VITAMIN SUPPLEMENTATION IN ANOREXIA NERVOSA: EXAMINING EXECUTIVE FUNCTION IN RELATION TO THE INTERACTION OF VITAMIN SUPPLEMENTATION AND ANOREXIC STATUS

by

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DEDICATION

This work is in memory of my friend and role model, Kaitlyn Elena Welch. Kaitlyn's resilience, empathy, and sense of humor has touched the lives of me and others who had the privilege to know her. She was compassionate toward all and was unafraid to advocate for the rights of others. I know that through her example, I've been inspired to stand steadfast in my values, pursue my dreams, and search for deeper connections in the world around me.

Kaitlyn was my role model not just in personal development, but in academia as well. Despite the many medical battles she faced, Kaitlyn fiercely pursued her undergraduate career in psychology and research in topics like stress perception in autoimmune diseases. In our last conversation, Kaitlyn urged me to take a leap of faith and pursue my interests in graduate school. I'll forever be thankful to her for pushing me when I needed it the most.

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"Why, sometimes I've believed as many as six impossible things before breakfast." – Lewis Carroll

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ABSTRACT

Anorexia nervosa (AN) has the highest mortality rate of psychological disorders and is characterized by food restriction, rigid and extreme weight loss behaviors, and altered self-perceptions (Hanachi et al., 2019). Cognitive deficits and nutritional deficiencies have been suggested to impact the progression of pathology and outcome of treatment in AN (Dahlgren et al., 2019; Hale & Logosimo, 2019). Investigations into the cognitive profile of AN have found evidence to suggest deficits in executive function (EF), particularly in domains of inhibitory control and cognitive flexibility (Smith et al., 2018). Though the precise effects of micronutrients on cognition have yet to be determined, vitamin supplementation has been examined in cognitive aging studies and is clinically used in the rehabilitation of AN (Cuerda et al., 2019). The goal of the current study was to identify differences in EF according to (a) the effect of AN status, (b) the effect of vitamin supplementation, and (c) the interaction of AN status and vitamin supplementation. Using a between-subjects design, 683 participants reported if they have a current or previous diagnosis of AN as well as vitamin supplementation habits via online survey. Participants also digitally completed the inhibition and set-shifting subscales of the Behavior Rating Inventory of Executive Function–Adult version (BRIEF-A; Roth et al., 2005), the Stroop Task (Stroop, 1935), and the Wisconsin Card Sorting Task (WCST; Grant & Berg, 1948). Results did not detect an effect of AN status, an effect of supplement status, or an interaction on the BRIEF-A inhibition subscale, performance on the Stroop Task, or performance on the WCST. A small-magnitude main

effect of AN status was found for the BRIEF-A set-shifting subscale ($p < .01$), whereby anorexic individuals ($M = 12.28$, $SD = .39$) exhibited more daily-life problems with cognitive flexibility than healthy controls ($M = 10.85$, $SD = .11$). Moreover, a small-magnitude main effect of vitamin supplementation was found for the BRIEF-A set-shifting subscale ($p = .03$), whereby supplementing individuals ($M = 11.15$, $SD = .20$) exhibited less problems with cognitive flexibility in daily-life tasks than non-supplementing individuals ($M = 11.98$, $SD = .34$). Limitations and implications of my findings are discussed.

I. INTRODUCTION

Anorexia Nervosa

Anorexia nervosa (AN) is a serious psychological disorder that has a relatively high prevalence of 1-2.2% in young women (Corbetta et al., 2015; Hanachi et al., 2019). Although eating disorders have been previously considered a Western issue, there is evidence to suggest increasing prevalence among non-Western populations (Espie & Eisler, 2015). AN incidence occurs most frequently during adolescence or young adulthood, as compared to later developmental stages, and often coincides with puberty (Kaye, 2008). An alarming disorder statistic, the AN mortality rate is 12 times that of the general population, the highest mortality rate of all mental disorders (Dahlgren et al., 2019; Hanachi et al., 2019). High risk for premature death in AN is greatest between 15 and 29 years of age, occurs in similar standardized ratios for males and females, and is most often the result of suicide or medical complications (Espie & Eisler, 2015; Hanachi et al., 2019; Stedal et al., 2021). Virtually every bodily system is affected by AN, and chronic starvation amplifies risk for physiological dysfunctions (Espie & Eisler, 2015; Lipsman et al., 2015).

Time of incidence and AN pathology collectively influence an array of long-term consequences. Herbrich et al. (2019) describe AN etiology as multifactorial with adolescent onset contributing to vulnerabilities in psychological development alongside metabolic changes. Elaborating on puberty and metabolic risk, functionality of endocrine systems, such as estrogens, is thought to influence serotonergic and stress system functions (Kaye, 2008). Alongside hormonal disorders, frequently reported physiological complications in AN include heart, blood, liver, and intestinal disturbances and bone

demineralization (Hanachi et al., 2019). In addition, nutritional rehabilitation is influenced by these complications, such when present alongside metabolic disturbances, risk for liver steatosis in severe AN increases (Corbetta et al., 2015). Relative to cognitive implications, synaptogenesis during puberty is thought to impact the integration of emotion and cognition (Kaye, 2008).

Chronic psychosocial and physiological dysfunction is high in AN, and emotional ambivalence toward treatment is thought to underly low rates of treatment seeking (Espie & Eisler, 2015; Herbrich et al., 2019). AN treatment requires a multidisciplinary team approach in which physicians, nurses, dieticians, psychiatrists, and psychologists manage cases collaboratively (Cuerda et al., 2019; Peterson & Fuller, 2019). Refeeding, the process of nutritional rehabilitation and weight restoration, is crucial for successful treatment of AN, yet the metabolic and hormonal changes caused by malnutrition can lead to refeeding syndrome (Hale & Logomarsino, 2019). Refeeding syndrome is a potentially fatal condition associated with all modalities of refeeding that primarily involves deficiencies in micronutrients in conjunction with volume overload (Cuerda et al., 2019). Moreover, refeeding practices vary, and the literature has yet to reach a singular consensus on treatment protocols (Hale & Logomarsino, 2019).

Diagnostic Criteria & Disorder Characteristics

The fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; American Psychiatric Association, 2013) defines the first criterion for diagnosis as energy intake restriction such that body weight is significantly low compared to age, sex, developmental, and physical health norms. The DSM-5 further classifies AN diagnosis into restrictive (AN-R) or binge-eating/purging (AN-BP) subtypes. Individuals

classified as AN-R primarily engage in fasting or excessive exercise to achieve weight loss, while AN-BP individuals abuse laxatives/diuretics or vomit following episodic binges (Lipsman et al., 2015). In addition, a new study found subtype differences, such that AN-R individuals typically exhibit lower body weight, experience greater organ dysfunction, and require more stringent supplementation in refeeding than AN-BP, whereas AN-BP individuals exhibit a higher body weight, greater dehydration and electrolyte imbalances, and increased gastrointestinal dysfunction compared to AN-R (Hale & Logomarsino, 2019). Prominent characteristics of AN include extensive weight loss or failure to gain weight, disturbances in body image and weight evaluation, restrictive eating patterns, and obsessive fears of becoming fat (Herbrich et al., 2019; Lander et al., 2020; Stedal et al., 2021).

Anatomically, magnetic resonance imaging studies suggest acutely underweight AN groups exhibit reductions in gray matter which normalize after nutritional rehabilitation (Bernadoni et al., 2018). Some studies suggest that this reduction in brain tissue may contribute to the relationship between malnourishment and cognitive dysfunction in AN (Peterson & Fuller, 2019). Overall, evidence in the literature paints a cognitive picture of poor decision-making, altered reward systems, attentional deficits, and executive dysfunction in AN (Ciszewsky et al., 2014; Collantoni et al., 2016; Fagundo et al., 2012). Other cognitive characteristics of AN are described as perfectionistic, obsessive, and neurotic with body-image distortion serving as a contributing factor in severity, relapse, and maintenance (Kaye, 2008; Lander et al., 2020). Those perfectionistic and obsessive tendencies are especially evident in the behavioral characteristics, whereby AN individuals strictly follow ritualistic and rule-

bound behavioral patterns as well as intensely plan and organize around the disorder (Herbrich et al., 2019). Furthermore, anxiety, poor emotion regulation, and the avoidance of emotional distress are believed to additionally contribute to the cognitive dysfunction and restrictive behaviors associated with AN (Lipsman et al., 2015; Steward et al., 2020).

Comorbidities

Rates of psychiatric comorbidities in AN range from 47-60% in clinical settings, yet how comorbidities contribute to intervention outcomes is variable (Espie & Eisler, 2015; Herbrich et al., 2019). Bipolar, depressive, and anxiety disorders are among the most common comorbidities, and pre-existing obsessive-compulsive disorder (OCD) has been described as occurring primarily in AN-R populations (Abbate-Daga et al., 2014; American Psychiatric Association, 2013; Stedal et al., 2021). Additionally, comorbid alcohol use disorder and other substance use disorders is not uncommon in AN-BP populations (Peterson & Fuller, 2019). Prevalence of autism spectrum disorder (ASD) is debated, but a systematic review found a mean rate of ASD in AN to be 23% (Westwood et al., 2016). As consequence of underconsumption in AN, many of the behavioral traits associated with premorbid conditions are often exaggerated by malnutrition (Kaye, 2008). While some research suggests that overlapping characteristics, such as behavioral rigidity and social and cognitive problems, may contribute to mechanisms of dysfunction in comorbid AN, distinct relationships have yet to be determined (Brown et al., 2018; Patrick & Ames, 2015).

Executive Function

Executive function (EF) is a cognitive construct derived from efforts to conceptualize functionality of the prefrontal cortex (PFC) in the 1840s (Barkley, 2012).

Despite an extensive history in the literature, there is a lack of agreement as to how EF is defined and its constructs conceptualized (Baggetta & Alexander, 2016; Cirino et al., 2018). Discrepancies in EF operationalizations can be understood, as the term itself implies the involvement of lower order cognitive processes (Stedal et al., 2021). For the purpose of this work, EF is defined as an umbrella term for a collection of cognitive abilities that allow for purposeful, goal-directed behavior (Barkley, 2012; Cirino et al., 2018; Spitoni et al, 2018).

Trends in Anorexia & Executive Function

Investigations into the role of cognitive function in eating disorders hypothesized that maintenance could be at least partly attributed to dysregulation between top-down and bottom-up processing (Ciszewsky et al., 2014; Collantoni et al., 2016). With these investigations, neurocognitive constructs of decision-making, central coherence, working memory, inhibitory control, and cognitive flexibility were suggested to influence disordered eating pathology (Smith et al., 2018). Continued research into the relationships between eating disorders and EF suggested weight maintenance and food intake could be attributed to EF differences (Dahlgren et al., 2019; Foldi et al., 2021). Research specific to AN highlighted executive dysfunction as a core trait in the maintenance of pathology with potential to indicate risk as an endophenotype of the disorder (Fagundo et al., 2012). In addition, some cognitive deficits were found to exist separate from starvation, providing evidence for EF as an endophenotype (Keegan et al., 2021).

The body of work between EF and AN is substantial but has been variable (Baggetta & Alexander, 2016; Lander et al., 2020). Longitudinal studies in adult AN

populations provided support for cognitive deficit as an endophenotype of AN as inefficiencies were found to persist post-recovery (Stedal et al., 2021). However, this perspective has been challenged. Child studies contradict the perspective of cognitive deficit as an endophenotype, demonstrating that cognitive function deficits in adolescents are less consistent, less pronounced, and can improve with recovery (Brown et al., 2018). A meta-analysis by Stedal et al. (2021) found no explanation for this discrepancy. However, some researchers suspect these differences may be partially attributed to the duration of undernutrition exhibited in adults with AN (Hemmingsen et al., 2021). Despite variability, reviews of the literature provide some consistency, suggesting deficits in decision-making, inhibition, and cognitive flexibility may characterize EF in AN (Collantoni et al., 2016; Lander et al., 2020; Spitoni et al., 2018).

Inhibitory Control

Inhibitory control refers to processes involved in the ability to suppress or interrupt behavioral and cognitive responses (Baggetta & Alexander, 2016; Smith et al., 2018; Westwater et al., 2021). As an EF, functionality of inhibitory control contributes to successful physical and mental adaptation to changes in environment (Collantoni et al., 2016). Considering discrepancies across the definitions of various EF constructs, inhibitory control can be difficult to differentiate from other EF domains (Cirino et al., 2018). For example, inhibitory control has been associated with cognitive flexibility, attention, and emotional regulation, among other EF constructs (Collantoni et al., 2016; Smith et al., 2018). Within inhibitory control, the filtration of irrelevant stimuli from memory, perception, emotion, and thought can be conceptualized as cognitive inhibition, while the ability to delay gratification and withhold motor response constitute behavioral

inhibition (Collantoni et al., 2016; Smith et al., 2018). Other conceptualizations describe inhibitory control as regulated by goal-directed or stimulus-directed processes, referred to as proactive and reactive inhibition, respectively (Westwater et al., 2021).

The eating disorders literature suggests pathology lies on an inhibition-disinhibition spectrum, such that binge-eating disorders exhibit below normal inhibitory control while restrictive-eating disorders exhibit excessive inhibitory control (Smith et al., 2018). Common examples of inhibitory behaviors in eating disorders include regular body-checking, excessive exercise routines, and rigid or ritualistic feeding patterns (Dahlgren et al., 2019). Specific to AN, associations between greater psychopathology and deficiencies in inhibitory control suggest inhibitory deficits in AN relate to perfectionistic traits and contribute to the disorder's development (Paslakis et al., 2019; Spitoni et al., 2018). However, there is considerable heterogeneity in findings across the AN inhibitory control literature.

A study by Kullmann et al. (2014) noted that past studies lacked inclusion of disorder-related stimuli and thus conducted a study including food and exercise stimuli. This group found that functionality varied in accordance with stimulus category, such that emotionally invoking stimuli elicited greater activation of inhibitory brain regions compared to non-disorder-related stimuli. Findings from this study aligned with those from other eating disorder studies, suggesting that emotional stimuli require greater activation of mental resources in response inhibition (Steward, et al., 2020). Additionally, the influence of emotional stimuli on inhibitory deficits in AN suggests a potential cofactor of attentional bias (Spitoni et al., 2018).

One review of the literature found that compared to controls, AN groups generally

performed worse on traditional neuropsychological inhibitory tasks, but with a small mean effect size and moderate to high variability (Stedal et al., 2021). Although few studies have examined inhibitory control differences between AN-R and AN-BP, some evidence suggests AN subtype may contribute to the variability across findings (Smith et al., 2018). In a study investigating inhibitory control in AN-R individuals, Collantoni et al. (2016) assessed functionality of behavioral inhibition and attention. This group found that the AN-R group performed worse than controls, exhibiting longer reaction times. One hypothesis is that extended reaction times in AN are consequence of perfectionism (Spitoni et al., 2018).

Collantoni et al. (2016) also found that impairments in performance were related to body mass index (BMI). This finding has been replicated and suggests that inhibitory control deficits may reflect disorder severity (Paslakis et al., 2019; Stedal et al., 2021). Recently, a study by Westwater et al. (2021) investigated the influence of stress and negative feedback on inhibitory control in bulimic and AN-BP individuals. Findings from this study further suggest inhibitory control in AN is influenced by weight. However, these researchers suggest that brain activity related to inhibition is impacted by the stress induced by starvation in AN.

Cognitive Flexibility

Cognitive flexibility refers to an EF construct broadly defined as the ability to effectively move back and forth between concepts or tasks in order to alter behavior in response to change (Baggetta & Alexander, 2016; Lander et al., 2020; Sato et al., 2013). The term set-shifting is often used interchangeably with cognitive flexibility, although some researchers operationalize the two terms separately (Baggetta & Alexander, 2016).

The term set-shifting is then described as the ability to shift between cognitive strategies and mental sets in response to environmental change (Abbate-Daga et al., 2014; Ciszewsky et al., 2014; Herbrich et al., 2019). For the purposes of this work, cognitive flexibility and set shifting will be operationalized together as one construct.

Cognitive flexibility as a domain within EF is essential for effective adaptation to situational demands (Dahlgren et al., 2019). Examples of cognitive flexibility dysfunction can be described as rigidity towards changes in rules, inflexible patterns of thought, and stereotypical or perseverative behaviors (Dahlgren et al., 2019; Keegan et al., 2021). On traditional neuropsychological tasks, eating disorder populations tend to perform worse than controls and exhibit a more inflexible cognitive style (Ciszewsky et al., 2014; Keegan et al., 2021). Deficits in cognitive flexibility are associated with perseveration of pathology in eating disorders from food-related behaviors to treatment resistance(Ciszewsky et al., 2014; Dahlgren et al., 2019; Sato et al., 2013). Of the work examining the roles of EF in AN, alterations in cognitive flexibility have been established as a key theme (Fagundo et al., 2012; Keegan et al., 2021).

Despite some inconsistencies, reviews of the literature suggest impaired cognitive flexibility performance in AN groups compared to controls (Lander et al., 2020; Stedal et al., 2021). Cognitive inflexibility has been hypothesized to underly AN characteristics of eating behavior rigidity, obsessive-compulsive personality traits, and perfectionism (Abbate-Daga et al., 2014; Brown et al., 2018; Paslakis et al., 2019). Some researchers propose that negative affect in AN may be modulated by impaired cognitive flexibility when adapting emotional regulation strategies (Steward et al., 2020). Additionally, some evidence suggests a relationship between deficits in cognitive flexibility and illness

duration (Lander et al., 2020). Impairments in cognitive flexibility persist post-recovery in AN and are unrelated to body weight, suggesting deficits may be a trait of the disorder rather than a consequence of starvation (Brown et al., 2018; Sato et al., 2013). However, deficits in cognitive flexibility have been primarily found in adult AN populations and are not characteristic of all AN individuals (Abbate-Daga et al., 2014).

Common methodology in the literature has employed traditional neuropsychological tasks to examine cognitive and behavioral flexibility in AN. Studies employing these tasks often present main findings that AN groups perform worse than healthy controls with small to medium effect sizes (Paslakis et al., 2019; Smith et al., 2018; Stedal et al., 2021). AN performance on these tasks demonstrates that AN groups are capable of acquiring initial rules but exhibit higher error rates when switching between rules or having to implement new rules (Fagundo et al., 2012; Sato et al., 2013). Similarities in cognitive flexibility deficits have also been observed in OCD, one of the comorbidities seen in AN (Westwood et al., 2016). Notably, there is some discrepancy between performance on verbal and perceptual cognitive flexibility tasks, such that, contrary to commonly described deficits, AN groups have been found to exhibit comparable or superior verbal set-shifting compared to controls (Stedal et al., 2021).

One possible factor contributing to discrepancies is again the intersectionality of EFs. Though validity of traditional neuropsychological cognitive flexibility measures is high, these tasks can involve different levels of complexity and often involve other EF constructs such as inhibition, problem-solving, and working memory (Herbrich et al., 2019). Therefore, involvement of other cognitive processes may influence cognitive flexibility performance outcomes. Methodology presents another possible factor. A

majority of the neuropsychological tasks used to evaluate cognitive flexibility were developed to examine functional differences in individuals with brain lesions or trauma, not psychiatric populations (Stedal et al., 2021). Because of this, some researchers question whether traditional neuropsychological tests are sensitive enough to identify cognitive flexibility in other samples (Herbrich et al., 2019). Recently, the use of ecological tests has become more common as clinicians have noted AN individuals exhibit serious real-life executive dysfunction despite normal performance on traditional tasks (Spitoni et al., 2018).

Vitamins & Other Nutrients

Vitamins are groups of organic compounds necessary for a wide variety of bodily functions (Kennedy, 2016). Vitamins are functionally classified as either fat-soluble or water-soluble and all water-soluble vitamins are involved in metabolic processes (University of Hawai‘i at Mānoa Food Science and Human Nutrition Program, 2020). Although the brain only makes up approximately 2% of one’s body weight, this organ requires over 20% of the body’s total energy expenditure in order to properly function (Kennedy, 2016). Maintaining cognitive function depends upon various complex biochemical and enzymatic processes that require vitamins, minerals, and other micronutrients (Hale & Logosimo, 2019; Patrick & Ames, 2015). Research on aging and cognitive function in older adults has examined the potential benefits of vitamin supplementation. Ginkgo biloba, vitamin B12, and vitamin E supplementation have received attention in the past with recent directions examining the efficacy of saffron, choline, and vitamin D supplementation (Lewis et al., 2021). However, the direct effects of nutrient deficiencies on cognitive functionality in AN remains inconclusive

(Hemmingsen et al., 2021).

Though the body can synthesize some vitamins, a significant portion must come externally from our diet (University of Hawai‘i at Mānoa Food Science and Human Nutrition Program, 2020). Adequate amounts of vitamins A, D, E, and K (fat-soluble) alongside vitamin C and eight B vitamins (water-soluble) are necessary for human function (Kennedy, 2016). As a consequence of food restriction, AN populations often exhibit micronutrient deficiencies that worsen with purging and sometimes even the rehabilitation process (Cuerda et al., 2019). Deficiencies in micronutrients during the chronic malnourishment phase of AN often initially present asymptomatically (Hanachi et al., 2019). However, the prolonged lack of nutrition in AN causes an energy availability deficit that leads to disruptions in hormone signaling and then to atrophy of gray and white matter in the brain (Paslakis et al., 2019; Peterson & Fuller, 2019). Nutritional protocols vary for the treatment of AN, with some practitioners including oral supplements immediately and others adding oral supplements when a patient’s weight gain stagnates (Cuerda et al., 2019).

B Vitamins

B vitamins, grouped as such for their water-solubility and co-enzymatic functions, play a role in almost all cellular processes (Kennedy, 2016). The first B vitamin (B1) is thiamin. Thiamin deficiency has been described in some populations with increased prevalence among individuals with alcohol use disorders or post-bariatric surgery (Hanachi et al., 2019). Thiamin acts as a co-enzyme in the synthesis of various neurotransmitters and contributes to the structural and functional integrity of neurons and neuroglia (Kennedy, 2016). The literature has described thiamin deficiency in AN

populations after controlling for the duration of malnourishment, vomiting, and alcohol consumption (Hanachi et al., 2019).

Wernicke-Korsakoff syndrome, which causes symptoms of memory impairment, confusion, loss of coordination, vision changes, and hallucinations, is both a serious and common condition of thiamin deficiency (University of Hawai‘i at Mānoa Food Science and Human Nutrition Program, 2020). Fortunately, oral thiamin supplementation has been suggested as a safe and cost-effective method for combatting thiamin deficiency (Winston et al., 2000). Though supplementation recommendations vary across clinical practices, some practitioners implement oral thiamin supplementation upon the first day of inpatient care (Cuerda et al., 2019).

Pyridoxine (vitamin B6) plays a critical role in the synthesis of some neurotransmitters as well as the development, maintenance, and function of neurons (Lewis et al., 2021; University of Hawai‘i at Mānoa Food Science and Human Nutrition Program, 2020). Specifically, dopamine, serotonin, γ-aminobutyric acid (GABA), noradrenaline and melatonin synthesis are differentially sensitive to vitamin B6 levels (Kennedy, 2016). Whether or not vitamin B6 supplementation directly impacts cognitive function remains elusive. However, one study using a traditional inhibitory control task found improved performance following increased blood levels of vitamin B6 via supplementation (Kennedy, 2016).

Vitamin B9 (folate or folic acid) is necessary for cellular growth and specialization within the central nervous system (University of Hawai‘i at Mānoa Food Science and Human Nutrition Program, 2020). Additionally, proper synthesis and regeneration of serotonin, melatonin, dopamine, noradrenaline, and adrenaline

neurotransmitters is directly impacted by functionality of the folate cycle (Kennedy, 2016). Deficiencies in vitamin B9 have been linked to psychiatric disorders, such as depression, bipolar, and schizophrenia, as well as cognitive dysfunction in dementia (Lewis et al., 2021). Furthermore, the AN literature suggests vitamin B9 deficiency may vary between 20% and 45% in AN groups (Hanachi et al., 2019).

Vitamin B12 plays an intimate role in some of vitamin B6's functions. Vitamin B12 is required for activation of an enzyme that then allows the inactive folate compounds from food to be activated, thus allowing folate-dependent enzymes to conduct DNA synthesis (University of Hawai‘i at Mānoa Food Science and Human Nutrition Program, 2020). Some researchers propose vitamin B12 may be useful in identifying preclinical liver dysfunction, as excess vitamin B12 in the blood has been associated with leakage due to liver damage (Corbetta et al., 2015). On the other hand, deficiency in vitamin B12 has been associated with neuronal dysfunction and psychiatric disorders (Lewis et al., 2021). Similarities between vitamin B12 and vitamin B6 deficiencies are suspected to relate to the intersectionality between the two vitamins' enzymatic functions (University of Hawai‘i at Mānoa Food Science and Human Nutrition Program, 2020). Relative to AN, elevated levels of vitamin B12 compared to controls is common in AN groups and may be a risk indicator for liver steatosis in refeeding (Corbetta et al., 2015).

Vitamin D

Vitamin D is the classification for a group of fat-soluble, cholesterol derived compounds that the body obtains through diet and sunlight exposure (University of Hawai‘i at Mānoa Food Science and Human Nutrition Program, 2020). Vitamin D is

recognized as a factor in cellular function relative to both skeletal and cognitive health (Lewis et al., 2021). Though the clinical effects of vitamin D are non-linear, severity of deficiency symptoms are more pronounced than those of insufficiency (Goodwill et al., 2018). Common disorders associated with low vitamin D include ASD, attention-deficit/hyperactivity disorder (ADHD), depression, bipolar disorder, and schizophrenia (Patrick & Ames, 2015).

Vitamin D deficiency is high in AN populations, and despite introduction of vitamin D food sources, individuals with severe AN tend to maintain significantly lower levels than healthy controls (Homan et al., 2021; Veronese et al., 2015). A retrospective study on 360 severe AN inpatients further supports deficiencies in this population, finding a prevalence of vitamin D deficiency in over 50% of the cohort (Hanachi et al., 2019). Relative to the skeletal function of vitamin D, low bone mineral density is one of the long-term and sometimes irreversible physiological consequences of AN (Homan et al., 2021). Hanachi et al. (2019) found that a loss of bone mineral density, particularly in the hip bone, was strongly related to vitamin D deficiency.

Vitamin D has been implicated in cognitive health from increasing neuron density in the hippocampus to complex planning and memory formation (Goodwill et al., 2018; Lewis et al., 2021). Additionally, some researchers propose that vitamin D may assay depressive symptoms, playing a protective role against mood disorders and suicide (Veronese et al., 2015). Furthermore, vitamin D deficiency in AN is suggested to negatively impact some of the long-term psychological symptoms of the disorder (Hanachi et al., 2019). The literature shows that supplementation restores blood levels of vitamin D in deficient adolescents and lends to improved attentional and hyperactive

symptoms in those with AHDH (Homan et al., 2021; Patrick & Ames, 2015). Moreover, findings from Veronese et al. (2015) demonstrate that vitamin D supplementation may protect against or even counteract bone loss in AN.

Zinc

Although not a vitamin, zinc is a trace mineral that participates in the function of over 200 enzymes in the body (University of Hawai‘i at Mānoa Food Science and Human Nutrition Program, 2020). Zinc deficiency in the general population is relatively uncommon with an epidemiological study in 1991 finding a prevalence of only 5% globally (Hanachi et al., 2019). However, zinc deficiency can have serious effects, such as symptoms of hair loss, diarrhea, skin sores, loss of appetite, and weight loss (University of Hawai‘i at Mānoa Food Science and Human Nutrition Program, 2020). Developmentally, zinc is an essential antioxidant that influences the structure and function of brain regions such as the hippocampus and amygdala (Lewis et al., 2021). Additionally, zinc acts as a synaptic modulator in one of the neurotransmitter systems suspected to influence AN pathology, the GABAergic system (Hanachi et al., 2021). Because of these roles, deficiency in zinc is a suggested mechanism for some cognitive developmental delays (Lewis et al., 2021). Furthermore, the retrospective study by Hanachi et al. (2019) found a 64% prevalence of zinc deficiency in severe AN and noted that previous research found zinc supplementation positively influenced BMI in AN.

Omega-3 Fatty Acids

Though not vitamins but lipid components, omega-3 fatty acids are a group of essential fatty acids obtained dietarily that impact the immune and central nervous systems (University of Hawai‘i at Mānoa Food Science and Human Nutrition Program,

2020). Two of the omega-3 fatty acids (docosahexaenoic acid [DHA] and eicosapentaenoic [EPA]) are common in fish oil while the third omega-3 fatty acid (α-linolenic acid) is found in plant oils (Lewis et al., 2021). During development, omega-3 fatty acids, particularly DHA and EPA, play a regulatory role in the serotonin system's function (Patrick & Ames, 2015). Maintenance of high brain concentrations of DHA within synaptic membranes is crucial to facilitate anti-inflammatory processes (Lewis et al., 2015).

A study by Cook et al. (2019) revealed that women with low omega-3 fatty acids exhibited worse attentional performance than controls. Additionally, populations with ASD, ADHD, bipolar disorder, and schizophrenia have been found to exhibit low levels of DHA and EPA (Patrick & Ames, 2015). Moreover, given that AN populations tend to restrict fat consumption and that both gray and white matter are largely composed of lipids, some researchers suggest that neuroanatomical changes may be related to lipid depletion rather than dehydration (Bernadoni et al., 2018).

Supplementation of omega-3 fatty acids has been shown to improve cardiovascular and immunological health (Lewis et al., 2021). However, the literature varies in its associations between omega-3 fatty acid supplementation and cognitive performance, such that some studies found improvements and some studies found no differences (Cook et al., 2019). Studies that found cognitive benefits from supplementation of omega-3 fatty acids suggest supplementation may aid in psychopathology-related cognitive function (Patrick & Ames, 2015).

Implications

The reviewed literature examines AN, executive dysfunction, and the functions of several vitamins and other nutrients. However, whether or not supplementation benefits EF in AN populations remains inconclusive. Best practice in the treatment of AN is multimodal, involving the work of medical, nutritional, and psychological professionals (Resmark et al., 2019). Relative to psychotherapeutic interventions, specialized family therapy, cognitive remediation therapy, and cognitive behavioral therapy among others have proved useful in the treatment of AN (Espie & Eisler, 2015; Herbrich et al., 2019; Keegan et al., 2021; Resmark et al., 2019).

However, one common bar to the success of intervention is cognitive dysfunction (Smith et al., 2018). Given the cognitive rigidity and ego-syntonic nature of AN, it is not surprising that treatment is difficult and may require different techniques based on individual differences (Resmark et al., 2019). From this difficulty, novel psychotherapeutic interventions focusing on cognitive training rather than disorder-related symptoms show promise clinically and in day-to-day life (Keegan et al., 2021).

Relative to the restrictive nature of AN, vitamin deficiencies may logically be expected. A large body of work has investigated the role of vitamins in both AN and cognitive processes from general trends to cellular functions. In addition, deficiencies in several of the B vitamins, vitamin D, zinc, and omega-3 fatty acids all relate to pathology in several of the psychiatric disorders comorbid with AN (Hanachi et al., 2019; Lewis et al., 2021; Patrick & Ames, 2015). Considering the various shared characteristics between AN and its comorbidities, supplementing these nutrients in early intervention may reduce the burden of comorbid symptoms. However, the explicit effect of micronutrient

deficiencies on expressions of cognitive deficits in AN has yet to be defined (Tenconi et al., 2021).

The following study will examine group differences in EF according to AN diagnosis and supplementation of vitamins. Particular constructs of EF explored are inhibitory control and cognitive flexibility, two EF domains consistently examined in the AN literature. This study aims to further elaborate on vitamin supplementation and cognitive function with the intent to inform future research on supplementation in early AN intervention strategies. Specifically, this study will address the question of whether vitamin supplementation may help alleviate cognitive dysfunction in AN populations. I hypothesize that individuals with AN who regularly supplement vitamins will demonstrate less EF deficits than individuals with AN who do not.

II. METHOD

Design

The principal focus of this study was to identify possible interactive effects between AN status and vitamin supplementation on executive dysfunction. Thus, this study followed a 2x2 between-groups design, examining differences in set shifting and inhibitory control between four groups. These groups were classified as follows: individuals with AN who consume vitamin supplements, individuals with AN that do not consume vitamin supplements, healthy individuals who consume vitamin supplements, and healthy individuals that do not consume vitamin supplements. Power analysis (α = .05, β = .80) indicated a minimum sample of 128 participants, 32 participants per group, would be needed to detect a large main effect of AN status or vitamin supplementation status.

Participants

Participant were adults of at least 18 years of age, the only requirement for participation. Recruitment emails were sent to students enrolled in psychology courses and nutrition courses at Texas State University. Additionally, participants were recruited online via an Instagram advertisement that targeted viewers of dieting and healthy eating content. All participants were provided the option to enter their email address (in a separate Qualtrics survey) into a drawing for one of forty $25 Amazon.com gift cards as compensation.

Procedure

Participants were administered an online survey, via Qualtrics. The survey initially asked participants to read a consent form to which they were provided the option

to either agree to and continue the survey or deny and exit the survey. The main body of the survey requested participants to disclose demographic information, AN status, and vitamin supplementation habits. The final section of the survey included two subscales from an ecologically valid measure of EF.

After completion of the survey, participants were directed to complete two computerized EF tasks online through the Inquisit software (millisecond.com). Participants first completed a measure of inhibitory control, followed by a measure of cognitive flexibility. Following completion of the cognitive flexibility task, participants were directed to a second, separate Qualtrics survey for compensation purposes. In this second survey, participants could elect to enter their email address in a drawing for the chance to win one of forty $25 Amazon.com gift certificates.

Materials

The demographics portion of the survey asked the participant to report their sex, race, level of education, age, and height and weight (to calculate BMI). Additionally, participants were asked to report whether they have a current diagnosis of AN and/or have a past diagnosis of AN. To control for any non-AN cognitive deficits, participants were asked to report whether or not they have a diagnosis of ADHD, ASD, intellectual or learning disability, or OCD. Specific inclusion of these diagnoses was to account for their relationships to AN and cognitive dysfunction as discussed in the introduction (American Psychiatric Association, 2013; Brown et al., 2018; Stedal et al., 2021; Westwood et al., 2016).

The vitamin supplement section of the survey asked participants to report the regularity (daily, weekly, monthly, yearly, non-regularly/not at all) of their vitamin

supplementation habits. Specifically, participants were asked to report how regularly they consume a multivitamin, vitamin B, vitamin D, fish oil or other omega-3 fatty acids, zinc, and any general vitamin supplement. Inquiry into the specific supplementation of vitamin B, vitamin D, omega-3 fatty acids, and zinc was included based on the body of work supporting the influence of these micronutrients in AN and cognitive function (Corbetta et al., 2015; Hanachi et al., 2019; Lewis et al., 2021; Patrick & Ames, 2015).

BRIEF-A

The final section of the survey included part of the Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A), a 75-item assessment that examines EF in adults based on every-day environmental behaviors (Roth et al., 2005). The BRIEF-A is structured inventory employed to assess behavioral regulation through set shifting, inhibition, emotional control, and self monitoring subscales. Furthermore, the BRIEF-A assesses metacognition through working memory, task initiation, task monitoring, planning/organizing, and organization of materials subscales. In the literature, AN performance on ecological EF tests has demonstrated more consistent deficits compared to traditional neuropsychological test performance, such that some researchers have suggested ecological tests may be more sensitive to clinical aspects of EF deficits in AN (Ciszewsky et al., 2014; Stedal et al., 2021). Therefore, the BRIEF-A was chosen for this study based on its ecological validity and past use in examinations of AN populations (Dahlgren et al., 2019; Spitoni et al., 2018).

Relative to this study, participants only completed the set shifting subscale and the inhibition subscale. The set shifting subscale consists of six items concerning cognitive flexibility (e.g., “I have trouble changing from one activity or task to another”),

and the inhibition subscale consists of eight items concerning inhibitory control (e.g., "I tap my fingers or bounce my legs"). To each item, participants selected from the following options how frequently they experience difficulties with the behavior identified in the statement: "never", "sometimes", or "often" (Roth et al., 2005). Higher endorsement of problematic behaviors indicated greater impairments in EF. With the data collected in the current study, Cronbach's α was .73 for the set shifting subscale and .77 for the inhibition subscale.

Stroop Task

After survey completion, participants were directed to the first computerized task, the Stroop Task. The Stroop Task (Stroop, 1935) is a well-established neuropsychological measure that has been extensively used in the AN literature. This task has a large body of work in the assessment of inhibitory control, attention, and flexibility (Ferro et al., 2005; Fagundo et al., 2012; Paslakis et al., 2019). The Stroop Task requires participants to quickly and correctly identify the font color in which a word is presented on a screen. Each trial presents a new word, in colored font, on a blank screen with instruction to press a key corresponding to the font color. Participants are directed to press a the 'D' key for the color red, the 'F' key for the color green, the 'J' key for the color blue, or the 'K' key for the color black. Instructions remain on the screen for all trials. This assessment includes three trial formats: congruent, incongruent, and control. Trials that present a color word in the font color of the word, such as BLACK in black font, are congruent trials. Trials that present a color word in a different font color than the word, such as BLACK typed in red font, are incongruent trials. Trials that present a non-color word, such as PAPER in black font, are control trials. Variables measured for this

task included percent error and average response time for each of the trial formats (congruent, incongruent, and control). Accounting for baseline performance on control trials (i.e., incongruent minus control difference scores), lower incongruent percent error and lower incongruent response time indicated greater inhibitory control.

WCST

After completion of the Stroop Task, participants were assessed for cognitive flexibility by completing the Wisconsin Card Sorting Task (WCST; Grant & Berg, 1948). Another well-established neuropsychological test, the WCST is a popular assessment tool for cognitive flexibility that has also been used to measure memory and visual perception (Paslakis et al., 2019; Stedal et al., 2021). Within the AN literature, the WCST has been demonstrated as a valuable tool in assessing EF in AN groups (Keegan et al., 2021; Sato et al., 2013; Spitoni et al., 2018). In this study, the WCST instructed participants to digitally sort a stack of 128 cards into one of four categories (by number, color, or shape). Categories were indicated by the following: a card with one red triangle, a card with two green stars, a card with three yellow crosses, and a card with four blue circles. The sorting rule was not provided and there was no direct indication of when the sorting rule changed. Instead, when the participant correctly placed a card in its category, the word "correct" appeared on the screen, and when the participant incorrectly placed a card in a category the word "wrong" appeared on the screen. After consecutively placing 10 cards in their correct categories, the sorting rule changed. The WCST is complete when participants either run out of cards or successfully complete two number categorizations, two color categorizations, and two shape categorizations.

Several variables are automatically computed for this computerized task: the total

number of errors made, the percent of errors that were perseverative (percent perseverative errors), the percent of all responses that were perseverative (percent perseverative responses), the number of completed categorizations, the number of errors made after five consecutive correct responses (failure to maintain set), the number of trials taken to correctly categorize the first consecutive 10 cards (trials to complete first category), and the average difference in the percent errors from completion of one categorization to the next. While some of these variables pertain to general cognitive ability, lower percent perseverative errors and lower percent perseverative responses indicated greater cognitive flexibility.

Statistical Analyses

The data from Qualtrics (survey responses) and Inquisit (Stroop Task and WCST variables) were merged into a single SPSS data file. The two quasi-independent variables were coded into dichotomous categorical variables. AN status was defined as anorexic individuals (participants with a current and/or previous diagnosis of AN) or healthy controls (participants without a current and/or previous diagnosis of AN), and supplementation status was defined as supplementing individuals (participants who regularly consume vitamins daily or weekly) or non-supplementing individuals (participants who consume vitamins monthly or non-regularly/not at all). Likewise, the covariate was coded into a dichotomous categorical variable, with non-AN cognitive deficits being defined as deficit (participants with a diagnosis of ADHD, ASD, intellectual or learning disability, or OCD) or non-deficit (participants without a diagnosis of ADHD, ASD, intellectual or learning disability, or OCD).

The six dependent variables were then calculated. The BRIEF-A inhibition and

set shifting subscale scores were computed by summing the eight inhibition items and six set set-shifting items, respectively, with higher scores indicative of greater impairments in EF. For the Stroop Task, incongruent percent error was computed by subtracting the percent error on control trials from the percent error on incongruent trials, and incongruent reaction time was computed by subtracting reaction time on control trials from reaction time on incongruent trials. For both of these variables, higher values were indicative of greater impairments in inhibitory control. For the WCST, percent perseverative errors was calculated as the percentage of errors that were perseverative (i.e., participant followed the same rule they did on the previous trial in spite of being informed that their sorting response was wrong), and percent perseverative responses was calculated as the percentage of total responses that were perseverative. For both of these variables, higher values were indicative of greater impairments in cognitive flexibility. Zero-order correlation analyses were conducted to examine the relatedness of these six dependent variables.

The primary analyses were six factorial ANOVAs, one for each of the dependent variables identified above. For each ANOVA, the two between-subjects factors were AN status (anorexic individuals vs. healthy controls) and vitamin supplementation (supplementing individuals vs. non-supplementing individuals), and the covariate was non-AN cognitive deficit status. Eta squared (η^2) was computed as the metric of effect size with $\eta^2 = .01$ representing a small effect, $\eta^2 = .06$ representing a medium effect, and $\eta^2 = .14$ representing a large effect.

III. RESULTS

Of the 683 participants who completed the demographic survey, 681 completed the BRIEF-A section, 400 completed the Stroop Task, and 365 completed the WCST. Participants were primarily young adults (M = 24.89, SD = 10.09) with an average BMI of 24.5 (SD = 5.62). The majority of the sample were classified as healthy controls (618, 90.5%; 65 anorexic individuals, 9.5%), were supplementing individuals (428, 62.7%; 255 non-supplementing individuals, 37.3%), and did not have a non-AN deficit (557, 81.6%; 126 deficit, 18.4%). Majority of participants were classified as healthy supplementers (379, 55.5%), followed by healthy non-supplementers (239, 35%), then anorexic supplementers (49, 7.2%), and lastly anorexic non-supplementers (16, 2.3%). Additional demographic details are provided in Table 1.

Zero-order correlations then examined the relatedness of the two BRIEF-A subscales (inhibition and set-shifting), the two Stroop Task variables (incongruent percent error and incongruent reaction time), and two WCST variables (percent perseverative errors and percent perseverative responses). Consistent with previous findings, no association between Stroop Task performance and BRIEF-A inhibition was found (see Table 2). Furthermore, in accordance with the previous literature, no association was found between WCST performance and BRIEF-A set shifting.

Table 1.

Demographics and Sample Characteristics

Factor	Level	*n*	Sample %
Gender			
	Male	97	14.2
	Female	565	82.7
	Non-binary/gender fluid	20	2.9
Race			
	White	217	31.8
	Hispanic/Latinx	356	52.1
	Black	43	6.3
	Asian American or Pacific Islander	31	4.5
	Native American	6	0.9
	Biracial or multiracial	17	2.5
	Other/Prefer not to say	13	1.9
Education			
	High school, no diploma	12	1.8
	High school diploma or GED	159	23.3
	College, no degree	238	34.9
	Trade/technical/vocational training	14	2.1
	Associate degree	32	4.7
	Bachelor's degree	168	24.6
	Master's degree	56	8.2
	Doctoral degree	3	0.4

Note. Total sample $N = 683$.

Table 2.

Correlations of Executive Function Measures

Variable	1	2	3	4	5
1. BRIEF-A inhibition					
2. Stroop % error	.04				
3. Stroop reaction time	-.02	.07			
4. BRIEF-A set-shifting	.57**	.10*	<.01		
5. WCST % perseverative errors	-.04	-.09	-.07	-.04	
6. WCST % perseverative responses	-.03	.01	-.04	-.05	.68**

Note. BRIEF-A = Behavior Rating Inventory of Executive Function–Adult version; WCST = Wisconsin Card Sorting Task.

*$p < .05$; **$p < .01$.

Results of the ANOVA analyses with the three dependent variables assessing inhibitory control are presented in Table 3, and results of the ANOVA analyses with the three dependent variables assessing cognitive flexibility are presented in Table 4. For five of the six ANOVAs, there were no significant effects of AN status, no significant effects of supplement status, and no significant interaction between AN status and supplement status.

Table 3.
ANOVAs with Inhibitory Control Measures

Measure	Predictor	*df*	*F*	*p*	η^2
BRIEF-A Inhibition					
	Cognitive deficit status	1	68.06	< .01	.09
	AN status	1	0.02	.88	< .01
	Supplement status	1	2.33	.13	< .01
	AN status * supplement status	1	0.42	.52	< .01
	Error	676			
Stroop % error					
	Cognitive deficit status	1	2.13	.15	.01
	AN status	1	0.08	.78	< .01
	Supplement status	1	0.17	.68	< .01
	AN status * supplement status	1	0.07	.80	< .01
	Cognitive deficit status	387			
Stroop reaction time					
	Cognitive deficit status	1	0.52	.47	< .01
	AN status	1	1.27	.26	< .01
	Supplement status	1	0.16	.69	< .01
	AN status * supplement status	1	0.13	.72	< .01
	Cognitive deficit status	387			

Note. BRIEF-A = Behavior Rating Inventory of Executive Function–Adult version.

However, small-magnitude significant main effects were found for the factors of AN status and supplement status on BRIEF-A set-shifting scores (see Table 4). For the main effect of AN status, anorexic individuals (M = 12.28, SD = 0.39) experienced greater deficits in set shifting than healthy controls (M = 10.85, SD = 0.11). For the main effect of supplement status, supplementing individuals (M = 11.15, SD = 0.20) experienced fewer deficits in set shifting than non-supplementing individuals (M = 11.98, SD = .34). The interaction between AN status and vitamin supplementation on set-shifting scores was not significant.

Table 4.
ANOVAs with Cognitive Flexibility Measures

Measure	Predictor	*df*	*F*	*p*	η^2
BRIEF-A set shifting					
	Cognitive deficit status	1	23.30	< .01	.03
	AN status	1	12.54	< .01	.02
	Supplement status	1	4.52	.03	.01
	AN status * supplement status	1	1.05	.31	< .01
	Error	676			
WCST % perseverative errors					
	Cognitive deficit status	1	0.16	.69	< .01
	AN status	1	0.66	.42	< .01
	Supplement status	1	0.37	.54	< .01
	AN status * supplement status	1	0.15	.70	< .01
	Cognitive deficit status	357			
WCST % perseverative responses					
	Cognitive deficit status	1	0.86	.36	< .01
	AN status	1	1.38	.24	< .01
	Supplement status	1	0.78	.38	< .01
	AN status * supplement status	1	3.00	.08	.01
	Cognitive deficit status	357			

Note. BRIEF-A = Behavior Rating Inventory of Executive Function–Adult version; WCST = Wisconsin Card Sorting Task.

IV. DISCUSSION

Anorexia and Executive Dysfunction

The first aim of this study was to test the hypothesis that, compared to healthy controls, AN individuals would exhibit deficits in the EF constructs of inhibitory control and cognitive flexibility. These EF constructs were examined both traditionally (Stroop Task & WCST) and ecologically (BRIEF-A). This hypothesis was only partially supported. On both assessments of inhibitory control (Stroop Task & BRIEF-A inhibition subscale), no group differences were found according to AN status. These findings were unexpected but aligned with several studies that show AN groups perform similarly to healthy controls on traditional, non-disorder-specific inhibitory control tasks (Kullman et al., 2014; Steward et al., 2020; Tenconi et al., 2021). Cognitive flexibility performance on the WCST also revealed no group differences according to AN status. These findings again differed from my expectations but are consistent with some of the past literature (Hemmingsen et al., 2021; Stedal et al., 2021).

However, group differences did emerge for the main effect of AN status on the BRIEF-A set-shifting subscale. As I had predicted, anorexic individuals experienced more daily-life problems with cognitive flexibility compared to healthy controls. I suspect one possibility for this result is that the BRIEF-A set-shifting subscale items present real-world scenarios where habits and routines are challenged. Considering the rigidity and the obsessive-compulsive nature of pathology in AN, it makes sense that anorexic individuals would exhibit greater challenges in cognitive flexibility when having real-world habits challenged. Past research has suggested that inflexibility in AN may be related to difficulties adapting new emotion regulation strategies (Herbrich et al., 2019;

Lipsman et al., 2015). From this perspective, changes in structure and routine may elicit inappropriate emotional responses, therefore reflecting cognitive inflexibility in AN.

More in-depth examinations of the mechanisms of EF constructs lead some researchers to suggest that AN differences in EF, especially in cognitive flexibility, may constitute an endophenotype of AN (Brown et al., 2018; Stedal et al., 2021). However, some researchers challenge this due to discrepancies between deficits in adolescent and adult AN populations (Abbate-Daga et al., 2014). One hypothesis for this discrepancy is that nutrition impacts brain maturation, such that chronicity of undernutrition in adults compared to adolescents may be a contributing factor in the development of the EF impairments seen more consistently in AN adults (Hemmingsen et al., 2021). Over time, nutritional deficiencies may ultimately lead to atrophy of gray and white matter in the brain (Peterson & Fuller, 2019), causing the EF impairments. Fortunately, through nutritional rehabilitation and weight restoration, alterations in grey matter can be restored in AN up to ten times faster than changes due to aging (Bernadoni et al., 2018). Moreover, many cognitive dysfunctions improve with nutritional restoration which lends to improvements in other areas of treatment, such as psychotherapy (Hale & Logosimo, 2019). This intersectionality of nutrition, physiology, and cognition contributes to the primary need to restore and correct malnutrition-related developments in AN for successful treatment of the disorder (Cuerda et al., 2019).

Vitamin Supplementation to Offset Executive Dysfunction

The second aim of the current study was to test the hypothesis that regular vitamin consumption may offset any deficits in EF that are exhibited in AN individuals. This hypothesis was only partially supported. For the inhibitory control measures and the

WCST, there was neither a significant effect of supplement status nor a significant interaction between AN status and supplement status. Given that anorexic individuals and healthy controls did not differ on any of these measures, though, the lack of improvement in EF due to vitamin supplementation is not surprising. However, analyses did reveal group differences for the main effect of vitamin supplementation on the BRIEF-A set-shifting subscale. As I had predicted, the vitamin supplementing individuals experienced less daily-life cognitive flexibility problems compared to individuals who rarely or never consume vitamin supplements. I suspect that this result may reflect the relationships between micronutrients and psychophysiological function. As one example, vitamin D is associated with complex cognitive processes and overall cognitive health (Goodwill et al., 2018; Lewis et al., 2021). Relative to the modern-day urban diet and lifestyle, the introduction of processed and refined foods has negatively influenced dietary micronutrient intake (University of Hawai‘i at Mānoa Food Science and Human Nutrition Program, 2020). When considering the array of the micronutrients needed for optimal cognitive function, vitamin supplementation may partially alleviate cognitive flexibility consequences of the modern-day urban diet.

Limitations and Future Directions

The results of this study should be interpreted within the context of its limitations. First, there are limitations related to my sample recruitment and categorizations. The recruitment of the AN group relied on self-disclosure via online survey rather than a clinical population, so I am unable to confirm diagnostic status, AN subtype, or severity of symptoms within the anorexic group. Additionally, due to low recruitment of anorexic individuals, I needed to combine participants with a current AN diagnosis and

participants with a past but not current AN diagnosis. It is possible that many of the latter group may have received sufficient nutritional rehabilitation and weight restoration to overcome any EF deficits experienced before their recovery from AN. Moreover, within the AN group, only 16 of 65 participants were classified as non-supplementing. Therefore, I did not have the statistical power to detect a strong effect as determined through my power analysis. Furthermore, there was a high rate of attrition with approximately half of the sample completing all of the study components.

Relative to participant supplementation status, data on the method of supplementation, the dosage of micronutrients consumed, and the active ingredients of supplements were not collected. Different brands and forms of vitamin supplements vary across these factors, such that the quality and amount of micronutrients supplemented was not standardized across the supplementing group. This may further be exacerbated by the grouping of daily and weekly supplementers, such that the regular added micronutrient consumption within this group was somewhat variable. Given the combination of the aforementioned limitations, generalization of results is strongly cautioned.

Second, results should be contextualized within the limitations of the EF definitions and measures employed in this study. Despite extensive use in the study of cognitive function, definitions and conceptualizations of EF remain highly debated (Baggetta & Alexander, 2016; Lander et al., 2020). This issue is further highlighted by the lack of relatedness between the measures employed in this study. The zero-order correlations revealed that the Stroop Task and WCST were unrelated, the BRIEF-A inhibition subscale was unrelated to the Stroop Task, and the BRIEF-A set-shifting

subscale was unrelated to the WCST. However, it is possible that these measures may assess different mechanisms of inhibitory control and cognitive flexibility.

Additionally, the Stroop Task and WCST were administered online where participants could complete the study in any environment that internet access is available. Since it is unlikely that all participants completed this study in a controlled environment, performance on these tasks may not be fully represented. Additionally, the reliability of computerized versions of the Stroop Task is variable (Penner et al., 2012). Furthermore, the versions of the Stroop Task and WCST employed in this study were not inclusive of AN-specific stimuli. As the literature has demonstrated, AN performance on traditional EF tasks differs across the type of stimuli used in the task (Herbrich et al., 2019; Kullman et al., 2014). Moreover, the Stroop Task and WCST were developed to examine EF in brain trauma populations and are known to measure more EF constructs than just inhibitory control and cognitive flexibility, respectively (Collantoni et al., 2016; Herbrich et al., 2019; Stedal et al., 2021). EF constructs vary in conceptualization and share considerable crossover (Baggetta & Alexander, 2016; Cirino et al., 2018). Therefore, the use of the Stroop Task and WCST may not have had the sensitivity to identify AN differences.

Although some studies have turned toward the use of ecological evaluations in AN populations, such as the BRIEF-A, reliability of these tasks are less established than traditional neuropsychological measures (Dahlgren et al., 2019). Relative to the BRIEF-A inhibition subscale, it is possible that the items were more related to impulsivity and hyperactivity rather than perfectionism and other AN-related characteristics. Therefore, by using the BRIEF-A inhibition subscale, this study may have lacked the appropriate

stimuli to detect AN-related differences in inhibitory control.

Future directions should explore new methods to systematically evaluate the observed differences in daily-life EF in AN populations. Discrepancies between normal performance on traditional neuropsychological evaluations and clinical descriptions of EF deficits merit developmental efforts to create AN-sensitive EF evaluations. Development of AN-sensitive measures may prove valuable in the ability to monitor pathology in AN and help identify risk factors for disorder relapse.

In addition, longitudinal studies should evaluate the influence of micronutrients on cognitive function in AN. A myriad of neurophysiological processes are influenced by micronutrients from metabolic processes to neurotransmitter function (Hanachi et al., 2019; Kennedy, 2016; Lewis et al., 2021). In the treatment of AN, emphasis of restoring nutritional and hormonal balance is crucial to the success of rehabilitation and the avoidance of refeeding syndrome (Hale & Logosimo, 2019). Furthermore, despite differences in protocols, vitamin supplementation is commonly implemented in AN treatment (Cuerda et al., 2019). Understanding the longitudinal effects of micronutrients on cognitive function in AN may contribute to the standardization of best practices and inform possible prevention strategies against AN.

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