levels may play a part in OA development through their impact on insulin-like growth factor 1 (IGF-1) (Bliddal et al., 2014). A recent study concluded that IGF-1 reduces the loss of chondrocytes and maintains matrix integrity by inducing the production of cartilage matrix components, thus protecting against OA progression. OA recently has been correlated with a reduction in IGF-1 levels (Wei et al., 2017). Finally, as a person gains weight, they acquire a greater total mass of ectopic adipose tissue (the form of adipose tissue related to weight gain), which induces both local and systemic inflammatory responses through the release of adipokines. At high concentrations, adipokines can often lead to cartilage destruction (Duclos, 2016).

To make matters worse, the impacts of obesity and OA work to increase the severity of each other. As a person gains weight, their body produces greater muscle mass to help move the extra weight around, but the rate of adipose tissue growth exceeds that of muscle tissue so that the muscles become increasingly inadequate in comparison to the weight they must bear. As a result, mobility decreases, leading to even greater weight gain and an increase of the impact upon the joints (Bliddal et al., 2014). In addition, arthritis leads to lessened joint mobility and considerable joint pain, which both lead to decreased physical activity and muscle atrophy. Compounding these factors, obesity, joint deterioration, and physical inactivity all result in inflammatory responses that further damage joint tissues. All of these factors create a vicious cycle.

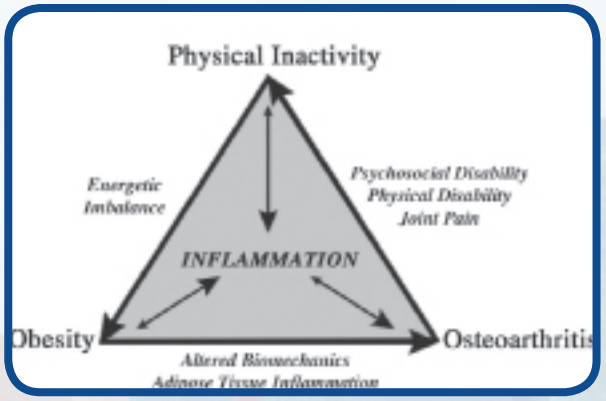


Figure 2: The self-recreating cycle of physical inactivity, obesity, and osteoarthritis.

Since obesity so strongly impacts joint health, reducing weight can be one of the most important aspects of OA treatment. A study by Bliddal et al. found that losing 5.1 kg over a ten-year period reduced one's odds of developing symptoms of knee OA by 50%. The standard weight-loss goal in OA patients in clinics is a loss of 10% of their body weight (Bliddal et al., 2014). Physicians typically regard successful weight loss in patients as maintenance of the loss for at least one year (Duclos, 2016).

Still, weight is hard to lose and harder to avoid regaining. If a patient's obesity leads to severe OA, surgeries such as total hip arthroplasty (THA) or total knee arthroplasty (TKA) will be considered. In these operations, a patient's joint's surfaces are completely replaced with artificial components. These operations are becoming increasingly common as the need for them is constantly increasing, and they are quite effective. Studies indicate that the number of THAs in the US soon will grow to 600,000 per year (Woo, Cha, Park, & Kim, 2019). Most patients, regardless of BMI, typically experience substantial improvements in levels of pain and joint functionality by six months after a total joint replacement (TJR) (Li et al., 2017). In addition, techniques for TJRs are constantly improving. One procedure currently under study is primary minimally-invasive TKA. This procedure uses smaller skin incisions and smaller soft tissue dissections to yield comparable results as standard TKA with less trauma to the patient's body (Yoo, Oh, Park, Kim, & Kim, 2018).

Despite modern procedures' abilities to repair joints in obese patients, obesity lessens the effectiveness of the procedures and increases risks for complications. Obese TKA recipients are more likely to experience post-operative infection and thromboembolic events. This increased risk of infection is largely due to the fact that obese patients have high rates of comorbidities (such as diabetes) that cause as

a weakened immune system or slower wound healing. A causative relationship between thromboembolic events and such obesity-linked comorbidities also is likely (Werner, Evans, Carothers, & Browne, 2015). In addition, the increased weight wears down the artificial joints more quickly, increasing the chances of the patient needing joint replacement revision at some point in his or her lifetime (Pellegrini et al., 2017). Another serious complication that can arise is aseptic loosening: failure of the bond between a bone and an implant. Obesity has been linked to primary THA failure due to aseptic loosening within five years after surgery (Goodnough et al., 2018).

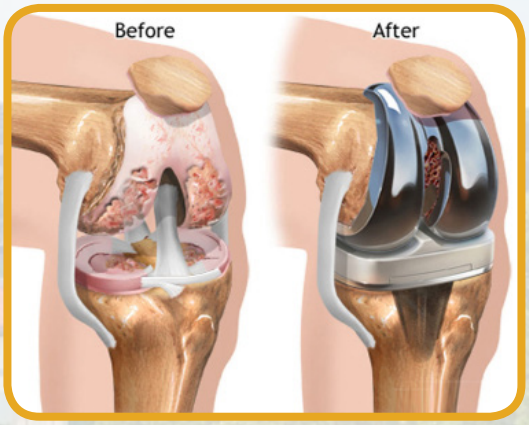


Figure 3: A pre- and post-primary total knee replacement operation knee joint.

Despite the advances of modern medicine, the most effective means of treatment still seems to be weight loss through diet and exercise. Patients tend to lose weight in the time surrounding a TJR surgery, likely because surgeons encourage them to do so in order to lower the risks of complications and improve outcomes in terms of post-operative comfort and mobility. A study by Pellegrini et al. found that 23% of patients lose at least 2.5% of their body weight in the time surrounding a TJR surgery. However, only 11% of patients lose weight following the TJR surgery, with the rest either maintaining the same weight that they reached during the surgical period or returning to their preoperative weight (Pellegrini et al., 2017).

Even with our recent advances in surgical procedures, OA healthcare costs, patient pain, and loss of functional movement will continue to rise without tackling the ever-growing problem of obesity. Truly, no aspect of human health can be completely isolated from the others, and how we approach the obesity epidemic will have a drastic impact not only on the frequently discussed problems of diabetes and cardiovascular health, but also on our very ability to move: a necessity for maintaining a healthy and social life.

References

Bliddal, H., Leeds, A. R., & Christensen, R. (2014). Osteoarthritis, obesity and weight loss: evidence, hypotheses and horizons – a scoping review. Obesity Reviews, 15, 578-586. doi:10.1111/obr.12173

Duclos, M. (2016). Osteoarthritis, obesity, and type 2 diabetes: the weight of waist circumference. Annals of Physical and Rehabilitation Medicine, 59, 157-160. doi:10.1016/j.rehab.2016.04.002

Goodnough, L. H., Finlay, A. K., Huddleston III, J. I., Goodman, S. B., Maloney, W. J., & Amanatullah, D. F. (2018). Obesity is independently associated with early aseptic loosening in primary total hip arthroplasty. The Journal of Arthroplasty, 33, 882-886. doi:10.1016/j.arth.2017.09.069

Jin, W. S., Choi, E. J., Lee, S. Y., Bae, E. J., Lee, T.-H., & Park, J. (2017). Relationships among obesity, sarcopenia, and osteoarthritis in the elderly. Journal of Obesity and Metabolic Syndrome, 26, 36-44. doi:10.1080/1354750X.2017.1315615

Li, W., Ayers, D. C., Lewis, C. G., Bowen, T. R., Allison, J. J., & Franklin, P. D. (2017). Functional gain and pain relief after total joint replacement according to obesity status. The Journal of Bone and Joint Surgery, 99, 1183-1189. doi:10.2106/JBJS.16.00960

Markenson, J. A. (2012). An in-depth overview of osteoarthritis.

Pellegrini, C. A., Song, J., Semanik, P. A., Chang, R. W., Lee, J., Gilbert, A. L., Pinto, D., Ehrlich-Jones, L., & Dunlop, D. D. (2017). Patients less likely to lose weight following a knee replacement. Journal of Clinical Rheumatology, 23, 355-360. doi:10.1097/RHU.0000000000000579

Plotnikoff, R., Karunamuni, N., Lytvyak, E., Penfold, C., Schopflocher, D., Imayama, I.,…Raine, K. (2015). Osteoarthritis prevalence and modifiable factors: a population study. BioMed Central Public Health, 15, 1195. doi:10.1186/s12889-015-2529-0

Prakash, J., Gabdulina, G., Trofimov, S., & Livshits, G. (2017). Quantitative genetics of circulating Hyaluronic Acid (HA) and its correlation with hand osteoarthritis and obesity-related phenotypes in a community-based sample. Annals of Human Biology, 44, 522-530. doi:10.1080/03014460.2017.1334822

Szumilas, M. (2010). Explaining odd ratios. Journal of the Canadian Academy of Child and Adolescent Psychiatry, 19, 227-229.

Wei, F.-Y., Lee, J. K., Wei, L., Qu F., & Zhang J.-Z. (2017). Correlation of insulin-like growth factor 1 and osteoarthritic cartilage degradation: a spontaneous osteoarthritis in guinea-pig. European Review for Medical and Pharmacological Sciences, 21, 4493-4500.

Werner, B. C., Evans, C. L., Carothers, J. T., & Browne, J. A. (2015). Primary total knee arthroplasty in super-obese patients: dramatically higher postoperative complication rates even compared to revision surgery. The Journal of Arthroplasty, 30, 849-853. doi:10.1016/j.arth.2014.12.016

Woo, S. E., Cha, D. H., Park, E. C., & Kim, S. J. (2019). The association of under-weight and obesity with mortality after hip arthroplasty. Age and Ageing, 48, 94-100. doi:10.1093/ageing/afy161

References

Yoo, J. H., Oh, H. C., Park, S. H., Kim, J. K., & Kim, S. H. (2018). Does obesity affect clinical and radiological outcomes in minimally invasive total knee arthroplasty? Minimum 5-year follow-up of minimally invasive TKA in obese patients. Clinics in Orthopedic Surgery, 10, 315-321. doi:10.4055/cios.2018.10.3.315

Image Citations

Health Jade Team. (2018). Knee replacement.

Issa, R., and Griffin, T. M. (May 2012). Pathobiology of obesity and osteoarthritis: integrating biomechanics and inflammation. Pathobiology of Aging and Age Related Diseases, 2. DOI: 10.3402/pba.v2i0.17470

Dearnley, P. (August 2005). A brief review of test methodologies for surface-engineered biomedical implant alloys. Surface and Coatings Technology, 198, 483-490. DOI: 10.1016/j.srfcoat.2004.10.067

The Vulnerability of Type I Diabetic Adolescents and Young Adults for Developing Mental Health Disorders

Authored by: Gabrielle Ruban
Edited by: Preethi Reddi **Reviewed by: Dr. Arri Eisen**

According to the Centers for Disease Control and Prevention's 2017 National Diabetes Statistics Report, 23.1 million Americans are living with diabetes, with an additional 7.2 million going undiagnosed. Diabetes comes in two main forms: Type I diabetes (T1), which is characterized by the autoimmune eradication of pancreatic insulin-producing beta cells, and Type II diabetes (T2), which involves insulin resistance (Centers for Disease Control and Prevention, 2017). Although T1 diabetes only encompasses about 5% of the diabetic population, just under 100 Americans are diagnosed with T1 every single day according to statistics.

Figure 1: Type 1 diabetes is a prevalent chronic illness in the United States, affecting populations of all ages, ethnicities, and genders. There is currently no cure for Type 1 diabetes, with insulin therapy being the only option to promote health stability and longevity in individuals with T1 diabetes.

T1 diabetes can be diagnosed at any age, yet the illness is most commonly diagnosed in childhood or adolescence. In addition to T1 diabetes, mental health disorders most commonly emerge in adolescence and early adulthood. As published by the National Alliance on Mental Illness, "50% of all lifetime cases of mental illness begin by age 14 and 75% by age 24." In addition to mental illnesses developing due to genetics and biomolecular imbalances, they can also emerge from poor lifestyle choices, such as irregular sleep, poor diet, and substance use, as well as from environmental stimuli, such as unsafe living conditions and traumatic events (Walsh, 2011). For instance, approximately 12% of T1 diabetics suffer from major depression and another 25% suffer from milder forms of depressive symptoms. Because the incidence of diabetes and mental illness co-occur most prominently in adolescence, the correlation between the two conditions, as well as how college life contributes to increased risk, needs to be examined.

"The diagnosis of a chronic illness, such as diabetes, can greatly impact an individual's mental health"

The diagnosis of a chronic illness, such as diabetes, can greatly impact an individual's mental health, especially when conditions emerge in the vulnerable time between childhood and adolescence. Because blood glucose levels are based on carbohydrate intake, diabetes management requires patients to be hypervigilant of timing meals and predetermining macronutrient quantities in order to regulate blood glucose levels rather than eating based on hunger and satiety. Whether it be syringes or pumps, diabetes requires insulin injections for blood glucose regulation. Seeing as insulin propagates fat storage, many T1 diabetics gain weight as a result of treating their autoimmune disease and soon discover the relationship between weight loss and restricted insulin intake (Larrañaga, 2011). Due to heightened difficulties with maintaining ideal weight, T1 diabetics are known to be more self-conscious about their weight compared to their non-diabetic counterparts (Larrañaga, 2011).

"Of those with T1 diabetes, about 38% of females and 16% of males have eating disorder behaviors (Hanlan, 2013)"

Although eating disorders can emerge in all demographics and at any point in life, they are most prevalent in young women from Western populations

where thinness is a beauty ideal and dietary restraint and calorie-counting are common practices (Larrañaga, 2011). In fact, 20 million American women and 10 million American men suffer from an eating disorder at some point in their lives (Wade, Keski-Rahkonen, & Hudson, 2011). Because diabetes management can provoke distress regarding food intake, body image, and weight, this can manifest as diabulimia, an eating disorder characterized by restricted insulin intake for weight loss purposes. Of those with T1 diabetes, about 38% of females and 16% of males have eating disorder behaviors (Hanlan, 2013). In addition to fear of weight gain from proper insulin therapy, women, in particular, were found to restrict insulin intake as a result of elevated diabetes-specific stressors, fear of hypoglycemia, and overall psychological distress. When insulin intake is restricted, various physiological complications can arise: dehydration, breakdown of muscle tissue, diabetic retinopathy, neuropathy, vascular disease, ketoacidosis, ketosis, high risk for infections, and even death (Larrañaga, 2011). Similarly to how the chronic illness of diabetes can provoke psychological distress, these related complications of improper insulin management can worsen emotional health in diabetics as they experience physical health deterioration (Larrañaga, 2011). Physical and psychological health are directly related, and when one deteriorates, the other usually follows. External stressors, such as acclimating to college, are often what provoke such

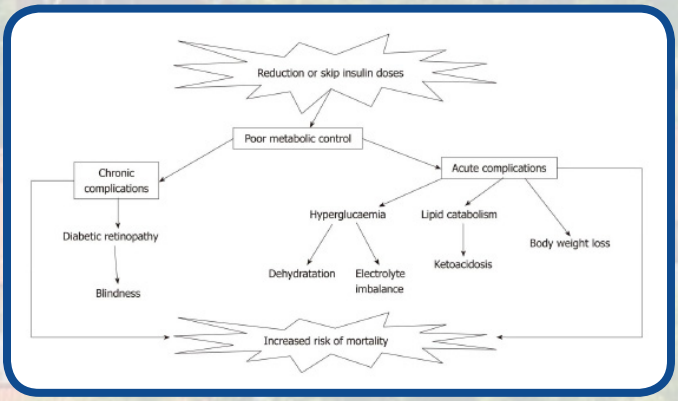


Figure 2: Proper attendance to glycemic control is essential for promoting the greatest quality of life for T1 diabetics, and diabetics in general. When insulin therapy is neglected, various physical complications can arise - some even fatal - that also can provoke the development of psychological distress or even disorders.

health degradation.

Whether or not students are diabetic, all incoming college students face a variety of challenges that come with transitioning into a new institution, environment, and lifestyle. Whether it is creating new relationships, managing new schedules, deciphering personal identity, or weighing which new experiences are worth pursuing, many students--especially in the beginning--can feel overwhelmed, uncertain, or distressed about their new life. Based on a 2007 comprehensive health survey of approximately 10,000 college students from Minnesota, 27.1% percent of students have been diagnosed with a mental illness at some point in their lives, with another 15.7% having been diagnosed within a year prior to the study

"Although diabetes affects a significant population of youths, a recent survey has shown that only 51% of four-year undergraduate institutions in the United States could provide on-campus resources for diabetes care (Lemly, Lawlor, Scherer, Kelemen & Weitzman, 2014)."

(University of Minnesota, 2007).

For T1 diabetics college students, there are additional obstacles. Depending on the institution, glycemic control can deteriorate through lack of access to health food options, decreased physical activity, and the inconsistent schedules of students who are balancing academic classes, clubs, and social life (Monaghan, Helgeson, & Wiebe, 2015). Although diabetes affects a significant population of youths, a recent survey has shown that only 51% of four-year undergraduate institutions in the United States could provide on-campus resources for diabetes care (Lemly, Lawlor, Scherer, Kelemen & Weitzman, 2014). Because the development of depression is so prevalent in college students, a T1 diabetic and depressed college student could lose proper regimens for self-care and insulin therapy as a result of deteriorating mental health. If diabetics lack resources and support in managing glycemic control, the discomfort may provoke unhealthy means of lowering their blood glucose levels or dealing with emotional distress. In addition to developing diabulimia or other eating disorders as a means of portraying control in one's life, T1 diabetics may also become victim to the most prevalent problem amongst college students: substance use disorders. According to the 2012 National Survey on Drug Use and Health, "...the rate of current use of illicit drugs was 22.0 percent among full-time college students aged 18 to 22" (NSDUH, 24). Although only about 5% of college students meet the criteria for substance abuse or drug use disorders (Blanco, 2008), 20% of college students are frequent binge drinkers and 25% of college students also relate drinking to academic consequences like missing classes or a lower

grades (White, 2014). Due to the regimens they must maintain to have proper glycemic control, T1 diabetic adolescents are more vulnerable to the consequences of the inconsistent and erratic lifestyles of college students and, thus, require more constant medical support and resources from their institutions in order to avoid developing or worsening mental health issues that could compromise their physical health as well.

Diabetes is an autoimmune disorder that is prevalent globally. T1 diabetes emerges particularly in adolescence and young adulthood, a time that is vulnerable to hormonal, emotional, and physiological changes. Whether it is puberty or the disruption of routine and regularity that comes with transitioning into college life, T1 diabetics are just as susceptible, if not more so than their non-diabetic peers, to developing psychiatric disorders that can compromise their glycemic control and overall physical health. With factors like new responsibilities, erratic and inconsistent daily agendas, and experimentation through relationships and substance use, college students are faced with a lot of disruptive change that, for T1 diabetics, can prove to be even more dangerous. T1 diabetics should feel confident and secure that they have the resources and support to maintain proper insulin therapy and healthy lifestyles that promote both a high quality of life but also help ensure low risks for diabetes' physical and psychological complications.

References

Blanco, C., Okuda, M., Wright, C., Hasin, D. S., Grant, B. F., Liu, S. M., & Olfson, M. (2008). Mental health of college students and their non-college-attending peers: results from the National Epidemiologic Study on Alcohol and Related Conditions. Archives of general psychiatry, 65(12), 1429-37.

Centers for Disease Control and Prevention (2017). National Diabetes Statistics Report, 2017. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services; 2017. https://www.cdc.gov/diabetes/data/statistics/statistics-report.html

Hanlan, M. E., Griffith, J., Patel, N., & Jaser, S. S. (2013). Eating disorders and disordered eating in Type 1 diabetes: prevalence, screening, and treatment options. Current Diabetes Reports, 13(6), 909-916.

Larrañaga, A., Docet, M. F., & García-Mayor, R. V. (2011). Disordered eating behaviors in type 1 diabetic patients. World journal of diabetes, 2(11), 189-95.

Lemly, D. C., Lawlor, K., Scherer, E. A., Kelemen, S., & Weitzman, E. R. (2014). College health service capacity to support youth with chronic medical conditions. Pediatrics, 134(5), 885-91.

Monaghan M., Helgeson V., Wiebe D. (2015). Type 1 diabetes in young adulthood. Curr Diabetes Rev., 11(4), 239-50.

Substance Abuse and Mental Health Services Administration. (2013.) Results from the 2012 National Survey on Drug Use and Health: Summary of National Findings. Substance Abuse and Mental Health Services NSDUH Series H-46, HHS Publication No. (SMA) 13-4795, 1-178.

University of Minnesota. (2007, November 16). Report On Health And Habits Of College Students Released. ScienceDaily. Retrieved February 27, 2019 from www.sciencedaily.com/releases/2007/11/071115125827.htm

Wade, T. D., Keshki-Rahkonen, A., Hudson, J. (2011). Epidemiology of eating disorders. Textbook in Psychiatric Epidemiology, 3rd edition. 343-360.

Walsh, R. (2011). Lifestyle and Mental Health. American Psychologist, 66(7), 579-592.

White A, Hingson R. (2014) The burden of alcohol use: excessive alcohol consumption and related consequences among college students. Alcohol Res. 35(2), 201–218.

Image Citations

Staff, Diabetes Daily. "What Is Type 1 Diabetes?" Diabetes Daily, www.diabetesdaily.com/learn-about-diabetes/what-is-type-1-diabetes.

Larrañaga, A., Docet, M. F., & García-Mayor, R. V. (2011). Disordered eating behaviors in type 1 diabetic patients. World journal of diabetes, 2(11), 189–195. doi:10.4239/wjd.v2.i11.189

The Neuroscience Behind Social Network Site Addiction

Authored by: Jinny Yoo
Edited by: Hannah Kelly **Reviewed by: Dr. Waqar Azeem**

Every second, six new Facebook profiles are created, amounting to 500,000 per day ("Facebook: global daily active users 2018"). Unsurprisingly, the emergence of social media technologies, such as Facebook, has allowed humans to amass a rapidly-expanding network of relationships. Today, social media users can interact with millions of new profiles, bridging communication and connection for companions across the globe. However, the first humans interacted with a mere 150 individuals in one's entire lifespan, and it is hypothesized that our brains are not fit for the thousands of interactions we may have today (Gluckman, et al., 2016). Advances in technology have therefore brought repercussions, including onset of addiction. Recently, scientists have attempted to identify the dynamic between the advent of social media and the neuroscience behind addiction disorder, and the observations, with changes in brain structure and reward pathways, are striking.

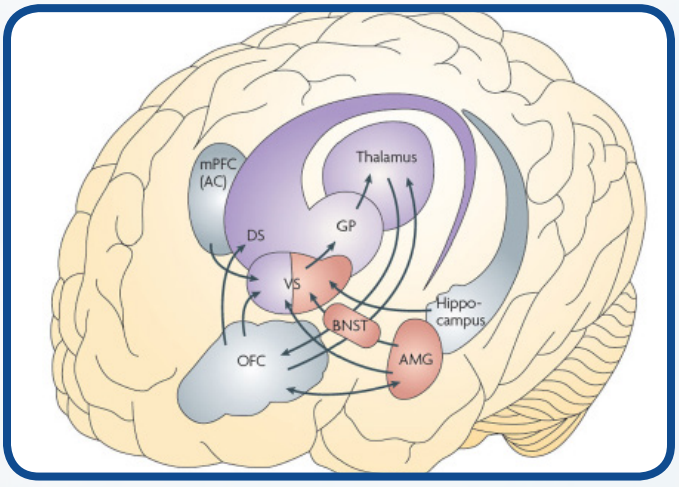
Since the development of the DSM-10, there have been 157 officially-diagnosable mental illnesses recognized in the United States (McCarron, 2013); among them are addiction, postpartum depression, bipolar disorder, and eating disorders to name few ("Online Assessment Measures", 2018). Interestingly, some of the symptoms of addiction, including "pre-occupation and craving, loss of alternative interests, social retreat, tolerance, withdrawal," have been identified with social media usage (Müller, 2015). Likewise, the University of Bergen in Norway has found a positive association between the Big Five personality traits of Neuroticism and Extraversion and social media addiction (Andreassen, C. S., et al, 2012). In 2016, a research study performed at Nanyang Technological University in Singapore explored the link between addiction and social media usage with a similar study. Accordingly, there are about 2.03 billion active social network site (SNS) users worldwide, and "SNSs excessive use" and "SNSs addiction" are two phenomenon thought to have problematic consequences, such as lack of sleep or delayed bedtimes. This study found that adolescents, particularly those with high levels of neuroticism and a need to belong, were prone to facing such results, while highly extroverted adults were also positively associated with these variables (Ho, 2017).

Facebook "pills" represent that the ultimate social media platform is associated with addiction.

From the psychological perspective to the biological, scientists have found parallels between the same neurological pathways in social media usage and addiction.

The addictive pathway in the brain occurs mainly in the limbic system, particularly with the amygdala (Meshi, et al: 2019). By exploring areas of the brain implicated in social media usage, scientists have found similarities in brain function and pathways between addiction and SNS. For example, Meshi and colleagues report that "the striatum and amygdala are smaller in both excessive SNS users and substance abusers" (Meshi, et al: 2019). A study at Michigan State University found that, similar to substance abusers and addicts, those with excessive social media usage also exhibit impaired decision making and a propensity towards risky behavior (Meshi, et al: 2019).

Social media usage not only affects decision making, but also may correlate with depression and SNS. A study conducted at Lancaster University

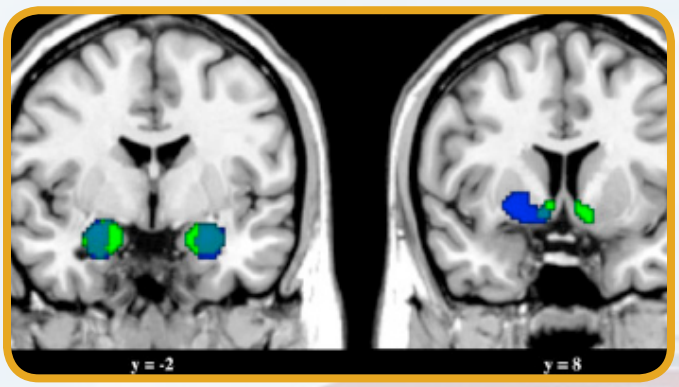


The Reward Pathway: this map highlights the reward pathway in our brains.

found that even after controlling for confounding variables such as socioeconomic status and gender, significant associations persisted between depression and social media usage (Baker & Algorta: 2016). Although the relationship is indubiously complex, there have also been explanations made for the benefits of social media and its protective factors against depression, such as the potential to establish online supportive networks.

The brain's reward pathway is not the only surprising difference for social media users; the brain morphology amongst users has been found to be distinct. In the amygdala, the gray matter volume for excessive social media users was found to be reduced, as seen in Figure 3. This can possibly be explained by fewer neurons in a smaller amygdala, leading to faster responses to conditioned stimuli, a possible outcome from notifications with SNS (He, Q., et al, 2017). Another study in Germany found significantly higher activity in the nucleus accumbens in those with an increased frequency of Facebook usage over a five week timespan. There was no such finding for the amygdala or the hippocampus, two structures also involved in the reward pathway, which acted as controls to detect significant activity in the nucleus accumbens (Montag, C., et al, 2017).

To make the comprehensive connection between neuroscience and social media usage, scientists must draw on diverse fields from anthropology to cognitive sciences. The motive for social media is, ultimately, to create, build, and resume relations while maintaining one's reputation: users



Brain morphology in social media users show a reduced amygdala, leading to questions about how the physiological difference could affect daily behavior.

can post information, photos, and experiences with one another while sending and receiving messages, comments, and likes.

Researchers in Princeton University have found specific parts of the brain that are involved with social media usage, and they have found contributions to negative performance in academics, occupation, and wellbeing (Meshi, D., et. al, 2015). This burgeoning field of research is essential as

> "Even the smallest of such notifications can activate brain's reward system, initiating a cycle of social media usage and feedback."

technology and the Internet continue to expand. As such, the links between personality and excessive social media usage have captured the interests of neuroscientists, who have mapped brain areas linked with the reward pathway, addiction, and SNS usage. Perhaps, it is useful to remind ourselves of life before such advancements in order to fully study the effects of social media.

References

American Psychiatric Disorders. (2018). Online Assessment Measures. Retrieved from

Andreassen, C. S., Torsheim, T., Brunborg, G. S., & Pallesen, S. (2012). Development of a Facebook Addiction Scale. Psychological Reports, 110(2), 501–517.

Baker, D. A., & Algorta, G. P. (2016). The relationship between online social networking and depression: A systematic review of quantitative studies. Cyberpsychology, Behavior, and Social Networking, 19(11), 638–648.

Facebook: Global daily active users 2018 | Statistic. (n.d.). Retrieved from https://www.statista.com/statistics/346167/facebook-global-dau/

Gluckman, P. D., Beedle, A., Buklijas, T., Low, F., & Hanson, M. A. (2016). Principles of evolutionary medicine. Oxford: Oxford University Press.

He, Q., Turel, O., Brevers, D., & Bechara, A. (2017). Excess social media use in normal populations is associated with amygdala-striatal but not with prefrontal morphology [Abstract]. Psychiatry Research: Neuroimaging,269, 31-35. doi:10.1016/j.pscychresns.2017.09.003

Ho, S. S., Lwin, M. O., & Lee, E. W. (2017). Till logout do us part? Comparison of factors predicting excessive social network sites use and addiction between Singaporean adolescents and adults. Computers in Human Behavior,75, 632-642. doi:10.1016/j.chb.2017.06.002

McCarron RM. The DSM-5 and the Art of Medicine: Certainly Uncertain. Ann Intern Med. ;159:360–361. doi: 10.7326/0003-4819-159-7-201310010-00688

Meshi, D., Elizarova, A., Bender, A., & Verdejo-Garcia, A. (2019). Excessive social media users demonstrate impaired decision making in the Iowa Gambling Task. Journal of Behavioral Addictions,1-5. doi:10.1556/2006.7.2018.138

Meshi, D., Tamir, D. I., & Heekeren, H. R. (2015). The Emerging Neuroscience of Social Media. Trends in Cognitive Sciences,19(12), 771-782. doi:10.1016/j.tics.2015.09.004

Montag, C., Markowetz, A., Blaszkiewicz, K., Andone, I., Lachmann, B., Sariyska, R., . . . Markett, S. (2017). Facebook usage on smartphones and gray matter volume of the nucleus accumbens. Behavioural Brain Research,329, 221-228. doi:10.1016/j.bbr.2017.04.035

Müller, K., Dreier, M., Beutel, M., Duven, E., Giralt, S., & Wölfling, K. (2015). A hidden type of internet addiction? Intense and addictive use of social networking sites in adolescents. Computers in Human Behavior,55, 172-177. doi:10.1016/j.chb.2015.09.007

Image Citations

Bui, J. (2016, March 24). [How to Know if You're Addicted to Facebook]. Retrieved from https://www.thrillist.com/health/nation/facebook-addiction-signs-youre-addicted-to-social-media

[Drug Addiction And The Brain]. (2018). Retrieved from https://www.drugrehab.org/drug-addiction-and-the-brain/

He, Q. (2017, September 9). [Excess social media use in normal populations is associated with amygdala-striatal]. Retrieved from https://www.sciencedirect.com/science/article/pii/S0925492717302159

How the Brain Works in Monolinguals and Bilinguals

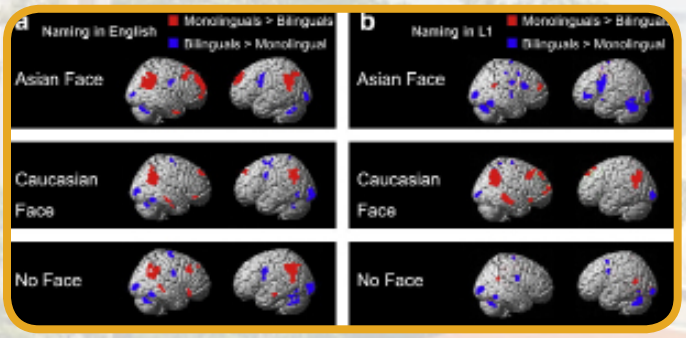
Authored by: Nivetha Aravind and Sarah Kim
Edited by: Haejin Kang **Reviewed by: Dr. Tyler Cymet**

In an increasingly globalized world, the acquisition of a second language has become a crucial asset. According to a survey conducted by the European Commission in 2006, about 56% of the world's population know more than one language (Marian and Shook 2012).

Bilinguals can be defined as those who may have chosen to study another language and those who have been exposed to two languages in the early or later stages of their life (Guadalupe). With the interest in how neural networking of monolingual and bilingual individuals differ, research studies have often emphasized whether the second language learning acts as an advantage or a disadvantage. Despite arguments regarding the advantages and disadvantages of bilingualism, the inherent differences between the bilingual and monolingual brains must first be established.

More than one language is perceived as an interference to language processing. A study tested both monolingual and bilingual speakers in their linguistic abilities through a wide range of tasks in one's first language. Results showed that bilingual speakers have reduced speech fluency and tend to produce fewer words when given syntactic tasks that require in-depth knowledge of vocabulary (Costa and Galles 2015). Monolinguals tend to have a greater breadth of knowledge about the syntactical choices of words that are needed to better represent what they are trying to say. Moreover, bilinguals tend to suffer more from "tip of the tongue" situations, in which they are essentially unable to express the exact word(s) they are thinking (Costa and Galles 2015). If metaphorically comparing this to multitasking of the brain, it is logical to argue that switching from one language to another may lead to a more superficial understanding of the first language, essentially disabling the speaker from full comprehension or full communication in either language.

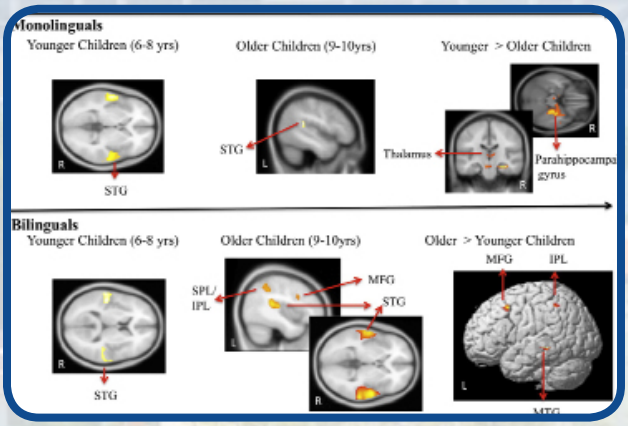
fMRI scans of brains suggest that bilingualism simply initiates different neural activations, which may lead to dissimilar performance in a given verbal task. Having to discriminate the appropriate language to use depending on the linguistic community of the speaker, listener, or interlocutor, bilingual individuals utilize nonverbal cues. The most prominently used cues are facial cues. In a 2013 study, Li, Yang, Scherf, and Li investigated the role of the race of a face in the lexical activation of the brain through fMRI. In a picture-naming task, bilinguals who spoke Chinese and English and monolinguals who only spoke English first saw either the face of an Asian or a Caucasian and answered a series of naming events in either language. In incongruent language-naming pairings, monolingual and bilingual individuals activated different areas of their brains for language processing. Primed with Asian faces and asked to name in English, the more active brain areas of bilinguals were the left inferior frontal gyrus, bilateral cingulate gyrus, right caudate, and occipital regions (responsible for eyesight). On the other hand, the right prefrontal cortex, right temporal regions, bilateral precuneus, and right supramarginal gyrus were more activated for monolinguals. These regions are mainly concerned with somatosensory and complex cognitive behaviors. In the opposite incongruent situation, bilinguals had a decrease in prefrontal and parietal activity and an increase in the right inferior posterior temporal area activity whereas monolinguals demonstrated no particular change from the prior condition (Li et al. 2013).



fMRI scans show the different linguistic activation of the brain areas between English monolingual and Chinese-English bilingual speakers when given the task to name objects after being primed with an Asian or Caucasian face.

In another fMRI study with English monolinguals and Spanish-English bilinguals, results demonstrated that "while monolinguals recruit perceptual areas in early and late childhood to process native speech, bilinguals recruit perceptual areas in early childhood and higher-order executive areas in late childhood to process non-native speech"

(Archila-Suerte et al. 2012). The results reject the conventional belief that the second language interferes with the bilingual individual's ability to process the first language. Facial cues were thought to promote the native language by fixating one's brain on the specific culture and linguistic contexts which inhibits the fluency of the second language (Zhang et al. 2013). In fact, facial cues amplify the processing of the first language in both bilingual and monolingual groups (Li et al. 2013). The focus is not on the advantages or disadvantages that the second language brings. The bilingual and monolingual speakers display contrasting neural activities that indicate that their brains function and process language differently from

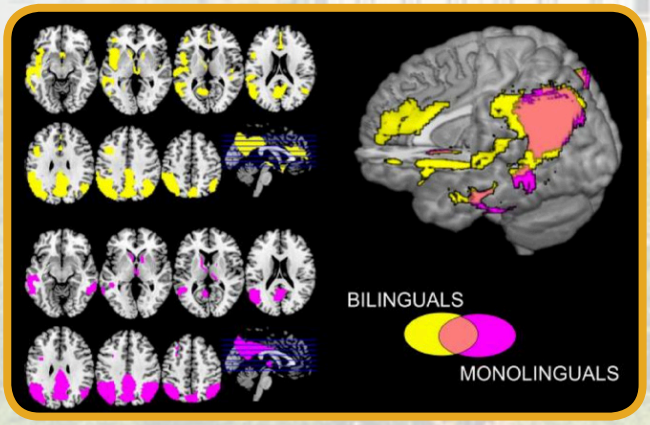


Monolingual individuals exhibit more neural activity for the native language in younger ages while bilingual speakers have more activity later in life for the second language.

each other.

As for bilingual and monolingual speakers and their susceptibility to neurodegenerative diseases, bilingual speakers tend to have different characteristics of their brains that allow them to react to neurodegenerative diseases in a different manner than monolinguals. A study by Duncan et al. has shown that bilingual speakers tend to have greater brain plasticity and increased amounts of gray matter (Duncan et al. 2018). Moreover, bilingual speakers are not less susceptible to the disease, itself, but are more likely to to develop the disease later on in life. A study conducted by Perani et al. showed that while the current mechanism is unknown, bilingual speakers have neural activity that delays the onset of neurodegenerative diseases (Perani et al. 2017) This, again, shows that the differences between bilingual and monolingual speakers rest in their different neural activities and does not necessarily give monolinguals or bilinguals an advantage over one another.

Whether monolingualism or bilingualism produces more wired brains have continuously been a topic of discussion. Language acquisition and sustainability are seen to be less common in bilinguals as they are able to communicate in multiple languages, but not to the full extent in either separate language. However, brain scans of these individuals all point at the varying neural activations which may explain the contrasting outcomes in different studies. While brain plasticity has shown to be greater in bilinguals, the only evidence shows that neural activities differ, not that bilinguals truly have a mechanism to fend off neurodegenerative diseases. Nonverbal cues produce enhanced language processing in both monolingual and bilingual individuals; however, more areas of bilingual brains are in activity to process the second language. Similarly, monolingual speakers utilize more brain areas earlier in life, but the brains of bilingual speakers exhibit more activity in older ages in order to operate a second language. Depending on what the task requires, monolingual and bilingual speakers may demonstrate higher performances due to dynamic differences in their neuroanatomy and neural feedback activities. Rather than making conclusive statements on the advantage of speaking one or more languages, more attention should be placed on how the contrasting activations of brains correlate to the various processing of diverse information.



Process of genomic paleopathology and resulting avenues of research (Andam et al., 2016).

References

Albert Costa and Núria Sebastián-Gallés. (2014). How does the bilingual experience sculpt the brain?. Nature Reviews Neuroscience.

Archila-Suerte, Zevin, Ramos, & Hernandez. (2013). The neural basis of non-native speech perception in bilingual children. NeuroImage, 67, 51-63.

Duncan HD, Nikelski, Pilon, Steffener, Chertkow, Phillips. (2017). Structural brain differences between monolingual and multilingual patients with mild cognitive impairment and Alzheimer disease: Evidence for cognitive reserve. Neuropsychologia.

Guadalupe. Multilingualism. Linguistic Society of America.

Li, Yunqing, Yang, Jing, Suzanne Scherf, K, & Li, Ping. (2013). Two faces, two languages: An fMRI study of bilingual picture naming. Brain and Language, 127(3), 452-462.

Perani, M. Farsad, T. Ballarini, F. Lubian, M. Malpetti, A. Fracchetti, G. Magnani, A. March, & J. Abutalebi. (2017). The impact of bilingualism on brain reserve and metabolic connectivity in Alzheimer's dementia. Proceedings of the National Academy of Sciences of the United States of America

Viorica Marian and Anthony Shook (2012). The Cognitive Benefits of Being Bilingual. Cerebrum.

Zhang, S., Morris, M., Cheng, C., & Yap, A. (2013). Heritage-culture images disrupt immigrants' second-language processing through triggering first-language interference. Proceedings of the National Academy of Sciences of the United States of America, 110(28), 11272-11277.

Image Citations

Archila-Suerte, Zevin, Ramos, & Hernandez. (2013). The neural basis of non-native speech perception in bilingual children. NeuroImage, 67, 51-63.

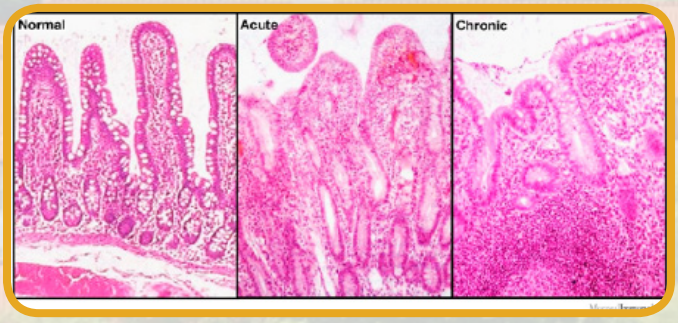
Li, Yunqing, Yang, Jing, Suzanne Scherf, K, & Li, Ping. (2013). Two faces, two languages: An fMRI study of bilingual picture naming. Brain and Language, 127(3), 452-462.

Inflammation: A Dietary Approach

Authored by: Monjori Mukerjee
Edited by: Jonathan Regenold **Reviewed by: Dr. Katherine Heiden**

Rheumatoid arthritis (RA), inflammatory bowel disease (IBD), and asthma all have one thing in common — inflammation. Today, 1.3 million adults in the US suffer from RA and in 2015, 3 million adults in the US were suffering from diagnosed IBD (CDC, 2016). In 2014, the estimated cost for IBD treatment in the US was between $14.6 and $31.6 billion(Mehta, 2016).

Inflammation itself is not always a cause for concern. There are two kinds of inflammation—acute (short term) and chronic (long term). While acute inflammation is an essential part of the healing process, chronic inflammation can lead to many of the health conditions plaguing people today, like RA, IBD, and asthma.. Treatments for these conditions (including corticosteroids and the newer biologic class of medications) are targeted at the symptoms of inflammation rather than the underlying cause (Mayo Clinic, n.d.). In an attempt to better understand the cause of chronic inflammation and autoimmunity, researchers have begun to look at our diets. There is a growing body of research suggesting that plant-based diets may play a role in reducing chronic inflammation.



Pathological differences between chronic (associated with prolonged disease states) and acute inflammation (associated with short-term disturbance or trauma) in the lining of the gut. https://www.nature.com/articles/mi200824?proof=trueln&draft=journal

A cursory glance of recommended diets by nutritionists for people suffering from IBD or RA shows an overwhelming shift towards veganism or vegetarianism. The American Society of Nutrition recommends a diet that is abundant in fruits and vegetables so as to increase the polyphenol content, soluble fiber and omega-3 to omega-6 ratio in the diet. (Dimitratos, 2019) This recommendation stems from large-scale longitudinal observational studies including the Women's Health Initiative Observational Study and Multi-ethnic Study of Atherosclerosis Study (MESA) (Dimitratos, 2019) (Women's Health Initiative Study Group, 1998) (Ma et. al, 2008) . That said, clinical trials have shown mixed results with respect to the effect of vegetarian or vegan diets on inflammatory conditions. In one study, a total of 604 adults who were either referred by primary-care physicians or self-enrolled (and who were not necessarily patients of chronic inflammatory disease), followed a vegan diet consisting of fruits, vegetables, nuts, seeds, legumes and grains for an average of 19 days. Dietary supplements, animal products and by-products were excluded from the diet. C-reactive protein (CRP), a marker of acute and chronic inflammation, was measured before and after the dietary intervention. Study subjects showed a significant reduction in CRP after the dietary intervention compared to baseline, as seen in Image 2 (Sutliffe et al., 2015).

Time period	CRP risk category		
	Low risk	Moderate risk	High risk
	n (%)	*n* (%)	*n* (%)
Pre-intervention	204 (33.8)	175 (29.0)	225 (37.3)
Post-intervention	286 (47.4)	163 (27.0)	155 (25.7)

A summary of the Sutliff et al. study showing reduced C- reactive protein after incorporating a vegan diet and other lifestyle changes. The different risk categories refer to the following: CRP <1 = Low Risk; 1.0–3.0 = Moderate Risk; and >3.0 mg/dL = High Risk for developing cardiovascular disease.

A limitation of this study is that CRP was the only marker tested, and more direct measures of systemic inflammation (IL-6 and TNF-alpha) were not included. Additionally, the study participants

also made other lifestyle changes including a regular sleep schedule and mental health counseling, both of which could have contributed to decreased CRP levels.

In another study published in the Scandinavian Journal of Rheumatology, 16 patients with RA selected at randomly underwent fasting for 7-10 days, followed by a 9-week period on a lacto-vegetarian (included dairy) diet. At the conclusion of the diet period, all patients were re-evaluated using objective criteria. Only one out of 16 patients showed objective improvement. On a whole, no significant differences were found between the diet and non-diet controls. However, this study had a small sample size and the dietary intervention period was relatively short.(Sköldstam, Larsson & Lindström, 1979) In a two-part study, researchers observed RA patients who did a vegetable fast for 7 - 10 days, followed by a gluten-free vegan diet for three and a half months, subsequently followed by a lacto-ovo-vegetarian diet for nine months (includes dairy and egg). "For all clinical variables and most laboratory variables measured, the 27 patients in the fasting and vegetarian diet groups improved significantly compared with the 26 patients in the control group who followed their usual omnivorous diet throughout the study period." One year after the patients completed the trial, they were re-examined. Compared with baseline, the improvements measured were significantly greater in patients who had previously benefited from the diet than in diet non-responders and omnivores. Further, the researchers were able to demonstrate that clinical improvements were not due to changes in psychological characteristics, antibodies against food antigens, or alterations in prostaglandin or leukotriene precursors. The authors made another interesting observation: a change in fecal microbiota in patients with clinical improvement compared to patients without clinical improvement. (Kjelson-Kragh, 1999).

Le Leu et al. (2013) reported that dietary red meat aggravates colitis, whereas starch attenuates inflammation in a colitis mouse model. In the case of IBD, a considerable amount of data exists connecting diet-induced changes in gut micro flora to the development of disease. In a small-scale observational study of adult patients with Crohn's disease, Chiba et al. (2014) reported excellent relapse prevention associated with consumption of a semi-vegetarian diet, and the authors attributed the disease to imbalance of gut micro flora and dietary metabolites. They concluded the importance of adhering to plant-based diets in patients with Crohn's disease as well as other inflammatory conditions. However, what exactly was happening in the microbiome remained unexplored.

"For all clinical variables and most laboratory variables measured, the 27 patients in the fasting and vegetarian diet groups improved significantly compared with the 26 patients in the control group who followed their usual omnivorous diet throughout the study period."

The mechanism by which a plant-based diet and the resultant changes in the gut microbiome may influence inflammatory disease remains largely unknown. Recent research has revealed that the chemical butyrate may be a key player in the inflammatory pathway. Butyrate is an end-product of fermentation by gut microbiota on fermentable fiber. It controls human dendritic cell maturation, which in turn is important for maintaining homeostatic immunity. Additionally, butyrate inhibits adipocyte–macrophage inflammatory interactions (Minihane et al., 2015). A diet which is high in fiber may increase the level of butyrate, hence reducing chronic inflammation.

Extensive research has revealed that a plant-based diet may reduce inflammation and improve symptoms in patients suffering from chronic inflammatory conditions like RA and IBD. More research on the composition of the microbiome and factors that influence and change it, as well as other possible effects of following a plant-based diet are needed to understand how these may be utilized to reduce, or even prevent, chronic inflammatory diseases.

References

A Kid's Guide to Vegan Nutrition. (n.d.). Retrieved February 22, 2019, from https://www.petakids.com/food/kids-vegan-nutrition-guide/

Chiba, M., Yoshida, T., & Komatsu, M. (2014). From Low-Residue Diets to Plant-Based Diets in Inflammatory Bowel Disease. Digestive Diseases and Sciences,59(12), 3129-3130. doi:10.1007/s10620-014-3399-5

Chronic inflammation Archives. (n.d.). Retrieved February

22, 2019, from http://uninhibitedwellness.com/tag/chronic-inflammation/

Data and Statistics. (n.d.). Retrieved January 06, 2016, from https://www.cdc.gov/ibd/data-statistics.htm

Dimitratos, S. (2019, January 31). Inflammation: What Is It, and how can my diet and behavior affect it? Retrieved February 22, 2019, from https://nutrition.org/inflammation-what-is-it-and-how-can-my-diet-and-behavior-affect-it/

Inflammatory bowel disease (IBD). (2017, November 18). Retrieved February 22, 2019, from https://www.mayoclinic.org/diseases-conditions/inflammatory-bowel-disease/diagnosis-treatment/drc-20353320

Jacques, P., & Elewaut, D. (2008). Joint expedition: Linking gut inflammation to arthritis. Mucosal Immunology, 1(5), 364-371. doi:10.1038/mi.2008.24

Kjeldsen-Kragh, J. (1999). Rheumatoid arthritis treated with vegetarian diets. The American Journal of Clinical Nutrition,70(3). doi:10.1093/ajcn/70.3.594s

Le Leu RK, Young GP, Hu Y, Winter J, Conlon MA. Dietary red meat aggravates dextran sulfate sodium-induced colitis in mice whereas resistant starch attenuates inflammation. Dig Dis Sci. 2013;58:3475–3482.

Ma, Y., Hébert, J. R., Li, W., Bertone-Johnson, E. R., Olendzki, B., Pagoto, S. L., . . . Liu, S. (2008). Association between dietary fiber and markers of systemic inflammation in the Womens Health Initiative Observational Study. Nutrition, 24(10), 941-949. doi:10.1016/j.nut.2008.04.005

Mehta, F. (2016, March 16). Report: Economic Implications of Inflammatory Bowel Disease and Its Management. Retrieved February 28, 2019, from https://www.ajmc.com/journals/supplement/2016/importance_of_selecting_appropriate_therapy_inflammatory_bowel_disease_managed_care_environment/importance_of_selecting_appropriate_therapy_inflammatory_bowel_disease_managed_care_environment_report_economic_implications_ibd

Minihane, A. M., Vinoy, S., Russell, W. R., Baka, A., Roche, H. M., Tuohy, K. M., . . . Calder, P. C. (2015). Low-grade inflammation, diet composition and health: Current research evidence and its translation. British Journal of Nutrition,114(07), 999-1012. doi:10.1017/s0007114515002093

Sköldstam, L., Larsson, L., & Lindström, F. D. (1979). Effects Of Fasting and Lactovegetarian Diet on Rheumatoid Arthritis. Scandinavian Journal of Rheumatology,8(4), 249-255. doi:10.3109/03009747909114631

Sutliffe, J. T., Wilson, L. D., Heer, H. D., Foster, R. L., & Carnot, M. J. (2015). C-reactive protein response to a vegan lifestyle intervention. Complementary Therapies in Medicine,23(1), 32-37. doi:10.1016/j.ctim.2014.11.001

W. (1998). Design of the Women's Health Initiative Clinical Trial and Observational Study. Controlled Clinical Trials, 19(1), 61-109. doi:10.1016/s0197-2456(97)00078-0