Moreover, individuals with high or low SES levels in childhood have different methylation patterns in gene promoters associated with functional signalling pathways. Similarly, Tehranifar et al. (2013) examined DNA methylation of three repetitive elements in adult women blood samples with varied childhood and adulthood SES. They found two repetitive elements having elevated methylation level associated with lower SES in childhood, yet only one element had lower methylation level associated with higher SES in adulthood, suggesting a greater association between changes in methylation levels and SES in childhood than SES in adulthood. Taken together, there is a clear association between childhood SES and DNA methylation values.

**DNA Methylation and Mental Health**

Studies by McGowan et al. (2009) and Yang et al. (2013) also investigated the association between epigenetic methylation and mental health. In McGowan et al.’s (2009) study, an increased level of methylation of NR3C1 promoter interferes with transcription factor binding and down-regulates the level of glucocorticoid receptor mRNA, resulting in a lower level of GR expression. Hippocampal GR expression controls the hypothalamic-pituitary-adrenal (HPA) responses to stress, in which lower GR expression level will result in a greater HPA stress response. Abnormal HPA axis responses are believed to be associated with a variety of psychiatric diseases, including depressive disorders and stress disorders (Ventura-Junca & Herrera, 2012). History of childhood abuse was associated with an increased methylation level of NR3C1 promoter, which in turns lowered the GR expression, results in abnormal HPA axis controls and increased likelihood to develop stress-related disorders later in life. Together, the results propose DNA methylation as one of the major mediators underlying the long-term effect of childhood stressful experience on mental health development.

Another study examining the epigenetic effect of child abuse identified 2868 significant CpG methylation sites and eight significant methylated genes (Yang et al., 2013). 20% of the methylation sites are intergenic regions that are associated with neuropsychiatric diseases, cardiovascular diseases and cancer (Yang et al., 2013). The remaining 80% are intragenic regions altering genes associated with cortical development, depression, and substance dependence (Yang et al., 2013). In addition, a recent study found that methylation values of three genes (ID3, GRIN1, and TPPP) act as significant predictors of depression in children (Weder et al., 2014). These experimental results suggest that DNA methylation is an important factor triggering a variety of health problems.

**Limitations and Future Direction**

As an emerging area, current studies on life experience and DNA methylation do have their limitations. One major limitation across most studies is the lack of longitudinal data. A very limited number of studies examined the variation of DNA methylation in a sample population from childhood to adulthood, and the majority of the existing data is collected at only one point of an individual’s life span. This limitation exists because of the recent and on-going development of methylome measurement technologies (Borghol et al., 2011). Methylome refers to the patterns of methylation modifications in the genome an organism. Methods of methylome measurement are relatively new-established, providing a relatively narrow time span for tracking the developmental path of individuals. Longitudinal studies are helpful in terms of revealing the changes of methylation patterns over time. In the future, research should focus on the formation of longitudinal DNA methylation data set, which facilitates a more extensive understanding of changes in methylations over time, and helps to establish a more explicit interaction mechanisms among experiences, DNA methylation and pathological outcomes.

Another limitation is the use of various tissue types in DNA methylation investigations. The majority of studies used blood samples or saliva samples, with only one group (McGowan et al. 2009) examining brain samples. The advantage of using blood or saliva samples is that these methods are non-invasive, and because the DNA methylation variability is relatively consist across the tissues of the same individual (Mehta et al., 2013), the DNA methylation pattern detected in peripheral blood or saliva can reflect the changes in the brain to some extents. However, as DNA methylation primarily serves as a mechanism assisting cell differentiation, tissue-specific methylation pattern always exists (Kundakovic et al., 2014), and the extent of how this pattern interacts
In conclusion, epigenetic changes such as DNA methylation provided biological linkage between childhood stressful experiences on mental health development. Epigenetic research inspired a deeper understanding of the nature-nurture interaction. More importantly, epigenetic research findings suggested that chromatin structure manipulation could potentially become a new possible therapeutic intervention for psychological abnormalities induced by childhood aversive experiences, proving a possible direction for more advanced psychologically assessments or interventions.

References


The Neural Basis of Dietary Self-Control
Vanessa Giuliano

Abstract
In today’s Western society, frequent overindulgence of unhealthy, high calorie food can lead to detrimental health effects such as obesity and heart disease. To combat these diseases, health practitioners recommend patients decrease their intake of unhealthy, high-calorie, low nutrient rich foods. Some individuals are better at following these recommendations than others. This review highlights the neural underpinnings that allow some individuals to better exercise dietary self-control. Cortical areas including the dorsolateral prefrontal cortex (DLPFC), ventromedial prefrontal cortex (VMPFC), and orbitofrontal cortex (OFC) are involved in crucial aspects of decision making such as inhibition of hedonic rewards, temporal discounting, and option valuation. These aspects of decision making are all used when making dietary choices, causing those who are better at reward inhibition and associated self-control mechanisms to be better dieters. This review suggests a neurobehavioral approach to dieting where dieters are taught cognitive strategies. These strategies can reinforce brain regions that help individuals exercise better decision making skills and aid dieters in making better food choices.
Inhibition studies show a causal link between the DLPFC and dietary inhibition, clarifying the role of the DLPFC in dietary regulation.

**Delay Discounting and Dieting**

One cognitive bias that humans particularly struggle with is delay discounting. Delay discounting is when humans place disproportionate value on immediate rewards while devaluing rewards that are presented later (Ely, Winter, & Lowe, 2013). Delay discounting plays a pivotal role in dietary regulation, as dieting is resisting immediately rewarding, high calorie foods to achieve weight loss, a long term goal. In comparison to women of normal weight, obese women have shown to perform worse on delay discounting tasks, often choosing more immediate rewards over later ones (Weller, Cook, Avsar, & Cox, 2008). Consequently, it is crucial to consider the neural underpinning behind this process in the context of dietary choice to understand what neural aspects allow some individuals to be more successful at dieting than others.

Activation of the DLPFC is a hallmark of successfully avoiding immediate awards in order to achieve goals present at a later point in time (Ely et al., 2013). Various studies have implicated DLPFC activation in the ability to focus on long-term goals (Peters & Büchel, 2011). Low frequency rTMS of the DLPFC, which decreases its activation, has shown to cause participants to be more likely to choose immediate smaller rewards over larger rewards presented at a later point (Figner et al., 2010). Individuals who experienced less activation of the pre-frontal cortex while performing tasks that involve delay discounting have been shown to experience more weight gain in subsequent years than those with greater prefrontal cortex activation (Kishinevsky et al., 2012). Further, a recent meta-analysis has provided support that stimulation of the DLPFC through both tDCS and rTMS has resulted in decreased food cravings (Jansen et al., 2013). Food cravings can often motivate an individual to choose immediate rewards over long term rewards. By reducing these cravings, avoiding delay discounting could be made an easier task. These results suggest that DLPFC activation allows for successful dietary impulse control through avoidance of delay discounting.

The orbitofrontal cortex (OFC) has also been implicated in delay discounting. Activation of the later-
al OFC (IOFC) has been associated with successfully inhibiting short-term rewards to achieve greater long-term rewards, while the medial OFC (mOFC) has been associated with motivating behavior for rewards closer in time. To examine this concept further, weight-concerned women, who had the long-term goal of weight loss, were placed into an fMRI scanner and were exposed to various dietary choices. Increased tastiness of food was negatively correlated with IOFC activity and positively correlated with mOFC activity (Laan, Ridder, Viergever, & Smeets, 2014). This suggests that those who are better at restricting intake of high-calorie foods may experience a greater activation of their IOFC and decreased activation of the mOFC. Recruiting this region may aid in focusing on long-term goals, despite immediately tempting rewards, and therefore benefit dieters.

Lesion studies directly address the OFC in dietary regulation. Dietary delay discounting was analyzed in rats with lesions either in their mOFC or IOFC. The IOFC lesioned rats displayed greater impulsivity and sought more immediate food rewards in comparison to rats with mOFC lesions who tended to seek temporally distant food rewards (Mar, Walker, Theobald, Eagle, & Robbins, 2011). To relate this evidence to humans, those who are more successful at dieting are better able to value long-term goals and refrain from the immediately rewarding high-calorie food. While this study supports the human data on OFC function with a method specific to animal research, differences in the animal and human OFC limit the direct translation of this finding to humans.

Studying those with eating disorders provides a unique opportunity to help understand potential abnormalities in delay discounting in these patients. Anorexic patients, who typically focus on long-term goals of weight loss over immediately rewarding foods, have revealed decreased grey matter volume in the left OFC (Brooks et al., 2011). Those with binge-eating disorders reveal increased medial OFC grey matter volume (Schäfer, Vaitl, & Schienle, 2010). Dietary restraint and avoidance of dietary delay discounting recruit the IOFC, whereas dietary delay discounting increases mOFC activity. Overall through imaging studies, lesion studies, and investigating clinical disorders associated with disrupted dietary regulation, it becomes clear that those who display successful dietary restriction reveal differences in OFC activity that reflects an ability to avoid delay discount within dietary contexts.

**Valuation of Food Rewards**

Lesion studies demonstrate that OFC damage leads to decision making deficits, potentially caused by the inability to effectively evaluate presented stimuli (Wallis, 2007). Supporting this idea, DelParigi et al. (2006) used PET to compare OFC activation differences between dieters and non-dieters when exposed to food choices. Successful dieters had decreased activation of the OFC after a satiating meal in comparison to non-dieter controls (DelParigi et al., 2006). The OFC receives visceral sensory input, which can use bottom-up visceral information about hunger to drive behavior. As a result, DelParigi et al.’s (2006) findings could indicate that successful dieters are better able to use bottom-up visceral cues about satiation to devalue further food intake after already eating. The DLPFC activation in successful dieters was inversely correlated to OFC activity. This reciprocal connection could be an inhibitory feedback circuit in response to meals. This circuit may allow successful dieters to use top-down environmental cues that are processed in the DLPFC, to further devalue food intake after eating. In line with this evidence, researchers have studied those with binge eating disorders and noted that in comparison to healthy controls, binge eaters showed increased activity in the mOFC when viewing food stimuli (Schienle, Schäfer, Hermann, Vaitl., & 2009). Increased activity in the mOFC may provide a value-based motivation that causes those with a binge eating disorder, and unsuccessful dieters, to overeat.

The value an individual places on certain goals drives the decisions he or she makes. The ventromedial prefrontal cortex (VMPFC) is another brain region that uses assigned values to drive dietary decisions. Evidence supports the notion that when making decisions, the brain computes the value of the options presented (the decision values) and will compare these values to drive an appropriate behavior (Hare et al., 2009). The VMPFC has been associated with computation of decision values (Sokol-Hessner, Hutcherson, Hare, & Rangel, 2012; Sripada, Gonzalez, Phan, & Liberzon, 2011). Keeping this in mind, Hare et al. (2009) conducted an fMRI study measuring decision value signals in dieters when making dietary choices. As expected, individuals who resisted tasty yet unhealthy foods had VMPFC
activity that correlated with considerations of both taste and health aspects of food. Dieters who were unsuccessful at rejecting tempting and unhealthy foods displayed VMPFC activity only in regards to taste aspects. These results suggest those who exercise a greater ability to refrain from high calorie foods are better able to endogenously activate the VMPFC in regards to health related cues. By recruiting this area, individuals can prioritize the health benefits of dieting over the temptation of food.

Those who successfully undergo dietary restriction have increased DLPFC activation. This was inversely related to activation in the VMPFC (Hare et al., 2009). This suggests a potential circuit involving the DLPFC and VMPFC implicated in decision making and more specifically, dietary choice. These results suggest that the VMPFC initially evolved to place value on short-term goals, but is now able to incorporate long-term consequences into its decision evaluations through modulation by the DLPFC (Hare et al., 2009). This circuit could have critical implications in dietary decision making. Damage to the frontal lobes has been associated with the development of hyperphagia, an eating disorder characterized by excessive uninhibited eating (Erb, Gwirtsman, & Fuster, 1989). Individuals with neurodegenerative disorders, such as frontotemporal dementia, that deplete grey matter in the fronto-temporal lobe, including the VMPFC, have been associated with disinhibited eating behaviors (Woolley et al., 2007). Those with VMPFC lesions have poor decision making skills, which can impact which foods they decide to eat (Fellows & Farah, 2007). This body of evidence suggests the VMPFC has a crucial role in dietary regulation through its ability to evaluate aspects of food intake to drive behavior.

**Dietary Regulation Failure**

The DLPFC plays a pivotal top-down role in controlling our mesolimbic and reward systems to regulate behavior. When individuals are under cognitive load, it may deplete DLPFC resources to inhibit impulsivity and restrict reward driven behavior. Consequently, self-regulation failure can occur. This was reflected in Ward and Mann (2000); participants who underwent cognitive depletion tasks engaged in more disinhibited eating than controls. Further, chronic dieters performed a task that depleted their cognitive resources and were later shown palatable food images (Wagner, Altman, Boswell, Kelley, & Heatherton, 2013). Those who underwent the cognitive depletion task revealed significantly increased activation in OFC and other brain structures that reflected the value of food with decreased activation in the lateral prefrontal cortex. The cognitive depletion task group also showed a reduced connectivity between these regions (Wagner et al., 2013). These results support the theory that high cognitive load can be detrimental to dieters. As high cognitive load depletes the resources of higher order brain regions to modulate the hedonic value of food, high cognitive load can result in disinhibited eating.

The environment in which one finds oneself can also affect the ability to inhibit impulses. Meule et al. (2014) investigated the effects of food cues on dieters. Showing participants visual food cues elicited impulsivity and automatic cravings for food, while the degree of impulsivity expressed was related to dieting success (Meule, Lutz, Krawietz, Stützer, Vögele, & Kübler, 2014). Because the OFC, VMPFC, and DLPFC receive input about external stimuli to drive behavior, these cues may interfere with cognitive control over impulsive behaviors, thus motivating dieters to make poor dietary choices. This presents a particular danger of dieting failure in today’s society, as ads promoting impulsive indulgence in high-calorie foods are almost unavoidable.

**Real World Implications**

The current approach for dietary regulation is to educate individuals on the nutritional content of their food choices and to emphasize personal choice (Appelhans, Whited, Schneider, & Pagoto, 2011). As a result of this method, humans believe that poor dietary choices reflect a personality flaw. This thinking stigmatizes failed dieters as being unmotivated. However, many failed dieters are motivated to lose weight (Appelhans et al., 2011). In this review, we show that dietary regulation extends beyond the intention of weight loss, and has complex neural underpinnings. There is support for a neurobehavioral approach to weight loss, moving away from ‘willpower’ as lacking in dietary regulation.

Inhibition is a crucial aspect of dieting which is linked to activation of the DLPFC (Appelhans, 2009). External cues from one’s environment can modulate DLPFC activity, which can in turn affect inhibitory behavior.
Surrounding dieters with health related cues, or removing cues that promote unhealthy food ingestion, can be strategies dieticians and practitioners recommend when treating those struggling with weight management. This review highlighted negative effects of cognitive stress on the ability of the DLPFC to modulate the VMPFC and OFC valuation processes. These studies suggest that dieters may benefit from training programs involving stress management. This may result in the reduction of cognitive load and the overall disruption of the inhibitory process—both necessary for diet maintenance.

All individuals, including dieters, struggle with the cognitive default of delay discounting. By educating dieters about temporal discounting and cognitive reappraisal therapy, dieters can learn to rethink food consumption in the context of long-term health benefits and weight loss. This dietary perspective can reinforce OFC and DLPFC activity among other regions to motivate dieters to continue through consideration of long-term goals.

Future Research
The majority of neuroscience research surrounding the complex human behavior of dieting has focused on understanding the brain regions involved in successful diet regulation. Recent findings indicate that behavioral intervention may facilitate self-regulation and inhibition by activating crucial brain regions that support top-down cognitive control (Kober et al., 2010). Few studies, if any, have investigated cognitive behavioral intervention on inhibition and dietary success. Future research should analyze the potential effects of cognitive reappraisal strategies to increase dietary success and weight loss of dieters. The neural underpinnings underlying this process may be understood through observable changes within the brain as individuals use these behavioral strategies. A longitudinal study could track the success of two groups: dieters taught reappraisal strategies and dieters unaware of these strategies. These strategies could increase dietary inhibition through reinforcement of brain regions involved in inhibition and self-control. Imaging studies along with voxel-based morphometric analysis could be conducted to test if these cognitive strategies affect activation and volume of brain regions associated with inhibition. Correlations between regional changes and dieting success can be examined. A study with this framework could support the implications in this review, and could further support neurobehavioral approaches to dieting as a recommendation by dieticians.

Although cortical brain regions appear to be playing a key role in dietary self-regulation, subcortical brain regions have also been implicated in dietary failure (Demos, Kelley, & Heatherton, 2011). Consequently, future studies should also analyze the effects that these cognitive strategies and potential cortical changes could have on subcortical brain regions associated with failure of dietary self-regulation.

References


