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**Exploring Culture and Mental Health**

**A spring 2012 Independent Study**

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## Abstract

While there is evidence for a relationship between culture and expression of mental illness, the nature of this interaction is ambiguous. In anthropological terms, culture is a behavioral pattern thought to help the individual best adapt to the surrounding social landscape. Culture can range from vague to specific spheres. Country of origin, city of residence, and even individual neighborhoods each have a distinct social environments. The multiple cultures to which an individual is exposed are determined by and thus encompass a variety of factors such as socio-economic and migratory status. These multiple social landscapes characterize environmental influence. The interface between genes and environment is known to have profound effects on mental health. Exploring this relationship exposes pathogenesis of some mental illnesses and the vulnerability of certain groups to pathologies.

## Introduction

At a young age individuals learn to interpret the meaning of events in their surroundings. This interpretation governs perceptions of the self as well as reactions to experiences throughout the lifetime. In the *Social Construction of Reality*, C. Wright Mills argues that these interpretations are largely subjective. Social reality governs how individuals view the world and in turn pass their views on to their offspring. In Sociological and Anthropological thought, the mechanism of constructing meaning and interpretations is culture. Mental illness effects a person's self-construct and interpretation of the world around them. On an abstract level, mental illness and culture both deeply effect phenomenology, indicating a relationship between the two. Bio-medical models have given little attention to the involvement of culture in development and outcome of mental disorders, instead focusing on primarily genetic factors. If not already obvious, mental illness itself proves that biology affects the psychological realm. Would it not be appropriate for the relationship to work the other way around as well? This paper explores numerous ways that culture potentially moderates outcome and development of mental illness. The hope is to demonstrate that human environment and biology are inseparable and consequently so is interpreting mental illness without respect to culture.

## Epigenetics, the link between environment and behavior

In the early nineties it was assumed that DNA was unalterable by individual lives. Inheritance was a fixed aspect and the only differences in genetic code due to changes in combinations of parental DNA. DNA is composed of four bases, Adenine, Guanine, Thymine, and Cytosine. It is the order of these base pairs which determine how an organism is built and maintained. When a cell replicates, a portion of DNA is carried with it. Genes, the functional unit

of heredity, are composed of DNA and form a set of instructions to make proteins (Watson & Crick, 1953). While each individual has a set of genes, genotype, not all of these genes will be expressed. Although not all genes are expressed in the individual, phenotype, the role of an allele, or gene type, changes according to other alleles present in the genome. Still, a belief in a sort of 'genetic astrology' remains pertinent. Even today it is not uncommon to hear of emerging researching claiming to have discovered a gene for obesity, criminality, and even religiosity (Lamb, Jablonka, 2007).

In the 90's the human genome project sought collected DNA samples from thousands of people around the world. Researchers expected to find some one hundred and forty thousand genes or more that would code as instructions for the variety of human biology. Instead they found around 30,000. The same amount of genes found in mice and far too few to account for the diversity of human life. It soon became apparent that a different mechanism played a large role in inheritance (Lamb, Jablonka, 2007; Palsson, 2008).

Recent studies suggest that diversity of the human phenotype expression is due not so much to our genetic makeup as it is to epigenetic coding. Initial evidence for epigenetic inheritance was first demonstrated in the Överkalix study. This study compared mortality risk ratios of 164 men and 139 women born in 1890, 1905, or 1920 as indicated by events in the lives of their 1,818 parents and grandparents. The mortality risk of the parents and children were determined by historical records of food availability during the grandparent's lifetime. They found that food availability on the paternal side was linked to grandsons but not granddaughters, while the food supply on the maternal side was linked to granddaughters but not grandsons. A high mortality risk ratio for granddaughters was indicated by a bountiful food supply during the grandmothers slow growth period (age 8-10) or during her time in the womb. A high mortality

risk ration for grandsons was indicated by a bountiful food supply during their slow growth period (age 9-12). Contrarily, low life expectancy for grandchildren was indicated by decreased food availability of the paternal (for boys) and maternal (for girls) grandparent during these times. Genomic imprinting, an epigenetic mechanism, explains this strange relationship between parents and children. A small number of inherited genes, .01 percent, have epigenetic tags which indicate whether or not they come from the paternal or maternal side. How the gene is expressed depends upon this tag. This study indicates that experiences during our lifetimes can be inherited by future generations through what has since been identified as epigenetic inheritance (Byrgen, 1986). Epigenetic mechanisms may be a possible interface between the environment, the genome and vulnerability to mental disorders.

Genetic factors are certainly linked to mental illness. While for some mental illnesses the genetic underpinnings are evident, for others they are not. These two types of mental illnesses can be categorized as neuropsychiatric disorders such as Huntington's and Alzheimer's and idiopathic disorders, such as schizophrenia, bipolar, and major depression, respectively. Idiopathic disorders are far more common, major depressive disorder affects 12.5 percent of the population and schizophrenia about 1.5 percent (Peedicayil, 2007). Genetic mapping has sought to characterize idiopathic disorders, yet no genetic mutation or polymorphisms has been indicated. Several researchers suggest that generic mutations or polymorphisms may not exist in these disorders. Rather the genetic basis may be defects in gene expression rather than in the DNA sequence, perhaps through epigenetic mechanisms. Epigenetic mechanisms may occur one of three ways (Peedicayli, 2006; Potash, 2006).

The first is DNA methylation. DNA is methylated by the addition of a methyl group to the cytosine nucleotide. This addition will result in silencing of a gene by reducing the likelihood

that it will be transcribed by Mrna polymers. Transcription is the process of replicating DNA when cells divide. Thus if a portion of DNA is not replicated it will not be transferred to the divided cell. Depending on the position of the addition in relationship to the position of the transcription start site this addition will result in gene silencing. Epigenetic factors, acetylation and methylation, are also involved in cell differentiation. Before cells are differentiated, they are known as stem cells. Different chemicals can be applied to stem cells to alter which pattern of DNA is expressed and consequently what the cells grow to be. Acetylation and methylation are the body's natural process for differentiating cells by reducing the likelihood that genes which are unnecessary for creating a certain cell will be expressed, and increasing the likelihood that those necessary for creating cells are (Rutten, Mill, 2008; Jones& Takai, 2001).

The second process is histone modification. DNA is wrapped in a histone protein coil which is susceptible to post-transformational chemical alterations such as methylation and acetylation. If genes are densely packed, they will be less easily accessible which reduces the likelihood they will be transcribed. If a methyl group, or a (CH<sub>3</sub>) bond, attaches to the Cytosine-Guanine portion of the DNA, the histone around the DNA thus reducing the likelihood that it will be transcribed (Rutten, Mill, 2008; Holiday & Pugh, 1975; Riggs, 1985; Champagne, 2002). Chemicals of the acetyl group on the other hand modify histones by loosening their coil around the DNA and increasing the possibility for RNA polymers to attach and transcribe DNA. Histone modification is a less permanent alteration than methylation changes. For example, histone modification increases breast cell size during menstruation but does not make lasting changes in the reproduction of these cells. If the change proves necessary for external circumstances histone modification can become more lasting by attracting Methyl groups which then attach to the DNA and transfer the methylation pattern to daughter cells (Jenuwein & Allis, 2001).

The third way epigenetic modification can occur is through RNA alteration. Small segments of RNA can silence genes before or after transcription takes place. The smaller RNA, 21 to 28 nucleotides long, targets the cleavage of larger RNAs which make proteins. When protein synthesis is inhibited, gene silencing occurs (Jenuwein & Allis, 2001).

Epigenetic mechanisms are thought to be the interface between genes and the environment in idiopathic disorders. Studies on animal models demonstrate that behaviors and stress responses may be passed down through generations without any genomic factors. Mother pub-liking behavior was shown to increase the number of glucocorticoid receptors in the hippocampus in rat pups. These increased glucocorticoids receptors were due to change in DNA methylation patterns and histone acetylation which effects expression of the glucocorticoid gene promoter (Francis, Szegda, Campbell, Martin & Insel, 2003).

In the prenatal period, drugs, toxins, nurtriance, and stress experienced by the mother, have a strong effect on epigenetic mechanism. In the postnatal period neglect, abuse and care all moderate epigenetic mechanisms as well. In the juvenile stage epigenetic alterations may be moderated by social contact and environmental complexities (Rutten, Mill, 2008; Champagne, 2002). Still many of the above mentioned factors potentially alter the genome at any stage in the organism's life. Research demonstrates epigenetic modifications by some of the above mentioned environmental factors may be involved in increased vulnerability to mental disorders, primarily Schizophrenia, Post Traumatic Stress Disorder, some developmental learning disorders, Anxiety disorders and Depression. Much of the literature concerning epigenetic alterations, especially those by social factors, has undergone little inter-subjective agreement and should be considered a primarily hypothetical possibility. Epigenetic factors are considered where relevant as they offer a potential biological mechanism for mediation by cultural factors of

mental illness development and recidivism. Epigenetic factors also leave open the possibility that environmental factors experienced in the parents' lifetime can effect phenotypic expression in offspring. Hypothetically, offspring could inherit genetic predisposition to mental illnesses due to certain cultural and social events experienced by their parents.

Nutrition, exposure to toxins, stress, and social defeat have been suggested to be involved in development of mental illnesses (Cools & Ellenbroek, 2002). The effects of stress and social defeat on mental illness in relation to culture are most apparent. Nutrition and toxins have both been indicated in development of mental illnesses but although evidence of their effects in adulthood does exist, it is less apparent. Exposure to toxins and nutrition are most impactful in the prenatal stage. The following two sections discuss effects of nutrition and toxins on mental illness and some evidence for their effects even in adulthood.

### Nutrition and Mental Illness

Studies suggest poor nutrition or autoimmune disorders may be involved in neurodevelopmental disorders such as neural tube defects, neurodegenerative disorders such as Alzheimer's and Huntington's and behavioral disorders such as Attention Deficit Hyperactive Disorder (ADHD). Feingold (1973) was one of the first few pediatric psychiatrists to suggest the involvement of artificial food coloring in ADHD. Although the Feingold diet receives much criticism for lack of sufficient scientific evidence, parents who adhere to it for their children defend it heavily (Feingold, 1973; Goldstein S. & Goldstein M., 1990). Recent research has also suggested that Autism may be related to celiac disease and be exacerbated by gluten or casein intake.

Reichelt (2002) found higher levels of exorphins derived from food proteins in autistic patient's urine than in non-autistic patients. Exorphins are a type of polypeptide created during digestion of the gluten protein. In a theoretical paper, Reichelt synthesizes previous research on the neurological effects of excess exorphins and traces these effects to a number of Autistic symptoms such as, social indifference, sterotypy and epileptic seizures among others symptoms (Reichelt, Knivsberg, 2003). Opioids, the group to which exorphins belong, inhibit social bonding. In animal models, injected opioids were shown to cause nullification of separation distress calls (Shanahan et. al, 2000; Reichelt, 2002). Domiminergic hyperactivity was also shown to induce stereotype in animal models (Rogeness etl al., 1991; Reichelt, 2002). Increased exorphin inhibit dopamine reuptake and consequently increases dopamine in the synaptasome (Hole et, al, 1979; Reichelt, 2002). Reichelt also notes that epilepsy increases with age in children with Autism while it decreases with age in non-autistic individuals. Celiac disease has been correlated with increased epileptic attacks. A group of children with high urine exorphin peptide levels showed a decrease in epileptic seizure when placed on a gluten free diet (Reichelt, 1990; Reichelt, 2002). Several studies suggest that removing gluten from the dies of children with Autism has little effect (Elder et. al., 2006; Irvin. 2006). However, Banks and colleagues (1996) found that exposing the blood-brain barrier to opioids during early growth periods resulted in permanent changes in the permeability of opioids in these membranes. Considering exorphin is a type of opioid which crosses the blood-brain barrier, early exposure could increase vulnerability to neurotoxic effects if children were immunologically sensitized to caroesin or gluten (Banks, 1996).

Dohen (1996) hypothesizes that dietary differences may account in part for lower prevalence of certain mental illnesses among specific cultures. After studying dietary

consumption in Papua New Guinea, Dohren (1966) found that inhabitants of these areas consumed far less wheat, rye, barley and oats and reportedly had fewer and far less severe cases of Schizophrenia. Though not verified, Dohren (1996) posed an interesting suggestion that increased rates of Schizophrenia in gluten and lactoid consuming cultures may be due to food intolerance of gluten and casein among Schizophrenic individuals. Neurological mechanism of this intolerance is indicated by peptides in milk which cross the blood brain barrier increasing C-fos activity in various brain regions and altering behavior. These same behavioral effects can be reversed by opioid antagonists, which also have been used to treat Schizophrenia (Sun & Cade, 1999).

The possible involvement of autoimmune disorders in mental illness in Autism is an interesting hypothesis (Panminerva, Lucarelli, Zingoni, 1996; Comi, Zimmerman, Fry, 1999; Reichelt, 2002). Similar suggestions have been made about gluten and involvement in ADHD and a number of other food groups in abnormal behavior. Given that diet varies significantly between regions, some researchers suggest that autoimmune disorders could explain variation of mental illness persistence between cultures. More research would be needed to verify this claim.

Having a healthy nutritional diet has been shown to change the epigenetic markers on more than 500 genes (Ornish et al., 2008). Studies on rats indicate that altering the dietary intake affects memory and environmental responses to stress. High protein diets and folic acid have been shown to regulate expression of the insulin-like growth factor Igf2 gene. Inducing Igf2 expression via fear extinction activities has been found to promote the survival of hippocampal neurons in 17-18 year old infants (Agis-Balboa et. al., 2011). This suggests that therapy strategies which promote IgF2 expression may be useful in treating disorders where memory plays a negative role, such as PTSD. (Dudley, J., Li, Xiang., Kobor, M., Kippin, E., 2011; Gong L, Pan YX, Chen

H., 2010; Agis-Balboa et. al., 2011). When sprague-dawley rats were fed high protein diets infused with folic acid, expression of the Igf2 gene was increased in the offspring. In this experiment rats were fed 180 g/kg of casein protein (control) or low protein diet of 90 g/kg. Low protein diets were infused with either one or three grams of folic acid. Low protein diets were shown to increase expression of folic acid and addition of folic acid increased Mrna expression. This study demonstrates that dietary factors such as protein and folic acid largely effect expression of the IfG gene (Gong L, Pan YX, Chen H., 2010). Folate is also required for normal development of the nervous system and plays a crucial role in programmed cell death and neurogenesis (Shea, Mattson, 2003). Incidentally, folic acid supplements taken during the gestational period have been shown to reduce a number of defects including susceptibility to mood disorders (Paul, McDonnell and. Kelly, 2004). Low folate levels were also found in patients with major depression. In one study, at least 56% of patients with affective disorder were found to have low folate levels (Shorvon et. al., 1960). Folate can also reduce DNA methylation which results in enhanced gene transcription. Increased gene transcription when unnatural can impair DNA and result in genetic mutations (Shea & Mattson et. al., 2003).

Folic acid intake can be affected by cultural factors or socio-economic status, for example, even in something as simple as the likelihood that a certain cultural group will take vitamin supplements or have access to healthier food options.

#### Cultural Barrier and Folic Acid Supplements

African American and Hispanic women living in the United States have a significantly lower intake of folic acid than Caucasian and non-Hispanic women. Studies indicate that Hispanic and African women have less awareness of the importance of folic acid intake during

pregnancy (Yang, Carter, Mulinare, Berry, Friedman, & Erickson, 2001). Studies show that lower levels of folic acid intake among Hispanic women arise not only from poorer nutrition but also from cultural beliefs concerning vitamin consumption. (Kimberlea, Hauser, Bell-Ellison, Rodriguez, Frías, 2003). Interviews with 144 Hispanic women in all across six major cities in the United States indicated that many American Hispanic women held culturally specific beliefs that caused them to not take vitamin supplements. For many of the women the word vitamin connoted medication, which they thought of in a negative light. When asked to comment on the effectiveness of an advertisement that states, “The most powerful pill in the world is not medicine”, a Hispanic woman living in Los Angeles responded, “What I do like the most (about the advertisement) is that it (a folic acid supplement) is not a medicine because here in the south we are always talking about it as a medicine.” (Quinn, Hauser, Ellison, Rodriguez, & Frías, 2003). Understanding differences in cultural perceptions surrounding nutrition is extremely important for public health campaigns, especially considering the importance of certain proteins and vitamins in preventing epigenetic mutations which can lead to birth defects such as spina bifida, and neural tube defects anencephaly (Daly, Mills, Molloy, Conley, Lee, Kirke, Weir & Scott, 1997). Low folic acid has previously been indicated in neurodegenerative disorders such as Parkinson’s and Epilepsy though evidence is debatable (Edeh and Toone, 1985).

Both access to nutritional supplements and healthier foods is in part determined by socio-economic position. It may also be due to the awareness of the importance of vitamins during pregnancy. These stratification of vulnerability is certainly cause for concern. Nutrition is certainly not the only area where social status and mental health are related.

### Toxicity

Thoughts and behaviors are regulated by processes of neurological chemical reactions. Changes in chemical balances in the brain can affect an individual's emotional and behavioral responses. Environmental chemicals such as oligodendrocytes, lead, and mercury have been strongly linked to behavioral changes. These chemicals have been shown to induce ADHD, cognitive/ developmental developments, and other Psychiatric illnesses. A review of each of these illnesses and chemical affiliates demonstrates the significance of the role of chemical factors in mental illness. While direct correlations between mental illness and chemical counterparts may be impossible to solidify, extra attention has to be given as exposure is preventable.

As use of chemicals in food production and development increase, bioaccumulation of toxins pose a public health concern. Levels of toxicity do not indicate recent exposure. Adipose tissues, or fatty brain tissues, accumulate lipophilic compounds. Toxins may remain in the system for a significant amount of time due to the circulation of bile acids between the liver and the gastrointestinal tract known as enterohepatic recirculation (Van den Berg, Birnbaum, Bosveld, Brunström, Cook, Feeley, Giesy, Hanberg, et. al., 1998). Thus in order to rid the body of toxins, it is not always enough to avoid the source of the poison, one may also have to undergo detoxification interventions. The Center for Disease Control recently carried out a study that found most Americans, adults and children, had bio-accumulated numerous potentially toxic chemicals, including heavy metals (Litovitz, Rogers, Cobaugh, Youniss, Omslaer, May, Woold, Benson, 2001). Additionally, at risk are newborns that are exposed to the same toxins as their mothers while in-utero. Core blood samples taken by the Red Cross found that infants on average had already bio-accumulated 297 toxicants including heavy metals, pesticides, gasoline by-products and fire retardants (Genuis, 2009).

One toxin, mercury, has been indicated in behavioral changes reminiscent of diagnostic criteria of psychotic disorders. Incidences of mercury poisoning date back to seventeenth century France where felt hat manufactures were required to lick brushes dipped in mercury in order to apply the compound to animal fur. In response to the mercury poisoning, workers displayed anxiety, agitation, melancholia and personality changes, earning the name, Mad Hatters.

Mercury poisoning is still a prominent health concern today. Nearly all seafood contains small amounts of mercury, though larger fish are thought to contain above the recommended limit >1ppm. While mercury poisoning from seafood is rare in the United States, case studies reveal that its effects can be severe (Weihe, Jørgensen, & Clarkson, 1992).

Childhood lead poisoning offers a vivid example of the role inequality plays in toxic exposure. Fifty eight percent of children in Detroit city still suffer the effects of lead poisoning (The Washington Post, 2010). Although the use of lead paint in homes was banned in 1978, it is low income kids, who are more likely to live in older and poorly maintained homes, at higher risk for exposure. Although pesticides have not been indicated in specific development disorders, they have certainly been shown to cause impairments in neurological functioning such as neuronal death leading to impaired cognition. Lead has been specifically linked to behavioral disorders, primarily Attention Deficit Disorder (ADHD).

ADHD is characterized by inability to focus or control behavior and hyperactivity. ADHD is one of the most prominent childhood disorders. As of 2007, approximately 9.5 percent of children have been diagnosed with ADHD. Moreover, ADHD has been shown to increase by 3% every year since 2003 (Center for Disease Control, 2007). In addition to being correlated

with a number of behavioral disorders, Lead poisoning and PCBs have been strongly indicated in ADHD.

### Lead Poisoning

A study by the Michigan Department of mental health, found that while nearly all children had traces of lead in their blood system, those diagnosed with ADHD had significantly higher amounts. None of the children studied had higher than 10 micrograms of lead in their system, indicating that even small amounts of the metal may have neurological effects (Michigan State University, 2007). Evidence supporting involvement of lead poisoning derives from comparing symptoms of children with lead poisoning and symptoms of children with ADHD.

Meta-analysis indicates that both verbal and non-verbal working memory is impaired in children with ADHD (Eubig, Aguir, Chance, 2010). A number of epidemiological studies found that lead exposure and poor working memory were also related. In a prospective birth cohort study, Stiles and Bellinger (1993) assessed lifetime lead exposure of a total of 148 children up to the age of ten. At all ages, the mean BLL, or lead present in the blood stream, were  $< 8 \mu\text{g/dL}$ . Children were asked to complete the Wechsler Scale or Children–Revised (WISC-R) Freedom from Distractibility Index throughout the study. This index includes a portion of Arithmetic and digital span which are thought effective measurements of verbal working memory. From the age of two on, high scores on the WISC-R test were inversely correlated with levels of lead poisoning, BLL (Stiles and Bellinger, 1993; Eubig, Aguir, Chance, 2010). A similarly designed study examined the association between BLL and performance on special working memory tests in a cohort of 174 children from Rochester. Working memory and spatial memory were measured using the Shape School task at age four and the Cambridge Neuropsychological Tests

Automated Battery (CNTAB) at age five. While no effects were observed at age four, impaired working memory and spatial performance on the CNTAB were evident at age five. A number of other studies have indicated BLL and performance on tests that measure attention, working memory, spatial memory and other symptoms of ADHD. The majority of these studies indicate that BLL impairs performance on these tasks in a similar manner as does ADHD (Ris et al., 2004; Chiodo et. al., 2004; Sukran et. al., 2007; Kordas et. al, 2006). Effects of lead on attention are also evident in Animal models. In these studies, levels of lead as low as 11–13 µg/dL have been shown to affect rodents ability to perform tasks related to spatial working memory, response inhibition, cognitive flexibility, and temporal information processing (Rice, 1993, 1996, 2000; Stiles and Bellinger, 1993; Eubig, Aguir, Chance, 2010).

#### Pesticide exposure

Epidemiological research also indicates a relationship between symptoms of ADHD and pre-natal exposure to polychlorinated biphenyl (PCBs). Pre-Natal exposure has been shown to negatively affect children's Attention, Cognitive Flexibility and Planning, Response Inhibition and working memory. Multiple studies on birth cohorts indicate that exposure to PCBs are associated with poor performance on these tasks as indicated by WISC tests (Jackobson and Jackobson, 2003).

A similar income disparity is seen in vulnerability to pesticide exposure. Individuals living in public housing were not only more likely to use organophosphate (OP) insecticide in their homes, but also more likely to use to chemicals at much higher frequencies. In order to maintain rampant roach problems in public housing, many New York Inner City residents reported using the insecticide at least once a week (Rausch, 2000). Although the use of this insecticide in homes is now banned, it is still used frequently for agricultural purposes. The

Federation for American Immigration reform indicates that non-documented immigrants comprise 36.3% of agricultural workers. Numerous research studies indicate that agricultural workers are the most vulnerable population to pesticide poisoning. Moreover many of these workers live within a few miles of the field, frequently exposing children and pregnant women to the chemicals.

Research demonstrates Organophosphate insecticides (Ops), the most commonly used pesticide worldwide, can affect the nervous system even at trace amounts by inhibiting Acetylcholinestarse. Acetylcholinestarse (AChE) is an enzyme which modulates the amount of aceylecholine neurotransmitter and acts as a neuromodulator upon plasticity, arousal and reward. It also has been shown to be involved in sustaining attention. When AChE is inhibited, aceetylcholine accumulates in the brain and over stimulates brain activity in these areas. Additionally, AChE has a non cholinergic role in cell adhesive functioning at neurodevelopment. This indicated that inhibition of AChE receptors may effect morphological development.

A study on organophosphate pesticides (Ops) effects on inner city mothers and their newborn infants born between February 1998 and February 2002 found significant neurological alterations. This study examined exposure to pesticides and effects on 254 children of black or Dominican women living in Harlem, New York. Level of pesticide exposure was indicated by biomarkers of chlorpyrifos and/or core blood samples taken at the time of delivery and interviews with mothers on their use of pesticides in the home. Effects were measured by a neurobehavioral outcome assessment at 12, 24 and 36 months. The Bayley Scale of Infant Development II was used to measure cognitive and psychomotor development. Behavioral problems were measured through maternal reporting on the 99 item Child Behavior Checklist (CBCL). Additionally, post natal observation of the child's home environment was performed in

order to assess for confounding variables. By the age of three, significantly greater proportions of children exposed to higher levels of pesticides scored in the range of mental and motor delays compared with those who with lower exposures; 6.5 points lower on motor development tests and 3.3 points lower on mental development tests. The mental development Index and psychomotor development index measurements at differing ages also indicated that these differences increased over time. Additionally children who were exposed to higher levels of pesticides more frequently scored in the clinical range for attention problems, ADHD and Pervasive Developmental Disorder.

A longitudinal study on populations showed that impaired neurological development in children was highly correlated with amounts of these pesticides in biomarkers taken from their mothers while children were still in utero. The women studied were all Mexican migrants who worked in the agricultural sector or whose husband worked in agricultural sector where they were likely to be exposed to high levels of organocholine and organophosphate pesticides. Level of pesticide exposure of the population was gathered from four sources; measurements of biological specimens, environmental measurements, information derived from detailed questionnaires and home walkthroughs, and the State of California Pesticide use data in the relevant geographic area. Biological specimens were also analyzed for other toxins in order to address confounding variables. The population also had relatively low in utero exposure of other toxins such as lead, polychlorinated biphenyls, cigarette smoke, and alcohol. Analyses of the infants at six, twelve and twenty four months revealed the neurological effects of the toxins. Using the Bayley scale of Infant Development exposure to DDE, an organocholine pesticide, adversely affected infants' psychomotor development index at six months. At twelve and twenty four months DDE was associated with lower PDI but not Mental Development indexes (MDI).

Similar results were found for DDT (dichlorodiphenyltrichloroethane) an organocholine, exposure. Researchers found that infants of mothers who tested high for Organophosphate pesticide exposure had three more abnormal reflexes than did infants from mothers who were not exposed to the pesticide. However there were no associations for BSDI scores or Mental Development Indexes of the children exposed to pesticides. This study makes it apparent that exposure to pesticide toxins in-utero can have neurological affects apparent at the neonatal stage and up to 24 months old (Eskenazi, B., Rosas, L., Marks, R., Bradman, A., Harley, K., Holland, N., Johnson, C., Fenster, L., & Barr, B., 2007).

A review study on the effect of PCBs and Lead poisoning on ADHD suggests that genetic factors have been proven to moderate diagnosis of ADHD. In fact ADHD has an inheritance rate of 76%. Moreover, the prevalence of ADHD diagnosis still increases 3% per year although prevalence of lead and PCB poisoning are declining (Brodum, 2011). Even so, the similarity of symptoms of PCB and Lead poisoning to ADHD is enough cause for concern. The effects of the chemicals may not cause ADHD, per se. Still, they cause psychological and behavioral symptoms that are nearly identical to diagnostic criteria for this developmental disorder. The relationship between ADHD and the socio-cultural landscape is ambiguous. Increased diagnoses may reflect academic pressure and tendency to over diagnose the disorder.

While it is clear that a number of factors effect development of mental illness, including heredity, gene-environment interaction, nutrition, and socio-economic status, research indicates that chemical exposure may also play a role. Given the difficulty of studying toxification in human models, conclusive human epidemiological studies are rare. Rather the scientific community relies on evidence that these chemicals can alter brain function to infer that they may have a profound effect on mental health. For some chemicals the weight of this evidence is

strong enough to indicate a causal relationship, for others the relationship is yet to emerge. The evidence above presents the case for a plausible role of chemicals in expression of mental illness symptoms. This plausibility is extremely important given the unequal exposure of chemicals to vulnerable populations and the preventability of these exposures,

### Stress, Trauma and Mental Illness

Nutrition and toxicity provide two interesting ways that culture may affect mental illness. These factors are primarily impactful in-utero. In adulthood, an increase of stress has been shown to be correlated with the likelihood of developing a mental illness. Interestingly, stress may be potentially mediated by socio-economic factors and migrant status. Strictly cultural differences also partially determine the impact of stress on health. The extent to which an individual feels stressed depends upon their interpretation of the event as stressful or not. Coping mechanisms also alleviate negative biological impacts of stress. The following discusses the biological impact of stress, migrant vulnerabilities and the role of cultural differences in experiencing and coping with stress.

### The Endocrinology of Stress

Endocrine stress response involves a number of components and cannot be easily simplified. It is primarily thought of as having two distinct mechanisms. These two components are perpetuated by two types of hormones, glucocorticoids and catecholamines. Glucocorticoids (GRs) indicate activation of the hypothalamic-pituitary axis. The HPA controls adrenal cortex secretion of glucocorticoids. Neuropeptides corticotrophin releasing factors (CRF) and arginine vasopressin (AVP) initiate the HPA when they are released from the Hypothalamus through the portal blood system and travel to the anterior pituitary. In the anterior pituitary CRF and AVP stimulate release of ACTH into

general circulation. ACTH travels to the adrenal cortex where it binds with receptors to stimulate steroid (GC) production. Type of glucocorticoid released depends upon the type of species. In humans GC secreted is cortisol, in reptiles and amphibians it is cortocosterone. Stimulated production of GCs results in higher levels of GCs in the peripheral circulation. GCs travel to target tissue and pass the cell membrane binding to the endocoplasmic reticula where they enter the nucleus and act on transcriptional factors. It takes 20-30 minutes for GC circulation in the blood stream to increase and for behavioral changes to be evident. After the stressor dissipates, GC circulation decreases through negative feedback mechanism 30-60 min after the presence of a stressor is gone. However as proteins will continue to act after the termination of the stressor, the increase of GCs have much longer lasting effects. Proteins modulated by GCs increase have been shown to have effects on a number of genes, however they are classified as having five main effects: increasing blood glucose concentration, altering behavior, inhibiting growth, inhibiting reproduction, and modulating the immune system. How GCs alter behavior is not exactly known and depends upon the context in which the stressor is presented. GCs have been shown to induce migration in birds (Silverin, 1997; Holsber, 2006). GCs can also promote behavioral strategies such as hiding and waiting out a stressor, or relocating and fleeing. They have also been implicated in having broad effects on the immune system. They inhibit synthesis, release and efficacy of cytokines (immune system proteins), and they reduce activation and proliferation of T cells and B cells, lower macrophages, and circulation levels of lymphocytes (Holsber, Kloet, 2006). Corticosteroids reach every organ of the body through blood circulation, gearing and coordinating the brain and the body for the stress response. This integrated response initiates through rapid hormonal changes in formation of neuroreceptors which lead to slower modulation of gene transcriptions (Romero & Butler, 2007; Kloet, Joels, & Holsboer, 2005).

The second class of hormones, Catecholamines are thought to be much faster acting than glucocorticoids (GRs). Catecholamines, epinephrine and norepinephrine, are secreted by Sympathetic Adrenal Medullary (SAM) system, also known as flight or fight. The SAM system is activated when the organism is challenged for control over the environment. Catecholamines do not pass the blood brain barrier but exert effects peripherally. Catecholamines induce an emergency response. They mobilize energy to the muscles, heart, and brain and inhibit gastrointestinal actions, internal organs, and blood flow to the skin. In modern society they are likely released in response to threats of a social or mental rather than a physical nature. Mental efficiency is associated with elevated catecholamine levels. Norepinephrine and Epinephrine orchestrate this response. Upon detection of a stressor, epinephrine and norepinephrine are released by the adrenal medulla and nerve terminals of the sympathetic nervous system. They activate a number of responses including decreasing visceral activity, shutting down digestion, increasing visual activity, increasing brain blood flow and arousal, and increasing gas exchange efficiency in the lungs. They also break down glycogen to release glucose stores. This in turn releases vasodilation in the periphery and increase heart rate (Holsber et. al., 2006).

### Stress effects on Animal Models

Adverse health effects have been shown to be caused by both prolonged activation of the HPA or the SAM system, although far more is known about the latter. Different styles of coping may mediate which stress pathway is utilized. Activation of the HPA is associated with passive coping mechanisms while activation of the SAM system is associated with more active coping mechanisms. The hippocampus is particularly vulnerable to glucocorticoids as it has an increased number of receptors for the hormone to allow for long-term potentiation and stimulation is a mild stressor (Sinha &Watson, 2007).

In Rats excess GC exposure causes atrophy of dendrites in hippocampal neurons over the course of weeks (McEwan, 2003). Consequences of dendritic atrophy can disrupt and simplify connections between other neurons, disrupting cognition. GC stress can also decrease the likelihood that hippocampal will survive subsequent stressful incidents (McEwan, 2003).

Stress induced in rats has been shown to significantly alter behavior. Wilber (2007) demonstrates that rats exposed to stress in utero have permanent increased anxiety responses to mild stress in adulthood.

### Mental Illness and Marginalized groups

In humans, stress has been indicated in depression, anxiety disorders, and post traumatic stress disorder. Recent studies indicate stress also plays a role in onset of psychotic disorders such as Schizophrenia and Bipolar. The association between increases stress and Schizophrenia was first evident through observation of abnormally high rates of the disorder among migrants and minorities (Odergaard et . al. ,1932; Smith, 2006). Pre-migration, migration, and post-migration expose individuals to a number of stressful events. Political or economic factors within the country of origin, the decision to leave, and planning the journey, and adjusting to the final destination may increase risk of psychosis.

Odergaards first noticed the correlation between migrants and mental illness in 1932. He and fellow researchers searched through hundreds of hospitalization records of Norwegian migrants vs. those born in the United States. Schizophrenia was significantly more prominent among Norwegian populations than it was among the native born (Oldergaard et al., 1932). A later study found the prevalence of Schizophrenia in patients born in Europe was 54% higher than prevalence of Schizophrenia in the native born population of British Colombia (Smith, 2006). Smith analyzed clinical records obtained between 1902 and 1913 for all psychiatric

admissions into a singular psychiatric hospital. Through use of clinical records, patients were diagnosed according the DSM IV and compared (Smith, 2006).

Correlation between immigration and Schizophrenia has been found across numerous studies. A postwar wave of immigration resulted in increased rates of psychotic disorder in the UK (Hemsi, 1967). Significantly higher rates of Schizophrenia in Caribbean immigrants in the United Kingdom have given weight to arguments of the role of stress in mental illness (Bhurga, 1997; Cochran, 1977; Coid et. al 2008; Littlewood & Lepsedge, 1981).

A WHO study investigated whether or not higher rates of Schizophrenia were due to migration or the tendency to diagnose individuals with the disorder. This study diagnosed a number of admitted patients to hospitals across England in a random sample using the DSM IV. Diagnoses were made over a period of two years by a panel of 72 multi ethnic individuals in three cities, London, Nottingham and Bristol. No significant difference was found between either Black Africans or Caribbean individual with white counterparts except with Schizophrenia and Bipolar disorder. Relative risk factor for Black Africans was 5.8 while relative risk factor for Black Caribbeans was 9.1, confidence intervals were 3.9-8.4 and 6.6-12.6 respectively. Interestingly enough, children of migrants were also seen to have higher diagnoses of Schizophrenia than both their parents and the native born population (WHO, 2000). Selective migration is an attractive hypothesis to explain higher rates of psychosis amongst migrants. However several arguments can be made against this hypothesis. Firstly, the emotional strain and planning involved in the migration process would require a level of mental stability. Secondly, prevalence of mental illness is higher among children of migrants than migrants, if the selective hypothesis were true it would likely be the opposite. Thirdly increased rates of mental illness are

not present in all migrant groups, but only some. Still these counter arguments do not disprove the selection hypothesis and further research should address pre-migratory factors.

Previous research suggests immigration to the United States may threaten the parental-child relationship by altering traditional familial structures and traditions leaving children with fewer coping resources (Choi, 2002; Escobar, Nervi & Gara, 2002; Gil, Wagner, & Vera, 2000). Identification with one's ethnicity and culture has also shown to be an important resource for stress coping. Mossakowski (1999) reports that Filipinos living in the U.S. with stronger cultural identification showed lower prevalence of depression. Conversely, Ganst (2002) reports that Latinos living in the U.S. with low cultural identification show a higher prevalence of depression. If stress were indeed a mediator of mental illness it would not be surprising that first generation adolescents showed higher rates of mental illness than their parents. First generation children go through a number of cultural stressor during childhood that their parents face at an older age or not at all. Some crucial examples are isolation from ethnic identity, disjunction between their parents and surrounding culture, and growing up as a minority in a potentially discriminatory environment.

Research indicates coping mechanism may play a role in predisposition for mental illness. Choi, Meininger, and Roberts (2006) found that Asian Americans living in Southwest Texas demonstrated higher levels of mental distress and suicidal intentions followed by Hispanic Americans and lastly European Americans and African Americans. There were no differences in mental distress between races after controlling for family characteristics, stress, self-esteem, and coping. In this study stress was measured through two dimensions, sociocultural stress and general stress. Asian Americans were shown to report increased stress in both dimensions as

were Hispanic Americans though to a lesser extent. The extent to which students indicated they felt stigmatized also predicted greater negative impacts of stress.

### Importance of coping mechanism

In addition to circumstantial factors, culture may also mediate whether or not an individual perceives an event as stressful and how they in turn cope with the event. Research indicates there is a significant relationship between stress coping and physical as well as psychological illness (Aldewin, 1994; Cooper, 2005; Tosevski & Milovancevic, 2006).

In animal models, types of coping mechanisms can be grouped into two categories, proactive and reactive. The type of coping mechanism utilized by the individual organism has been shown to mediate physiological effects of stress. Kugler (1984) found that Roman high avoidance rats, thought to reflect a proactive coping style, and Roman low avoidance rats, thought to reflect reactive coping styles, showed differential responses to trauma. After being deprived of food and water for five days, Roman high avoidance rats had more stomach ulcers than Roman low avoidance rats. Differences in coping mechanism have been reflected between organisms across species. Adrichem (1987) showed that veal calves fed only milk developed different intensities of a tongue-playing stereotypy as a stress response. Calves that performed a higher intensity stereotypy, in this case increased repetitive tongue playing behavior, had fewer stomach wall ulcers when slaughtered at 20 weeks old. Calves that did not develop tongue playing all developed ulcers at the same slaughtering age. Sterotypies are thought to reflect a proactive coping mechanism. Their implication of stereotypy behavior in decreasing stomach ulcer provides evidence that coping mechanisms moderate adverse health effects of stress.

Future studies confirmed that a high number of stereotypies reduced sympathetic activation caused by the chronic stress of tethering. Less activation decreased the animal's heart rate helping them to cope (Wiepkempa, Schouten, 1992). While these coping mechanisms are not easily applied to human behaviors, the effect of coping on physiology demonstrates its importance.

### Coping mechanism and Culture

Intra-individual differences in human coping mechanisms are partially culturally dependent (Lazarus, Folman, 1884). Psychologically stressful events are often subjective and culture is an important determinant in subjective interpretation. Individualist and collectivist cultures demonstrate different coping mechanisms and interpretations of events as stressful or not. Numerous cultural nuances affect differential stress coping mechanism. Still research primarily studies the difference between individualist and collectivist cultures due to the utility of these concepts to effectively differentiate cultural practices. Individualist cultures are classified as conceptualizing the self as the central unit and the group as the periphery. Independence, personal success, and concern for one's self and immediate family are emphasized (Hofstede, 1980). Collectivist cultures are classified as conceptualizing the group as the central unit and the individual as marginal in comparison. Individuals in collectivist societies are seen as bound to their roles in the society as a whole rather than focused on personal success. Individualism and collectivism have been measured multiple ways, cross-national surveys, individuals reports, and exposing individuals to cultural cues. Meta-analysis suggests that respondents in the United States represent the extreme end of individualism while respondents from East Asian countries collectivist (Oyserman, 2002)

Chang (1996) found that Asian-American students were more likely to use avoidance and social-withdrawal coping mechanisms than European American students. Avoidance social withdraw coping means excluding one's self during hardship. Individuals utilizing this strategy will engage in isolated activities such as watching television, reading a book, or other solo activities. This study compared 111 Asian-American students with 111 Caucasian American for optimism, pessimism, and coping mechanisms. Health outcomes were assessed six weeks later. Asian-American students expressed more negative psychological health but not physical health. Further analyses indicated that two thirds of the outcome could be attributed to pessimistic viewpoint while one third of the outcome could be attributed to coping strategy (Chang, 1996). Perhaps a cultural disjunction may be responsible for less effective coping mechanism by Asian student abroad rather than poorer coping mechanisms in general. In one study, Students were assessed for independent vs. interdependent self-constructs and proactive vs. reactive coping. Asian students whose coping mechanisms and self-constructs were consistent with their cultural norms experienced far less psychological stress than Asian students whose coping mechanisms and self constructs were more aligned with American norms (Cross, 1996). Transitioning between cultures can be traumatic. In addition to reinterpreting the surrounding environment according to different norms, individuals may also be exposed to negative stereotypes or social defeat.

In rodents, newly introduced males will typically be treated with social antagonism and aggression by cage mates. Examination of these introduced males revealed that they had numerous altered behavioral and neuroendocrine states. These states include decreased social behavior, increased self-drug administration and locomotion. The epigenetic basis of these behavioral changes has been traced to transcriptional activity of the BDNG gene. In socially

ostracized mice, BDNF gene expression was seen to be significantly decreased in the hippocampus, the effect of which appeared to be mediated by BDNF II and BDNF IV transcripts which can be accounted for by methylation at these sites, indicating that the methylation patterns may be passed on to offspring (Carnevali et. al., 2012). Differential levels of histone H3-K27 dimethylation observed in the hippocampus are also found across the genome in the nucleus accumbens, both in response to chronic social defeat and prolonged adult social isolation (Carnevali, et. al., 2012). Post mortem analysis of humans diagnosed with depression similarly indicated that increases in H3-K12 acetylation and decreased HDAC2 levels similar to those observed in socially defeated mice (Mill, Ruten, 2009; Mill, Dempster, Caspi, Moffitt, 2006).

Mother's experiences of 9/11 provide a real life example of socially stressful events effect on an individual's offspring. A study on women who developed post traumatic stress disorder in response to witnessing the attack on the World Trade Center on 9/11 2001 revealed abnormal stress responses in their children who were in-utero at the time. This study took cortisol samples and administered behavioral questioners to assess severity of PTSD in 98 women who witnessed the attacks while pregnant. The tests took place nine months after the birth of their children who were in-utero at the time of the attacks. Mothers also rated their children's distress to novelty, such as loud noises or startling stimuli. Mother's cortisol levels were inversely correlated to the child's distress response, in other words, the lower the cortisol level, an indicator of poor stress adaptation, the more likely the child would have a high distress response to novelty stimuli. This study further suggests that traumatic events experienced by the mother have an impact on the child. The glucocorticoid receptor, a mediator of the HPA stress response, is prone to epigenetic modification, still, longitudinal studies would be needed to observe inheritance of abnormal stress responses across generations (Canfield ,&Yehuda , 2006).

Though purely hypothetical, epigenetic research indicates offspring may inherit abnormal behaviors induced by social defeat or stress. Considering extensive research examining the role of stress, migration, and racial prejudice on vulnerability to mental illness, even hypothetical implications of epigenetic inheritance by these experiences are horrifying.

### Conclusion

Predisposition to mental illness is moderated by a number of cultural factors many of which reflect socio-economic status. Exposure to certain toxins and diet vary by birth place (neighborhood or country) which in turn reflect global income disparities. Inner city children and migrant workers may be more frequently exposed to toxins as safety regulations seem to elude poorly maintained neighborhoods and lower wage professions. At every life stage, excessive exposure to stress or negative coping mechanisms may negatively impact well-being. A mismatch between learned coping mechanism and standard coping mechanisms may also reduce affectivity of coping, as seen in acculturation. Still, little is known about individual differences to stress responses and whether or not these differences may be culturally mediated. Acculturation may also induce a stress reaction which in turn may alter brain structures, such as the hippocampus. It is highly likely that correlations between migration and mental illness reflect this negative impact of stress on the brain. The possible role of epigenetic alternations in expressing mental illness implies that many of these effects may be inherited by future generations. If not for the sake of simply improving the lives of many who suffer from mental illness, the role of culture and mental disease should be more thoroughly explored on the basis of its creating a health disparity.

There are an additional number of ways that culture effects effectively of treatments for those with a mental illness that were not addressed in this paper. Current research on the effectively of pharmaceutical drugs on those of different ethnicities may eventual reveal important differences in biological reactions, especially considering most psychological pharmaceuticals have been tested on Caucasians living in the Untied States or Europe. Concern of culture's role in mental illness is certainly widespread, still further research into its effect on predisposition to mental illnesses is needed.

## References

- Brunton, P., Russell, J.A. (2010) Prenatal Social Stress in the rat programmes neuroendocrine and behavioral responses to stress in the adult offspring: sex-specific effects. *Journal of endocrinology*. 22: 258-271
- Banks, W. (2006) Perinatal treatment of rats with opiates affects the development of the blood-brain barrier transport system PTS-1. *Zadina* 18(6) 711-715.
- Choi, H., Meininger, J. C., Roberts, R. E. (2006). Ethnic differences in adolescents' mental distress social stress and resources. *Adolescence* 41(162).
- Balboa, A., Arcos-Diaz, D., Wittnam<sup>2</sup>, J., Govindarajan, N., Blom, K., Burkhardt, S., Haladyniak, U., Agbemenyah, H., s Zovoilis, A., Salinas-Riester G., Opitz, L., Sananbenesi, F., Fischer, A., A hippocampal insulin-growth factor 2 pathway regulates the extinction of fear memories
- Edeh J, Toone B K (2006) Promoting Pre-Conceptional Use of Folic Acid to Hispanic Women: A Social Marketing Approach. *Maternal and Child Health Journal* 10(5).
- Elder, J., Shankar, M., Shuster, J., Theriaque, D., Burns, S., and Sherrill, L. (2006) The Gluten-Free, Casein-Free Diet In Autism: Results of A Preliminary Double Blind Clinical Trial. *Journal of Autism and Developmental Disorders* 36 (3).
- Ellenbroek, B., Cools, A. (2002). Aporphine Susceptibility and animal models for psychopathology: Genes and Environment. *Behavioral Genetics* 32(5).
- Irving, D. (2006) Using Analog Assessment Procedures for Determining the Effects Of A Gluten-Free and Casein-free Diet on Rate of Problem Behaviors for an Adolescent with Autism. *Behavioral Interventions*, 21: 281-286
- Koolhas, J.M., Korte, S.M., De Boer, S.F., Van Der Vegt, B.J., Van Reenen, C.G., Hopster, H., I.C., Jong, M.A.W., Ruis, H.J., Blokhuis (1999) Coping Styles in animals: current status in behavior and stress-physiology. *Neuroscience and biobehavioral reviews*. 23: 925-935
- Koolhas, J.M. (2008). Coping style and immunity in animals: making sense of individual variation. *Brain, Behavior, and Immunity*. 22:662-667.
- Chun, C., Moos, R., Cronkite, R. (2006 ) Culture: A fundamental Context for the Stress and Coping Paradigm.
- Harris, K., Edlund, M., Larson, S. (2005) Racial and Ethnic Differences in the Mental Health Problems and Use of Mental Health Care. *Medical care* 43(8) :775-784
- Myers, N. (2010). Culture, Stress and Recovery from Schizophrenia: Lessons from the field for global mental health. *Cultural Medical Psychiatry*. 34: 500-528.

Menard, J., Wilkin, M. (2012) Intermittent physical stress during early and mid-adolescence differentially alters rats anxiety and depression like behaviors in adulthood. *Behavioral Neuroscience*. 126(2):344-260

Mattson, M., Shea, T. (2003). Folate and homocysteine metabolism in neural plasticity and neurogenerative disorders. *Trends in Neuroscience*. 26(3)

McEueun, J., Beck, S., Bale, T., Failure to mount adaptive responses to stress results in dysregulation and cell death in the midbrain raphe. *Journal of neuroscience*. 28(33): 8169-8177

Romero, M., Butler, L. (2007). *Endocrinology of Stress*. *International Journal of Comparative Psychology*. 20: 89-95

Sinha, B., Watson, D. (2007). *Stress, Coping and Psychological Illness: A Cross-Cultural Study*. *International Journal of Stress Management*. 14(4).

Folkman, S., Lazarus, R., Dunkel-Schett, C., et. Al. (2000). The dynamics of a stressful encounter. In: Higgins, E. T. & Kruglanski, A W. (eds.) *Motivational science: social and personality perspectives*, pp. 111-127. Philadelphia: Psychology Press.

Goldstein, S. and Goldstein, M. (1990) *Managing Attention Disorders in Children*. New York: Wiley.

Gong L, Pan YX, Chen H. Gestational low protein diet in the rat mediates Igf2 gene expression in male offspring via altered hepatic DNA methylation. *Epigenetics*. 2010 Oct 1;5(7):619-26. Epub 2010 Oct 1.

Gould, E. and Gross, C. (2002). Neurogenesis in adult mammals: some progress and problems. *Journal of neuroscience* 22, 619-623

McEwan, B. (2002). Sex, Stress, and hippocampus; allostasis, allostatic load and the aging process. *Neurobiology of aging* 23, 931

Haynes, Feinleib (1980) Women, Work and coronary disease; prospective findings from the Framingham Hear Study. *American Journal of Public Health* 70, 133-141.

Kloet, Joels, Holsber (2006). *Stress and the Brain: From Adaptation to Disease*. *Nature neuroscience review*, vol.6

Kaplan J, Manuck S, Adams M, Williams J, Register T, et al. (1993) Plaque changes and arterial enlargement in atherosclerotic monkeys after manipulation of diet and social environment. 13: 254–263.

Oloff, Brosschot, Godaert, Benschop, Ballieux, Heinjnen, Smet, & Ursin (1995). Modulatory Effects of Defense and Coping on Stress-Induced Changes in Endocrine and Immune Parameters. *International Journal of Behavioral Medicine*, 2(2), 85-103).

Oyserman, Daphna; Coon, Heather M.; Kimmelmeier, Markus (2002) . Rethinking individualism and collectivism: Evaluation of theoretical assumptions and meta-analyses. *Psychological Bulletin*, Vol 128(1), 3-72.

Petticrew M, Davey Smith G (2012) The Monkey Puzzle: A Systematic Review of Studies of Stress, Social Hierarchies, and Heart Disease in Monkeys. 7(3)

Reichelt, Knivesberg, 2003. Can the Pasthophysiology of Autism be explained by the Nature of the Discovered Urine Peptides? *Institute of Pediatric Research* 6 (1) 19-28.

Sapolsky R. (200). Glucocorticoids and hippocampal atrophy in neuropsychiatric disorders. *Archives of General Psychiatry* 57, 925.

Sapolsky R. (1999) Stress, glucocorticoids and their adverse neurological effects: relevance to aging. *Experimental Gerontology* 34, 721.

Veenema, Meijer, Kloet, & koolhaas, (2003) Genetic Selection for Coping Predicts Stressor Susceptibility. *Journal of Neuroendocrinology* vol. 15, 256-267

Williams JK, Vita JA, Manuck SB, Selwyn AP, Kaplan JR (1991) Psychosocial Factors Impair Vascular Responses of Coronary Arteries. *Circulation* 2146-2153