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BEHAVIORAL ECONOMICS APPROACH TO PERIMENOPAUSE,

A LEARNING CULPABILITY OF WOMEN IN DEVELOPING NATIONS

by

Brenda Nelson-Porter, Neutral, ND, DM, MIT, BAS, AAS

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The Thesis Committee for Brenda Nelson-Porter, ND, DM

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Grand Phd Eduard Everinov
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ABSTRACT

This mixed method novel clinical trial explored the selections of natural health remedies to approach perimenopause symptoms that impact the acquisition, comprehension, and transmission (ACT*ION) of knowledge in higher education settings. The cohort-reported clinical trial involved three phases: qualitative preliminary data, descriptive quantitative outcome data, and qualitative outcome data. African American perimenopausal women aged 20 to 40 responded to descriptive closed question on natural healthcare choices and open-ended questions about their experiences in an academic setting representing an empirical phenomenological approach to complete the clinical trial. Nutritional selections that were categorized across predictor subcategories to show common medical outcomes, which were validated by transitive or intransitive judgements, resulted in the emergence of three major themes: **[CONTACT WIDU FOR FINAL VERSION]**

DEDICATION

I dedicate this doctoral thesis to All Female Academic Learners around the world who are experiencing and coping with hormonal imbalances that negatively impact their lifestyle and educational endeavors.

ACKNOWLEDGEMENTS

First, I acknowledge God for allowing me to pursue this journey and continue to study to show myself approved. For allowing me this opportunity, I would like to sincerely thank the World Information Distribution University (WIDU). I appreciate the support of Shana Philyaw of the United States and former research assistant for her support during this journey. I acknowledge the participants in my research and express my appreciation for sharing their experiences and beliefs. Finally, I would like to thank all those who provided words of encouragement and believed that I would one day become an International Scholar.

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Chapter 1: Perimenopause: A Learning Culpability Introduction

Hormonal imbalances derived from either ovarian failure or estrogen (estrone [E_1], estradiol [E_2], and estriol [E_3]) deficiency have been found to impede the acquisition, comprehension, and transmission (ACT*ION) of knowledge when the interruption of the brain functions causes memory loss, confusion, and poor concentration (Greendale, Derby, & Maki, 2011; Luo, Li, Zhu, Ding, & Deng, 2013; Maki, Rich, & Rosenbaum, 2002; McCormick, 2013; Monteiro, Teixerira, & Calhau, 2014; Pinkerton, 2012). Some prior studies, however, have failed to conform that substantial cognitive change or decrements, short-term memory, episodic memory, visual working memory (WM), remembering, problem-solving, reasoning, natural language understanding, mental rotations, and decision-making are absolutely impacted by hormonal changes (Berent-Spillson, Persad, Love, Sowers, & Randolph et al., 2012; Henderson, 2008; Maki et al., 2002; Sommer, 1992). Episodic verbal memory, which processes involve verbal retrieval, encoding (forming new memories), consolidation, storage, and fluency based on mere sensations or personal experienced events, and WM (i.e., visual memory retention), which manipulates information, are rich in estrogen receptors (Berent-Spillson et al., 2012; Greendale et al., 2011; Mednick, Cai, Shuman, Anagnostaras, & Wixted, 2011; McKoon, Ratcliff, & Dell, 1986; Reas, Gimbel, Hales, & Brewer, 2011; Smith & Mizumori, 2006). Studies have concluded that the premenstrual phase has no effect on reaction time (RT) and reproductive hormones are not correlated to executive function and processing speed; however, few have shown that hormonal women experience slower choice RT or articulation because regional activation is correlated with levels of hormones, which differ in each hormonal phases, for verbal and not visual tasks (Berent-Spillson et al., 2012; Sommer, 1992).

Perimenopause (rajonivrutti), a condition resulting from the decline of ovarian function, has received little scientific attention maybe because menopausal phases continue to be considered a normal process for aging woman (Prior, 1998; Setorglo, Keddley, Agbemafle, Kumordizi, & Steiner-Asiedu, 2012; Shylaja, Jithesh, & Gayal, 2015). The effects of perimenopause or reproductive aging are difficult to distinguish from the effects of chronological aging at the regional (behavioral, neuroanatomical) and the executive levels (e.g., memory systems; Berent-Spillson et al., 2012). Various symptoms associated with declining ovarian functions or perimenopause include but may not be limited to hot flashes/night sweats (vasomotor/physical symptoms), insomnia, fatigue/exhausted, stress, mood swing, depression, poor memory or concentration (psychological symptoms), headaches, dry eyes, burning mouth sensations, muscle spasms, autonomic reactions (heart palpitations; somato-vegetative symptoms); urinary tract infections (UTI), urinary incontinence, vaginal dryness urogenital symptoms); breast tenderness, bloating, visible distension, adiposity (obesity), and cycle changes to include but are not limited to "oligomenorrhea (infrequent) or dysfunctional uterine bleeding, symptoms of estrogen deficiency, and elevated gonadotrophins" (Collin, Rosano, Casey, Daly, Gambacciani et al., 2007; Goodman, Cobin, Ginzburg, Katz, & Woode, 2011; Greendale et al., 2011; Livdans-Forret, Harvey, & Larkin-Thier, 2007; Mangweth-Matzek et al., 2013; "Perimenopause Symptoms," n.d.; Prior, 1998, p. 397; Setorglo et al., 2012; Shylaja et al., 2015; Subhankar et al., 2011; Sunil, Mukunda, Gonsalves, Basheer, & Deepthik, 2012; Wang, 2011a). Under the Ayurveda systems traditionally practiced in India, perimenopause symptoms are classified by three stages of life: Vatika, Pittaja, and Kaphaja (see Table 1 for listing; Dhiman, 2013; Shylaja et al., 2015).

Research has shown that the physical symptoms associated with perimenopause are impacted by sociocultural conditions well into senescence and stressors may be further heightened when external stimuli and lifestyle factors influence the natural ability of the body (living machine) to regulate hormones (Malone, 1990; Setorglo et al., 2012). Senescence signifies the period of cession of the normal ovulation function (Klein et al., 2004). A healthy diet has been found to have a positive influence on the body during the start of the natural menopause phase (Spencer et al., 2013).

Table 1

Dosha Predominance Classification of Symptoms of Menopause

Vatika	Pittaja	Kaphaja
Irregular Menstruation	Angry Outbursts	Weight Gain
Nervousness	Irritability	Sleepiness
Anxiety	Short Temperedness	Sluggishness
Insomnia	Hot Flushes, Night Sweats	Fungal Infections
Mild Hot Flushes	Urinary Tract Infections	Slow Digestion
Depressive Symptoms	Skin Rashes	Fluid Retention
Poor Skin And Muscle Tone		
Constipation		
Vaginal Dryness		

Note. Adopted from "Perimenopausal Depression and Its Ayurvedic Management," by C. K. Shylaja, M. Jithesh, and R. R. Gayal, 2015, *International Journal of Scientific Research (IJSR)*, 4, pp. 1-6. Permission to reprint from the International Journal of Scientific Research, 2016.

Sociocultural factors, however, have been reported to limit the dietary intake of African women (Manuh, 1998). The determinant of African women's health and nutrition has resulted from their high illiteracy rate that derives from a lack of education, training, and employment (Manuh, 1998). The interconnection identified between poverty and powerlessness of African women has been associated with their precarious health status, which encompasses how

perimenopause impacts learning (Manuh, 1998). Perimenopause as well as premenopause, thus, will be further researched to discuss its uniqueness and identify dispersed resources (e.g., natural foods and remedies) that may be accessible to female African learners to approach the symptoms or underlying causes of the symptoms associated with this unique condition (Setorglo et al., 2012). This research assessed the beliefs and a level of awareness of learners about how their perimenopause symptoms impacted their ACT*ION of knowledge in higher education systems after the consumption of natural remedies and nutritional medicines as a field of study cannot mature unless the field is recognized by the academic community as an essential element for learners (AACE Nutrition Guidelines Task Force; 2003; Linnekin & Broad Leib, 2014).

Problem Statement/Decision Problem

Hormonal imbalances and changes that result from estrogen deficiency impact the ACT*ION of knowledge because estrogen stimulates neurotransmission (McCormick, 2013; Parnell, 2007). Research has found that deductive reasoning, spatial ability, and mental rotations decrease and fine motor skills and verbal articulation enhance during the midluteal phase when estrogen is high (Maki et al., 2002). "Mental rotations, fine motor coordination, and verbal fluency" are known as sexually dimorphic skills (Maki et al., 2002, p. 520). Estrogen deficiency or low estrogen during follicular phase or as a result of the ovarian function ceasing during the reproductive age disrupts the normal hormonal systems causing an increase in mental rotations and a decrease in non-declarative implicit memories, declarative semantic memory, verbal memory, and facilitation of epigenetic alterations during learning, fine motor skills, fluency, or articulation (Berent-Spillson et al., 2012; Frick, 2013; Maki et al., 2002; Wang, 2011a).

When any of the normal hormonal systems become disrupted by either extracellular triggers, such as microbial invasion and generation of reactive oxygen species (ROS), which are

known as free radicals, and so forth, we have to consider if cellular inflammation is a precursor to estrogen modulation or fluctuation (Dauqan, Abdullah, & Sani, 2011; Monteiro et al., 2014; Sears, 2012). The protein complex, NF-κB, mostly controls "the expression of several inflammatory factors including adhesion molecules, TNF-α [tumor necrosis factor alpha], interleukins, and inducible nitric oxide synthase (iNOS)" (Kim, Tarhuni, Elmageed, & Boulare, 2015, p. 2). Because of limitations of this study, NF-κB and its association to the various stressors were not assessed. The influence of psychological, biological, emotional, physical, and cognitive stressors associated with perimenopause on learning was assessed after identifying selections of natural remedies to approach these stressors.

Biological stressors, which drive cognitive or behavior changes that impact the ACT*ION of knowledge, stimulate physical and emotional stressors (Prior, 1998). During the perimenopausal transition phase, when the body may undergo abnormal uterine bleeding (AUB), many young African women fail to meet attendance at school doing their menstrual cycle because of limited or lack of sanitary products (Subhankar et al., 2011; Taylor, 2011). The condition of AUB is defined as "Patients having either metrorrhagia defined as vaginal bleeding separated from expected menses or menorrhagia defined as patients' subjective complaints of either increased duration or increased volume of flow or both" (Subhankar et al., 2011, p. 189). Biological stressors associated with the symptoms of perimenopause, thus, tend to heighten negative sociocultural conditions.

Physical symptoms associated with perimenopause, which are heighten by behavioral or cognitive stressors, may further suppress the regular functioning of the nervous system, which may further impede the ACT*ION of knowledge (Nelson-Porter, 2014c). Based on speculation, when knowledge derived from external stimuli (KES) differs from knowledge stored in the

subconscious (KSS), the brain may experience a lapse resulting in the inability of the mind to acquire, organize, store, retrieve, analyze, and transmit supplemental knowledge and perform automatic processing. New subsequent learning interferes with previously learned information, which is known as retroactive interference, when the time between them is relatively short (e.g., 1 hr; Booth, 2008; Mednick et al., 2011).

"Our earliest memories are often created through the sense of touch . . . the sense of smell creates some of our strongest and most vivid long-term memories" (Parnell, 2007, pp. 23-24). Brain freeze is characterized as an event whereby information becomes difficult to retrieve when estrogens fluctuate during the menopause phase (Parnell, 2007). Natural remedies and the processes and preparations of foods and remedies of which learning is gained have evolved over the course of decades; thus, the current sense of sight, touch, and smells of foods may not register with the stored memories causing disorientation and behavior changes.

Learning has been claimed to be associated with the flexible conscious mind, which emerged from the cognitive sciences that follow logical structured reasoning (Jan van de Kaa, 2010; Loftus & Klinger, 1992; Skinner, 1985). The conscious mind whereby internal stimuli influence adaptive behaviors is considered analytical (Loftus & Klinger, 1992). Adaptive refers to learned responses as a result of environmental relations that enable avoidance of other stimuli (Powell & Lumia, 1971). When ongoing behaviors are disruptive or behaviors are prevented to reoccur by the individual or by society, then the responses (phobias, voidances) are considered unadaptive (Powell & Lumia, 1971).

The behavior choice to select natural remedies vice the cognitive choice to select natural or conventional remedies, thus, may be difficult to adapt because the unconscious mind whereby external stimuli influence adaptive behaviors are considered intuitive although here errors are

usually minimized (Bouquet & Warglien, 1999; Jan van de Kaa, 2010; Loftus & Klinger, 1992; Skinner, 1985). Greenwood, author of the 1992 article, "New Look 3: Unconscious Cognition Reclaimed" claimed the unconscious is analytically unsophisticated warranting limited capabilities and nonresponse in the presence of stimuli (Loftus & Klinger, 1992). In regards to the two forms of thinking being seen as complimentary and revisiting the notion that the awareness and experiences of consuming natural remedies prompted choice of selecting natural remedies as an approach to perimenopause symptoms, "Beach might be right: 'We suspect that, as a general rule, if intuition (gut feeling) conflicts with analysis, analysis seldom wins'" maybe when there is biases in judgement under uncertainty (Jan van de Kaa, 2010, p. 302; Rabin, 1998).

"Conventional medicines that have been used to treat [perimenopausal] symptoms, such as fuzzy thinking and memory lapses, include but are not limited to Prempro® and Cymbalta®. Natural remedies that have been used to approach the symptoms include but are not limited to Remifemin® and GEM™" (Kronenberg & Fugh-Berman, 2002; Nelson-Porter, 2015a, p. 58). The increased manufacturing of conventional medication increases the distribution and selections of conventional medications (Mann, Gaylord, & Norton, 2004; PhRMA, 2007). Western methods, to include deliberate, conscious, and analytical processing and intuitive processes by physicians and hormone replacement therapy (HRT), have been priorities in approaching medical issues (De Vries et al., 2010; Stolper et al., 2010; Wang, 2011a). When natural remedies are consumed, behaviors and cognition may be monitored to further gain an understanding of their selective nature. The awareness of natural approaches via clinical trials and academic learning platforms may stimulate awareness and prompt behavioral selection because "consumptions can also be unknowingly influenced by environmental cues" (PhRMA, 2007; Wansink, 2010, p. 454).

Purpose/Therapeutic Value Proposition Statements

The purpose of this novel mixed methods clinical trial was to identify selections of natural remedies and assess which remedies (independent/experimental variables) positively approach perimenopause symptoms (intervening variables) that negatively impact the ACT*ION of knowledge (dependent/response variables) in higher education setting by evaluating the effects of the selection processes and choices based on if improved memories or beliefs about the outcome are implicit intransitive inferences (ITIs) or transitive inferences (TIs) about the influences of higher education processes, learning, and practices (Frank, O'Reilly, & Curran, 2006; Dougherty, Franco-Watkins, & Thomas, 2008; Gigerenzer, 1997; Wansink, 2010). Natural remedies include but are not limited to foods, vitamins, herbs, flowers, homeopathic formulas, and nature (Ballentine, 1978; Hoffman, 2007). Although many natural remedies are not found in certain communities, the therapeutic value of natural remedies has been found to respond to various symptoms associated with perimenopause and result in minimum harm; whereas, the financial value of natural remedies may be expensive if access is limited, a negative outcome emerge, and medical insurance does not cover the cost as with conventional medications (Mann et al., 2004; Nelson-Porter, 2015a). Mixed methods case studies aim to integrate research approaches to confirm or complement inferences drawn from the data about the behavior choice, effects, and beliefs (Cameron, 2009).

This clinical trial (knowledge domain) may also transform beliefs about the effects of certain compounds in natural remedies stimulating activities (hidden connections) that decrease the symptoms associated with perimenopause or control the fluctuations of estrogen when symptoms fail to advance and awareness become permanent (intermediate domain), and the transfer of knowledge become further enhanced in classroom settings whereby learning

processes and capabilities become leveraged and conscious and unconscious competences arise (e.g., target domain; Batra, Harper, & Liang, 2003; PhRMA, 2007; Roche, 2013; Rubio et al., 2010; Tan, Song, Zhong, & Yang, 2015; Workman, 2010). Thus, if processes become clearer, comprehension levels become enhanced, and collaborations become understood and adaptive, then the effects of a targeted natural remedy may become further validated (PhRMA, 2007). The beliefs about the having a clearer understanding of the processes, an enhancement of compression levels, and an collaborations adaptation, however, can further validate the effects of the natural remedies consumed through future clinical trials. The mixed methods design was appropriate because the integration of the qualitative preliminary data, descriptive quantitative outcome data, and qualitative outcome data assisted in gaining a better understanding of a unique population (Curry, Nembhard, & Bradley, 2009). Reporting patient-reported outcomes (PROs) are revealed in the questionnaires completed by the participants; whereas, observer reported outcomes (OROs) are revealed from the responses asked by the primary investigator (PI) prior to the start of the study and during daily phone calls (Deshpande, Rajan, Sudeepthi, & Nazir, 2011).

The population for this clinical trial was African American women, because Black women have been reported to experience premenstrual symptoms (PMS) more often than women of other races and "population-based samples concerning cycle-by-cycle changes in interval, flow, and ovulatory characteristics are still lacking" (Batra et al., 2003; Prior, 1998, p. 402). Because African American women in the United States who share similar deoxyribonucleic acid (DNA) as women in Africa continue to experience economic and health disparities, African American women participated in this clinical trial (American College of Obstetricians and Gynecologists [ACOG], 2015; NCHPEG, 2015; PhRMA, 2007; Salas, 2004). Although scholarly literature indicates that O+ is the most abundant and stable blood group, literature is

scarce concerning the ABO phenotypes (blood type) of Africans; whereas, literature reports that African Americans have high O+, A+, and B+ blood types (American Red Cross, 2015; Buettner-Janusch, 2009). "Two individuals chosen from different continents would be expected to differ genetically by just 10 to 15%" maybe as a result of natural selection, positive or negative (Halima, Bahri, Esteban, Moral, & Chaabani, 2015; NCHPEG, 2015, para. 22).

Findings revealed which dispersed resources African American and African women may need to access and consume to approach perimenopause symptoms. "Capability leverage increases the value delivered by flexibly connecting resources that otherwise might not be accessible to customers or that might require great effort by customers to assemble on their own" (Hagel, 2011, para. 8). Although the costs associated with purchase of each food group was collected, this study did not primarily focus on cost effectiveness, which is associated with economic evaluations whereby the value is measured based on cost and outcome (The University of Sheffield, 2016). After deploying the conditional logit model, to achieved capability leverage, alternative selections were immediately generalized across populations as each selection within each subcategory of nominal variables shared similar characteristics or nutritional value (McFadden, 1973).

This research may further help emerge natural alternatives tracks and training sessions that are pertinent to help women alleviate or cope with physical symptoms and sociocultural conditions that heighten the symptoms associated with perimenopause. Within clinical trial settings whereby learners engage with patients, graduate learners may acquire knowledge about natural health solutions aimed to enhance their critical appraisal skills, which include but are not limited to randomized controlled trial, systematic reviews, cohort studies, and economic evaluations (Siminoff, 2013; Singh, 2013). "Learning leverage adds even more value by

enabling individual participants to deliver higher levels of performance to the marketplace as they learn more rapidly from each other" (Hagel, 2011, para. 8). Researchers, however, posited that behavior change derive from a community of encouragement by providing weekly reminders, asking about progressions, sharing ideas, or obtaining feedback instead of education and awareness through instructions; researchers believed a field of study cannot advance unless the academic community embraces the field (Linnekin & Broad Leib, 2014; Wansink, 2010).

Research has shown that no special arrangement needs to be made for college entrance exam or any other situation that involves cognitive competence except for severe dsymenorrhea or disabling symptoms (Sommer, 1992). Naturopathic practitioners as faculty members and acquiring, full-time, and tenured professors, however, may find this research useful to raise awareness about the benefits of intuitive evaluations of learners and the importance of natural health by establishing hybrid university healthcare clinics, incorporating natural remedies into cafeteria selections, and devising clinical programs to evaluate each remedy choice of women experiencing perimenopause and integrating the outcomes of consumptions of natural healthcare remedies into higher education curriculums to stimulate group discussions or in applied scholarship or flagship programs to stimulate conferences and research initiatives (AACE Nutrition Guidelines Task Force; 2003; Boston University, 2010; Nelson-Porter, 2015a; PhRMA, 2007; Roche, 2013; Slavin, 2008; Stolper et al., 2010). Access to natural approaches, however, may prove limited because of environmental factors and government restrictions (Sharad, Manish, Mayank, Mitul, & Sanjay, 2011). Learners may find that acquiring more knowledge about natural approaches may stimulate their interest to pursue a natural healthcare career, initiative selecting natural approaches can empower learners to personally enhance self-

health, and using natural remedies may enhance their ability to acquire, process, and apply an unprecedented amount of knowledge (Wansink, 2010; Workman, 2010).

Behaviorism v/s Rationalism Framework

Research has shown, to approach problems, societies have to form cultures that embrace a norm (Richerson & Henrich, 2012). The behavior or personal characteristics of individuals influence the environment based on what is observed (logical positivism) and heard (radical behaviourism), or the environment, situational factors, or stimuli influences the behaviors of individuals based on the consequences aroused from the interactions with the environment (Maddux & Yuki, 2006; Richerson & Henrich, 2012; Skinner, 1985). Referring an object, one is actually observing a copy (presentation) of the world not the actual world (representation) because stimuli alter perceptions (Berg, 2003; Skinner, 1985). "Nonrational behavior in economics [behaviorism] is a bit like an optical illusion. Just as you cannot always trust your eyes, you cannot always trust your behavior to be rational" (Zeckhauser, 1986, p. S440).

Behaviorists study and explain the unobserved, such as personal habits, through experiments and micro evidence of non-rational choices (Berg, 2003; Zeckhauser, 1986). Rationalists compute solutions for reoccurring situations, such as prescribing a certain amount of conventional medications to balance the fluctuation of estrogen and approach the symptoms associated with perimenopause (Pharmavite, 2015; Zeckhauser, 1986). Rationalists who make decisions based on observable variables believe behaviorists make predictable and systematic errors in judgement as a result of illusions or biases in thinking, which is faster, automatic, and largely nonvoluntary (System 1) or slower, more deliberate, and more controlled (System 2; Berg, 2003; Quigley, 2013). The administering of the conventional medicines has followed the concept of rationalism; however, although the effects of some conventional medications are

compatible to natural medications, the elements surrounding the nature of the medications are extremely different (Hoffman, 2007; Nicolazzzo, 2009; Panos & Heimlich, 1980; PhRMA, 2007; Zeckhauser, 1986).

Behaviorism involves being flexible while seeking to find a solution to unique situations (Zeckhauser, 1986). Perimenopause may be categorized as a unique condition because the condition is not readily diagnosed unless a female hormonal panel, to include blood or salivary testing, is administered to simultaneously view the profiles of estrogen and progesterone (Diagnos-Techs, 2012; Jasienska et al., 2006). Behaviorism may be further defined as signal equilibrium by identifying which natural source(s) as unique to approach underlying symptoms of perimenopause vice treating the symptoms (Pharmavite, 2015; Zeckhauser, 1986).

Decision-making about a more effective approach to hormonal imbalances continue to lean, however, towards administering conventional medications in modern societies, which derive from rational market behaviors (Mann et al., 2004; Zeckhauser, 1986). Conventional approaches have been reoccurring due to market influences, manufacturing, and political interests (Mann et al., 2004; PhRMA, 2007). Rational behaviors seem to stem from control systems as economists have little to do with any results that stem beyond rationalism, such as preferences and values (Zeckhauser, 1986). The pursuit of food (even as a natural medicine) based on non-rational market behaviors have been reported to derive from poorly behaving markets, price fluctuations, and unpredictable financial markets (Zeckhauser, 1986).

Here, we may reflect on natural selection, the evolutionary process that maintains balance of the polymorphism, which are conditions (e.g., poverty; abnormal hemoglobin and ABO(H) blood groups) that emerge when the effects of natural mutation stimulate a greater amount of a less dominant species that occupy the same environment as other discontinuous forms of a

species (Buettner-Janusch, 2009). Based on the opinions of the reader William Godwin on Robert Malthus' population essays whereby Malthus observed the poor in England, Godwin believed a change in attitude about how to approach problems could counteract the population growth and misery associated with the limited food supply; that is, if personal, political, and moral attitudes embrace abstinence, celibacy, or a certain number of births per family unit (Avery, 2005). Here, we may consider if presentations (copied belief/heuristics about the actual food supply/type of blood/an approach to problems) trump the representations (factual information about the actual food supply/type of blood/an approach to problems) because perceptions become altered based on the stimuli (Skinner, 1985).

Solutions, known as checks are noted to become essential to reduce the population to the level of food supply (Avery, 2005). Malthus posited that vice (abortion/birth control) is one type of preventive check, but also believes that misery (e.g., death by disease/war), although is a positive check to control the population, can be seen as a preventive check (Avery, 2005). Here, an increase in agriculture improvements, to include biotechnologies, to approach misery can be considered a preventive check; although the population may grow even larger because improvements tend to stimulate reproduction, the growth, however, may lead to more vice and misery unless the concept if embraced personally, politically, and morally (Avery, 2005; Bakshi, 2003; Fernandez-Cornejo, Wechsler, Livingston, & Mitchell, 2014; Pinkerton, 2012). For example, because the long-term effectiveness, safety, medical risks, and adverse effects of compounded bioidentical hormone treatments (BHT) have yet to be studied, effects may result in sterilization and death (Pinkerton, 2012).

The human behavior can be compared with organizational behaviors in relations to competing for resources whereby the environment selects the best resources for survival (Dobbin

& Schoonhoven, 2010). Considering cultural difference, Western cultures consider a more independent, narrow, and analytical view, as the Asian culture considers a more holistic and broader view of the environment (Maddux & Yuki, 2006). Research has reported when analyzing the environment, the subconscious mind is inflexible, however, is where learning takes place; whereas, the conscious mind is more adaptable to situations (Loftus & Klinger, 1992). The transformation of the subconscious to become more flexible to acquire additional learning, thus, is warranted to form organizational or cultural behaviors whereby all stakeholders can consider multifaceted views (Maddux & Yuki, 2006).

Skinner (1985) implied that the concept of behaviorism differs from the more embraced contemporary concept of cognitive science, which considers stimuli that derive from within the stored systems of the organism, which in turns drives human behaviors. Cognitive science is mostly understood in accordance with assessing the dynamics of information transfer associated with neuroscience, brain science, and computer science (Skinner, 1985). Computer science involves studying how technologies may be used to assess how the brain encodes and retrieves information, the menstrual blood flows, and the immune system or compounds in nutrients attack pathogens (Gallagher & Chakavarti, 2008; Goncharenko et al., 2013; Norheim et al., 2012; Protopopescu et al., 2008; Subhankar et al., 2011; Thompson-Schill, 2003).

This research may further revitalize the concept of behaviorism because external stimuli and environmental factors have been found to contribute to hormonal imbalances that influence behaviors and the selection and consumption of natural remedies to approach hormonal imbalances (Berg, 2003; Dobbin & Schoonhoven, 2010; Fehr & Rangel, 2011; Maki et al., 2002; Setorglo et al., 2012). If this research can further validate that perimenopause is a unique condition impacting women between the ages of 20-40 by accessing their learning capabilities

before and after the consumption of natural remedies, then behaviorism may be revitalized as an acceptable contemporary belief system ("American Society for Reproductive Medicine [ASRM]," 2008; Duda, Harris, & Wehbe, 2014; Jarvis & Morin, 2010; Shylaja et al., 2015; U.S. Food and Drug Administration [FDA], 2015). Societies, as well as academic societies, may then form cultures that embrace the consumption of natural remedies as a norm when subconscious minds prime that natural remedies provide a more positive reaction in the healing processes than conventional medications as a result of experimentations vice classroom instructions (Hell, Gigerenzer, Gauggel, Mall, & Müller, 1998; Mann et al., 2004; PhRMA, 2007; Richerson & Henrich, 2012; Stolper et al., 2010).

Definition of Terms

Behaviourism. Knowledge derived from experiences or hearsay (Zeckhauser, 1986).

Cognition. "The mental processes that are involved in acquiring knowledge and to the integration of these processes into the conscious aspect of emotions, which influences mood and has psychiatric manifestations" (Gómez-Pinilla, 2008, p. 2).

Context. "A theory of the world which encodes an individual's perspective about it" (Bouquet & Warglien, 1999, p. 2; Smith & Mizumori, 2006).

Hormones. Molecules that regulate the cells' chemical processes (Ballentine, 1978).

Human choice behavior. "A mental process that transforms perceptions of several optional courses of action into a choice. It is considered to cover any kind of intuitive, automatic and impulsive choice behaviour as well as conscious-deliberate decision making" (Jan van de Kaa, 2010, p. 301).

Markets. Places where buying and selling commence between two parties (D. Lomulen, social media communication, May 18, 2014).

Neuroeconomics. Because the brain activities do not solely explain behaviors, this discipline based on the integration of economics, psychology, and neurosciences approaches or neurobiological and social approaches to show how the brain produces decisions (Fehr & Rangel, 2011; Klucharev, 2014).

Oxidative stress. "An imbalance between reactive oxygen species (ROS) production and the efficient scavenging of these species by cellular defensive mechanisms, which include both enzymatic scavengers . . . and low-molecular-weight reductants (e.g., vitamin E, glutathione, and ascorbate;" Taha & Blaise, 2014, p. 510).

Preferences. A stable and coherent description of choice determined by calculated absolute levels/characteristics of outcomes/situations/present according to economists, which makes preferences observationally equivalent to a choice; wants and needs of agents (human, market, firm) according to psychologists, which are independent of the choices the preference described, deriving from references (i.e., aspiration level or externalities; heuristic, which is copying what others want or did for one's future/copying what one did from the past) or changes in outcomes based on one's reference level (Bossaerts & Murawski, 2015; Gigerenzer, 2001; Library Economic Liberty, 2012; Rabin, 1998).

Rationalism. Knowledge derived from reason (Zeckhauser, 1986).

Villages. "In Indonesia, we do have areas where they are underdeveloped in terms of economic growth, living standards, and education, but only very rarely with huts. In rural areas, you will still see people living in bamboo walled houses, with very minimum furniture and lifestyle, usually elder farmers. In Java, that is not that many. Indonesia has many islands, the main one is Java. I think in other islands, they are generally less developed in Java" (R. Pramadita, social media communication, May 12, 2014). "They are in the outer parts of the

country Zimbabwe, middle of bushes, huts; they keep livestock and do vegetation for survival-that's if the rains are there too, without rains it's a big problem for the community" (L. Moyo, social media communication, November 8, 2015). "In Kenya, many households (bomas) made a village. Due to land fragmentation and partly due to 'development' it's hard to find demarcated villages in existence" (L. Isuyi, social media communication, November 11, 2015).

Scope and Research Questions

This novel mixed methods clinical trial involves identifying natural remedies or interventions to approach symptoms associated with perimenopause that negatively influence the ability of the brain activities to acquire and transmit knowledge during the perimenopausal phase by using qualitative and descriptive quantitative designs (Cameron, 2009). This clinical trial is novel in the sense that the application model is uniquely designed based on multiple-faceted research approaches used to identify diverse and of perimenopause symptoms and the perceived magnitude on how the symptoms impact the ACT*ION of knowledge. Perimenopause symptoms can be associated with or signifies other conditions or diseases, however, comparative interventions were not identified as approaches to the other conditions, but to solely approach perimenopause or symptoms associated with perimenopause (McCormick, 2013; Rice, 2013).

Throughout the research, the word, "natural remedies" will be used to collectively to refer to plant foods, vitamins, nutraceuticals, amino acids, enzymes, minerals, herbs, and homeopathic formulas (Ballentine, 1978; Hoffman, 2007). The Dietary Supplement Health and Education Act (DSHEA) passed by the U.S. Congress in 1994 also defined what constitutes a natural remedy (AACE Nutrition Guidelines Task Force, 2003; Krasny, 2004; National Institute of Health [NIH], 2015). "Nutraceuticals are dietary supplements that contain a concentrated form of a presumed bioactive substance originally derived from a food," such as concentrated

omega-3 fatty acid; whereas, crude drugs are the actual raw materials/roots used to make various herbal formulas (AACE Nutrition Guidelines Task Force, 2003, p. 423; Jearasakulpol, Tipduangia, Teekachunhatean, Chiranthanut, Chansakaow, 2015).

This mixed methods clinical trial required the privacy and security of perimenopausal women between the ages of 20-40 who are transitioning from the reproductive to the non-reproductive years (ASRM, 2008; Duda et al., 2014; Jarvis & Morin, 2010; Shylaja et al., 2015; U.S. FDA, 2015). Perimenopausal women could have been categorized as women who had at least one cycle in the prior year with a FSH between 11 and 45 IU/liter; however, the study was limited in obtaining FSH levels (Berent-Spillson et al., 2012). Premenopausal or early menopausal women who may be classified as women between the ages of 41-50 or who has regular menstrual cycles and FSH < 11 IU/liter and postmenopausal women who may be classified as having no menses because of their reproductive age and a FSH > 40 IU/liter were not be solicited for this trial (Berent-Spillson et al., 2012; Shylaja et al., 2015). The participants were solicited by electronically or verbally asking African American women. If the women meet the criteria, then the trial will commence as planned and in compliance with human subject protection principles.

The pathway of this virtual clinical trial involves multiple natural technology appraisals (MNTAs) aimed to assesses the effectiveness of a variety of natural technologies for one or more outcomes (Egger, Davey-Smith, & Altman, 2001; The University of Sheffield, 2016). The intuition of the PI with expert knowledge was not used in this trial to determine which intervention was used in the selection processes or be administered to the participants (Stolper et al., 2010). To improve the outcome, a participant-centered approach was used whereby the

female participants recorded their natural intervention selections and perspectives about the outcome of their preferences or choice (Siminoff, 2013).

Intervention (natural remedies) effectiveness was measured by positive change or satisfaction based on the beliefs about the effectiveness that the remedies had on their knowledge, learning, and interaction. The results of the trial, however, did not reveal the level of satisfaction of the participants (Rice, 2013). The expected and anticipated outcomes of the pathway were to improve self-knowledge about natural interventions and means to find natural interventions and to signify how natural interventions may enhance academic-related processes and interactions. "Clinical pathways define expected or anticipated outcomes of care and are used as a tool for process and outcome audits" (Cheah, 1998, p. 534).

The outcome data provided by the female participants was further used to answer the following central research questions and serve as a measure for future clinical trials whereby the specific clinical questions relate to the central research questions (Cheah, 1998; Ravindran & Shankar, 2015). Central research questions, which is based on a problem, were inquires guiding this trial (Leedy, 1997). Associated Sub questions are inquires based on factors associated with the primary problem. The following central research questions guided this clinical trial:

RQ_1. How do hormonal imbalances impact learning?

RQ_2. Which economic beliefs guide food selections to approach hormonal imbalances?

The care associated with the changes of perimenopausal women in response to conventional medicines has followed individual care whereby over-the-counter medications have dominated; whereas, with natural remedies or medicines, perimenopausal women most likely have not been aware the variety of choices to approach the condition or the symptoms associated with the condition (National Institute of Health and Care Excellence [NICE], 2016). To ensure

adherence to ethics and medical oaths, the PI continued to acquire learning throughout and will after the trial, ensured the benefits of the participants by checking on the participants throughout the trial, and encouraged the participants to continue to follow their self-management plan after the trial (Rancich, Pérez, Morales, Gelpi, 2005). Following the virtual clinical pathway, the perimenopausal women were advised to devise and follow a self-management pathway and discuss any changes to include reoccurrences or progressions, with a naturopathic practitioner (Thompson & Subar, 2013). After appraisals of the results of the trial, limitations and delimitations were recorded, conclusions were drawn, and recommendations were suggested to approach perimenopause or individual symptoms associated with perimenopause (Singh, 2013).

Summary

Chapter 1 introduced the nature of a novel mixed methods clinical trial that may give insight into which economic beliefs guide natural remedy selections and consumptions to approach hormonal imbalances by using varies research designs (Cameron, 2009). The selection and consumption of natural remedies have been reported as essentials to approach any learning incapability stimulated by symptoms that are associated with perimenopause and heightened by external stimuli, sociocultural conditions, and lifestyle factors (McCormick, 2013; Parnell, 2007; Setorglo et al., 2012). Natural remedies include but are not limited to plant foods, vitamins, herbal formulas, such as Remifemin® and GEM™, and homeopathic formulas (Ballentine, 1978; Hoffman, 2007; Nelson-Porter, 2015a, p. 58). A conceptual framework emerged from both forms of data that focused on how the stressors associated with perimenopause impact the ACT*ION of knowledge when the natural ability of the body to regulate hormonal changes becomes imbalanced (Cameron, 2009; Setorglo et al., 2012).

Chapter 2: Literature-Based Discovery: Factors Impacting the Acquisition of Knowledge

The purpose of this novel mixed methods clinical trial was to identify selections of natural remedies and assess which remedies positively approach perimenopause symptoms that negatively impact the acquisition, comprehension, and transmission (ACT*ION) of knowledge in higher education setting by evaluating the effects of the selection processes and choices based on if improved memories or beliefs about the outcome are implicit ITIs or TIs about the influences of higher education processes, learning, and practices (Bøyum, 2013; Dougherty et al., 2008; Gigerenzer, 1997; Greendale et al., 2011; PhRMA, 2007; Wansink, 2010). "Peri-menopause includes the period beginning with the first clinical, biological and endocrinological features of the approaching menopause and ending twelve months after the last menstrual period" (Subhankar et al., 2011, p. 192). Many Ghanaian women, however, believe that perimenopause is a natural aging process and no remedies exist while others continue to debate if the condition is real (Batra et al., 2003; Setorglo et al., 2012). Age-related cognitive decline (ARCD) have been said to be individual and to some degree inevitable (Kidd, 1996).

The literature provides an overview of various medical conditions associated with perimenopause impact the ACT*ION of knowledge and natural remedies that stimulate brain activities to increase academic performance. The overview derives from qualitative and quantitative research methods, which aim to control biases (Cooke, Smith, & Booth, 2012; Kostoff, 2007; Ravindran & Shankar, 2015). One study found that during the cycle phases, the perception of performing poorly and not the actual performance on concept formation becomes influenced (Sommer, 1992). Natural remedies that include foods, vitamins, and herbs, however, have been found to alleviate perimenopause symptoms enhancing the brain activities that stimulate learning (Collin et al., 2007; Gómez-Pinilla, 2008; Wentz & Magavi, 2009).

Learning (performance) tends to increase when knowledge is acquired from a diverse population, and capabilities tend to increase when knowledge becomes assessable (Hagel, 2011). Knowledge has been categorized as either mythos or logos; however, each has some element present of the other (Kakabadse, Kouzmin, & Kakabadse, 2001; Tahko, 2011). Mythos (e.g., implicit/intuitive/tacit knowledge) involve information about and interpretations of personal goals/abilities and are not readily visible or communicable; whereas, logos involve specific (e.g., explicit/formalized/written/coded) knowledge based on scripts (e.g., reason, curriculums) to achieve an expected sequential flow (Kakabadse et al., 2001). A priori knowledge precedes experience and experiential knowledge derived from non-perceptual information/deductions of perceptual information; a posteriori knowledge is nonempirical and empirical knowledge that derive from the actual perceptual information (Tahko, 2011).

Procedural (e.g., implicit/habitual/non-declarative) knowledge is the intact or repertoire of mental procedures and processes of the mind used to select, order, and manipulate information to derive at a decision (Kakabadse et al., 2001). Intact procedural memory derived from enhanced instructions or augmented feedback information during the learning processes (Oudman, Van der Stigchel, Wester, Kessels, & Postm, 2011). Factual (e.g., declarative/a posteriori) knowledge metaphorically can be related to knowledge stored in a database (e.g., the mind) that may be expressed easily as a result of experiences (explicit) or studying the meaning of concepts and facts (semantic) to include the definitions and descriptions, word/phrase associations, sentence completion, and perceptional information (Kakabadse et al., 2001; Nessler, n.d.; Thompson-Schill, 2003). This research, thus, may show that when learners acquire knowledge about effects of natural remedies on perimenopause symptoms that impact learning, economic (capability/learning) leverage increases when inferences are made about formalized

knowledge that is available and shared across domains, and capability leverage increases when inferences are made to formalized knowledge applied to the self and the general population and thus increase learning leverage and performances, in either professional or academic structures or domains (Hagel, 2011; Tan et al., 2015).

Economic Sociocultural Conditions Impacting Learning Processes

Social issues continue to impact the ACT*ION of knowledge. Social issues experienced by Africans are accompanied by economic and cultural issues and may be compared with issues experienced in other developing nations. For example, "Thirteen percent of adult women in Bolivia cannot read and write" (Global Campaign for Education [GCE], 2012, p. 5). The absence of women teachers are presented in these stats: women make up 33% of secondary school teachers in South and West Asia, fewer than 3 in 10 in sub-Saharan, and fewer than 1 in 10 in Ethiopia at the tertiary level (GCE, 2012).

A 26-year-old woman living in *Yemen*, a 3rd world country (M. Alsofy, social media communication, May 2, 2014) shared the following:

> In regards to the difficulties of taking courses online, the biggest issue is electricity . . . we have it only 6 to 10 hours a day. Rest of day is off. Yemen has been through many crises right after the revolution in 2011. Some group of bad people demanded things from the government, and when the government rejected, they just attack the electricity . . . the power station. Sometimes, the Ministry of Electricity acts like an idiot and just turn electricity off for no reason. We have our main and biggest university (Sanaa university), and since the revolution had started from the university and took place in all the streets near to it . . . they start to use the university as a military point, a battle ground. So teachers stopped coming to teach and students were not allowed to come to the university

> in order to be safe. In regard to adding photos on social media, girls in Yemen do not use their original pic in public. It is not allowed.

A male Doctoral candidate studying computer science in Mahrashtra, *India* (A. Ahmed Ali, social media communication, May 8, 2014) shared the following:

> Businessmen rent a building and take permissions to open a university. No staff and faculties. Just register students and come for exam. Any student of those universities paying fees gets a degree regardless of his exam. Most of the students belong to a high cast. After 1 or 2 years, some businessmen found their universities do not get good money, so they close.

The 27-year-old research assistant (RA) living in *Indonesia* (R. Pramadita, social media communication, May 12, 2014) shared the following:

> We do have mandatory education for 9 years, starting from elementary school until junior high school. I think only recently, since a few years ago, our senior high school main fees are free, a new program from the government. I think when I got into a University in 2006, I read or heard somewhere several times that in Indonesia, from 240 million population, only around 2% could go to higher education (university). Not so many people go to university. Reasons, well, it varies, mostly economic factor. Either they have to work so they do not have the time and money, or they simply do not have money.

Women continue to experience stress, such as economic, situational, and emotional stress (Prior, 2013). "Among low-income families, stressors may include living in overcrowded, substandard housing or unsafe neighborhoods; enduring community or domestic violence, separation or divorce, or the loss of family members; and experiencing financial strain, forced mobility, or material deprivation" (Jensen, 2009, Chapter 2, Theory and Research section).

Millions of minorities in the United States with low incomes most likely live in the estimated 6,500 food deserts (Dutko, Ver Ploeg, & Farrigan, 2012). Low income areas differ from food deserts in that residents of deserts have limited access to healthy and affordable foods (Dutko et al., 2012; Sullivan, 2014). Income inequality and racial segregation from wealthier neighborhoods have stimulated the growth of small food markets that consist of higher priced foods (Dutko et al., 2012). Individuals with low income are driven to purchase foods that are expensive, however, low in nutritional value (Freudenberg, Mcdonough, & Tsui, 2011).

Food and antihunger activists, who advocate against hunger and food insecurity and for food justice and distribution, partner with food chains and the community to expand the access to quality foods (Freudenberg et al., 2011). Food mirage emerge as a result of new retail developments that are often not utilized for regular food shopping by seasoned residents, minorities, and lower-class residents because of social class, which embodies being less educated or having a feeling of being unwelcomed (Sullivan, 2014). Time and cost of the trip and the attractiveness of each shopping designation are factors considered when choosing an alternative destination (McFadden, 1973). Increased usability of new developments may arise as a result of promoting healthy living (Sullivan, 2014).

Sociocultural conditions that influence the natural ability of the body to regulate estrogen heighten hot flashes as well as other premenstrual and perimenopause symptoms (Prior, 2013, p. 19; Setorglo et al., 2012; Zhao, 2015). Psychosocial stressors play a role in the risk of having psychiatric disorders (e.g., depression; image/eating disorder), which are heightened in persons with brain injuries or women over 40 experiencing menstrual changes, such as amenorrhea or irregularities (Cancelliere, 2011; Mangweth-Matzek et al., 2013). While advocating for societal justices, we thus have to consider, “feminist arguments that blame eating disorders on the

expectation that women will be able to manage both careers and their domestic responsibilities are found to ignore African American married women's history of labor force participation" (Avakian & Haber, 2005, pp. 20-21).

Although left-handedness have been said to deal with pain and distress better, academic-related suppression, which also include suppression in writing, eating and drinking, leads to reduced social interactions and problems, depression, confusion, personality damage, and so forth (Masud & Ajmal, 2012). Left-handedness in many cultures impacts learning. In Nigeria, teachers more often than others have encouraged learners to suppress using the left hand. Learners who primarily use their left hand may be considered evil (Masud & Ajmal, 2012).

Many young girls between the ages of 4 and 12 or prior to marriage in Africa experience female genital mutilation/cutting (FGM/C), which stems as a result of social power and results in infections, cysts, hemorrhage, "infertility, incontinence, painful sexual intercourses, obstructed labour, and psychological trauma" (Manuh, 1998, Health section, para. 4; Population Reference Bureau, 2008; Ukoha, 2015). Many African women under 20 also experience fistula, the obstruction of labor when the access to obtaining a Caesarean section (C-Section) is absent, have been abandon by their community to include the healthcare workforce (United Nations Population Fund [UNPF] and EngenderHealth, 2003). "Obstruction can occur due to malnutrition and pregnancy at a young age (which both lead to small pelvis width, and thus pronounced cephalo-pelvic disproportion)" (UNPF and EngenderHealth, 2003, p. 4). The obstetric fistulas are unable to remain dry, because the fistuals between the vagina and urine cause excess urine leakage and bowel movements (UNPF and EngenderHealth, 2003).

In other region, lots of young women who live in sub Saharan Africa are unable to afford sanitary care or facilities at educational institutions. "In research conducted in Uganda, 61% of

girls reported staying away from school during menstruation" (GCE, 2012, p. 7). In poor living condition, young women may have to substitute pads for rags, newspaper, or bark (Taylor, 2011). During the menstrual cycle, many "women and girls in Africa use anything from rags, tree leaves, old clothes, toilet paper, newspapers, cotton wool, cloths or literally anything that can do the job. Most girls from poor, rural communities do not use anything at all" (Biriwasha, 2008, para. 2). In Demark, women use Libresse and Always (Bind). Many African women reside in Copenhagen, Denmark and speak Danish (L. F. Larsen, social media communication, January 13, 2016). In the United States, Always, up & up, fresh times, Kotex®, and Family Wellness are familiar trademarked sanitary napkins. Always seems more absorbent although expensive. The Family Wellness and fresh times brands are very absorbent and cost effective.

After showing an image link of what sanitary pads were on social media, the 26-year-old woman living in Yemen (M. Alsofy, social media communication, May 2, 2014), shared, pads made by Sofy are used by girls and women. "But still in some villages, women believe pads because some kind of health issues, so the just use piece of cotton instead." The 27-year-old RA (R. Pramadita, social media communication, May 12, 2014) shared the following:

> Here in *Indonesia* it's all pads. Popular brands are Charm, Laurier, and Kotex. We do not recognize tampons yet. Well, some people theorize it's because the concept of virginity is still very much relevant here. People think that using tampons would damage the hymen. To be honest, I think most people in Indonesia do not even know what a tampon look like or what it is.

Quality education and healthcare are needed in many regions of Africa because many women need knowledge beyond and skills beside sex work to earn an income. The lack of knowledge about and access to various resources by African women disappeared as a result of

colonialism and external religions giving decision-making power to men who changed the economic structures and social relationships throughout the nation in the 1970s and 1980s (Manuh, 1998). Since the 1980s, many countries in Africa lack significant imports because their exports (mainly coffee, cocoa, and spices) are not drawing ample financial means to pay the import bills (Rakotoarisoa, Iafrate, & Paschali, 2012). During the 50s, many women in rural or urban Africa who belonged to women-only mutual-aid societies and market groups had leverage to negotiate with men. Female human investments had great knowledge about herbs and healing powers and access to many resources to include food sources (Manuh, 1998; Sharad et al., 2011). The reconstruction of Africa to sustain economic growth depends upon developing or participating in stronger higher education systems and applying the knowledge learned within African nations instead of in countries external of Africa, known as brain drain (UNESCO Institute of Statistics, 2012). The ACT*ION of knowledge may involve developing curriculums about environmental stressors (i.e., associated with import and export trade taxes and policies, soil fertility, animal disease [pathogens] and control, and the lack of assess to nutrients found in cereals and livestock products) influence on biological stressors (e.g., the decline of cells, neutrons, and gonadal hormones stimulating perimenopause symptoms; Deecher & Dorries, 2007; Rakotoarisoa et al., 2012).

Brain Association with Cognition and Learning

The brain, which consists of four lobes, include the hippocampus and the hypothalamus, which stimulate or influence metabolic regulation and cognition; whereby the former has been reported to associated with stimulating the external memory that may be used to draw TIs (Frank et al., 2006; Gómez-Pinilla, 2008). The hippocampal neural activity/responses during episodic memory (experiences of events; autobiographical memory) retrieval may be influenced by sub-

processes as the interactions are not fully understood as “episodic memories involve a neural system that extends beyond hippocampus” (Reas et al., 2011; Smith & Mizumori, 2006, p. 12). Episodic memory involves event-relations, such as speech, audio, and visual-spatial associations (Crespo-Garcia, Cantero, Pomyalov, Boccaletti, & Atienza, 2010). Sub-processes include the strength of the memory and the extent of task engagement, mental searches, to which associated source details are recalled, the depth of processing, or post-retrieval monitoring, such as judgement (Reas et al., 2011).

The theory of mental models (TMM) explains the process of the underlying disjunctive reasoning tasks assuming that a unique space (mental blackboard, canvas, comprehensive picture, local mental models [LMM]) exists in which distinct mental models (states, thoughts, representations, individual choice selections, and potential solutions) are individually listed comprising of partially sets (contexts/vector) about a situation/group used to enable search to draw conclusions or validate decisions to solve a problem (Bouquet & Warglien, 1999; Gigerenzer, 2001; Toplak & Stanovich, 2002). Based on cognitive science and artificial intelligence theories, a contrasting reasoning theory of TMM, a unique space exists in which more structured domains, *sets* of initial LMMs or target contexts, are listed whereby other sets (input targets) can be added while enabling search to draw putative conclusions or validate decisions to solve a problem (Bouquet & Warglien, 1999). Targets are classified as imperative stimulus of which has to be responded to complete a task (Ameqrane, Pouget, Wattiez, Carpenter, & Missal, 2014). Targets are imperative stimulus of which has to respond to complete a task (Ameqrane, Pouget, Wattiez, Carpenter, & Missal, 2014). If input targets are in target contexts, then input targets and target contexts are not processed separately (Bouquet & Warglien, 1999; Iban˜ez & Manes, 2012).

Contextual processing (recall from continuously present background/foreground cues), contextual and cued fear conditioning, spatial place-based navigation (uses allocentric strategies/ locale-based navigation/object-to-object relation spatial memory [visual contextual temporal information] to directly see location on a map), and novel object recognition (NOR) memory conditioning, which are depended on the mutation of the protein histone, stimulate hippocampal learning (Frick, 2013; Oudman et al., 2011; Protopopescu et al., 2008; Smith & Mizumori, 2006). Context associated with background stimuli, "refers to a particular situation or set of circumstance that must be differentiated from other situations in order for subjects to retrieve the correct behavioral or mnemonic output" (Smith & Mizumori, 2006, p. 2). Context-specific neuronal responses that differentiate based on the episode (reward) and the location of the episode may provide information to prepare for different behavioral responses, which are experienced during spatial alternation tasks (Smith & Mizumori, 2006).

Research revealed when the explicit (episodic/specific knowledge understood and stored about the world) memory processes of the hippocampus is suppressed, other brain areas (Basal ganglia) become increased to include the increase of Basal ganglia learning (habitual learning/ procedural), which rely on the non-declarative memory consisting of various firing patterns to include motor control (Frank et al., 2006; Smith & Mizumori, 2006; Sukumar, Rengaswamy, & Chakravarthy, 2012). Episodic memories extend beyond the hippocampus because spatial information is included in the general context processing function of the hippocampus (Smith & Mizumori, 2006). The memorized or recorded patterns in the environment using mental or cognitive maps of surroundings are known as spatial memory or spatial place-based navigation (Smith & Mizumori, 2006; Sukumar et al., 2012).

Temporal information, which is an internal timing system, clock constructs, information space, and relations between points of times and intervals, used to predict, anticipate, or target a time to start, pause, or complete the movement prior to the occurrence of a predictable cue, are foundations to approaching tasks to complete temporal goals, to include expected time to prepare and consume foods and observe foods to consume to suppress appetite or to speak during a team presentation (Alonzo, Baeza-Yates, Strötgen, & Gertz, 2011; Ameqrane et al., 2014; Zelaznik, Spencer, & Ivry, 2002). Although neural phenomena are found throughout the brain network whereby predictions occurs about the past, present, and future, preparatory-set cells in the prefrontal or parietal cortex mainly contribute to temporal expectation, preparation, and anticipation to include imagining the future and remembering the past (Bubic, von Cramon, & Schubotz, 2010). Before a prediction of time, distance, or duration is made, time perceptions, which are depended on a scale, activity, rest, emotions, or pathologies, are estimated to include the appearance of the stimulus and the perception of elapsed time (Ameqrane et al., 2014).

Task performance is directly guided by explicit representation of time, whereby the estimation of temporal variables/expressions (i.e., time, distance, frequency, duration) is associated with intentional movement initiation. An example of temporal (relational) information that requires using explicit timing (capacity) to make an overt intentional precise decision or to qualify the facts about the temporal nature of the task includes, “We will eat dinner in 10 min or approximately 15 min” (Ameqrane et al., 2014; Beecham, Reeve, & Wilson, 2009; Zelaznik et al., 2002). Explicit duration estimation, which derives from using the right-sided fronto-striatal network, may be expressed as, “We should eat dinner for 30 min” (Ameqrane et al., 2014). *Explicit timing* and *implicit timing*, derived from different networks, are underlying timing processes involving controlling time, not task requirements (Zelaznik et al., 2002, p. 586).

Implicit representation of time, which includes timing of movement duration or when an expected event may occur based on the recall of prior motions, however, does not directly guide task performance (Ameqrane et al., 2014; Zelaznik et al., 2002). An example of implicit temporal information (regularities extracted from or judgements about the world/environment) used to time action precisely requires using implicit timing (the capacity) to qualify that influence on temporal variable of movement is, "We ate dinner last week at 7 pm and was late for class, so we need to eat dinner by 6 pm" (Ameqrane et al., 2014; Zelaznik et al., 2002). Implicit temporal expectations derive from using the left inferior parietal cortex whereby implicit duration (cue stored in memory) may be expressed as, "It took an hour to eat dinner last week, so we will eat dinner for 30 min" (Ameqrane et al., 2014).

The saccadic system, which consists of the same movement or motor response (a saccadic) in response to different contexts, may be viewed (a) in temporal domains/brain whereby explicit responses are internally-generated from the recall of the stored sensory information (episodic) in the neurons, and (b) in spatial domains whereby implicit responses are visually-guided by targets and cues from diverse knowledge domains to include academic discliplines, such as Natural Healthcare, Higher Education, and Law (Ameqrane et al., 2014; Beecham et al., 2009; Oudman et al., 2011; Suthan & Fried, 2012). In regards to higher visual attention processing and cognitive load, fixation number and fixation duration increase, which involve showing more or longer fixation on paired categorical/attribution cues (oatmeal/good), when the cues disconfirm negative implicit beliefs and attitudes (oatmean/bad; Mele, Federic, & Denni, 2014). Eye movements may result from lateralization (cognitive processes domination if cues presented in a fixed position--on the right or the left), most recognized or salience, or gaze biases (Mele et al., 2014).

Pertaining to mapping, upon completing task performances, the time, number, and pitch are putatively spatial (space) described using terms that reflect a relation, such as dimensions (narrow/wide), directions (front/back; up/down; before/after), or symmetries (right/left; Beecham et al., 2009; Genter, 2001). Time in terms of space expressed as an ego-moving metaphor (move towards the future/future in front) reads, "I am looking 'forward' to eating dinner", and as a time-moving metaphor (move towards the past/past in front) reads, "Dinner follows lunch" (Beecham et al., 2009; Genter, 2001). The effects of the visual or sound stimuli result in numbers, tones, emotions, or relationships described as being "low" or "high" (Beecham et al., 2009). The following individual examples of Space (base) →Time (target) mapping reflect system mapping; however, when the effects are compared to determine similar spatial processes, the combined mapping technique reflects domain mapping, whereby two stimuli derive from different domains (Beecham et al., 2009; Genter, 2001).

The effects that reflect a faster response for "compatible" conditions are expressed in two knowledge domains--numbers and pitch (Beecham et al., 2009; Taft, Castles, Davis, Lazendic, & Nguyen-Hoan, 2008). Responses to number magnitude (explicit condition) judgement and responses to parity (implicit condition) judgements were the means to measure RTs for symmetric temporal sequences/learning. The button keys, near to ("lower") or further from ("upper") the body, were pressed when the tone was heard: The correct response to high number was when the right button was pressed, and the correct response to low number was when the left button was pressed. The RT of the explicit tasks is influenced by the judgement of the sound magnitude of the verbally spoken number words; and the RT of the implicit tasks is influenced by judgement of odd and even parities (Beecham et al., 2009; Taft et al., 2008).

Responses to pitch height (explicit condition) of the tone and responses to different timbre instruments (implicit condition) programmed to sound like a different instrument were the means to measure RTs (Beecham et al., 2009). The button keys, near to ("lower") or further from ("upper") the body, were pressed when the tone was heard: The correct response to high pitch was when the upper button was pressed, and the correct response to low pitch was when the lower button was pressed. The RT of the explicit tasks is influenced by the judgement of the pitch of the tone; and the RT of the implicit tasks is influenced by judgement of the timbre (Beecham et al., 2009; Taft et al., 2008). Based on domain mapping, the number and pitch experiments did not share similar spatial representation possibly because the cues did not map into the position of the response button keys (Beecham et al., 2009).

Cue competition whereby alternative cues compete for recognition are expressed in the blocking and high lighting of learning, which are evident in effecting functional and category learnings whereby selective attention might be considered (Kruschke, 2001). Blocking of learning involves two or more cues (fruit/vegetables) that predict the same outcome (influence cognitive functions); however, some of the predictive cues (e.g., vegetables, such as white potatoes) will not be associated with the outcome because the primary focus is on the stronger predictive cues (fruit/vegetables, such as butternut squash) that were first learned (Gómez-Pinilla, 2008; Kruschke, 2001; Prior, 2008). The shift from the white potatoes to the butternut squash, thus, demonstrates blocking cues supercede the blocked cued (Kruschke, 2001). When the control cue dominant the blocked cue, a positive association exist; however, when neither the control cue nor blocking cue dominate the other, a negative association exist (Kruschke, 2001).

Highlighting of learning (i.e., inverse base rate effect) involves rapid shifts of attention during learning (Kruschke, 2001). An example of highlighting include: (a) a pair of cues (fork-

>oatmeal) used to predict an estimated outcome (eating breakfast), such as a fork (imperfect predictor based on past experiences) can be used to eat oatmeal (perfect predictor), (b) followed by the introduction of another pair of cues (fork->baked chicken) to predict an outcome (eating lunch) whereby the baked chicken is the perfect preditor (Kruschke, 2001; Pástor & Stambaugh, 2009). A stronger association emerged from the consuming the baked chicken than the oatmeal because the association was tested with both pairs (meals); a stronger association emerged from the fork used with oatmeal than baked chicken because the breakfast association was tested alone (Kruschke, 2001). A positive association exists when responses to conflicting cues (oatmeal and baked chicken) show a preference for the later learned outcome (having lunch w/the fork); and a negative association exists when responses to only imperfect cue (fork) show a clear preference for the early learned outcome (having breakfast w/ the fork; Kruschke, 2001). The results confirmed a function appropriate to baked chicken has a stronger relationship/peak during the shift than the function appropriate to oatmeal; in regards to cue completion, selecting both cues and averaging their implied responses have not shown a strong inclination (Kruschke, 2001).

Functional-learning tasks are performed based on the continuous cues/information provided about metric values, magnitudes, and averaging, such as distance or the amount of consumptions (Kruschke, 2001). Spatial memory for coordinate object-to-location binding occurring in the right hemisphere of the brain involves using fine-grained, metric information (contextual information) from the world/environment to remember the position of the object and to make precise movement and for categorical (relative) object-to-location binding occurring in the left hemisphere of the brain involves using directional (above/below) and symmetric (right/left) relations/viewpoints independent object recognition (contextual information) from the world/environment to remember the position and make precise movements (Bullens & Postma,

2008; Oudman et al., 2011; van Asselen, Kessels, Kappelle, & Postma, 2008). Spatial memory, thus, has relations between objects/locations or features within objects/locations (Bullens & Postma, 2008; Oudman et al., 2011).

Category-learning tasks, which are performed based on nominal cues about labels (without size/order) or categorical values, such as the group of which naturals belong (fruit, vegetable, meats), are as follows (Ashby & Maddox, 2005, Abstract section; Kruschke, 2001; Linck, Osthus, Koeth, & Bunting, 2013):

- Success in rule-based (explicit reasoning) tasks depends on frontal-striatal circuits and requires WM and executive attention.
- Success in information-integration tasks requires a form of procedural learning and is sensitive to the nature and timing of feedback.
- Prototype distortion tasks induce perceptual (visual cortical) learning.
- A variety of different strategies can lead to success in the weather prediction task.

The relocation phase of conditioning is the time and process of repeating what was observed (van Asselen et al., 2008). Object recognition condition relocation phase involves placing the breakfast foods consumed during breakfast time from the stove containing of all meal foods on the table but not in a particular location (van Asselen et al., 2008). The visuo-spatial construction condition involves viewing two breakfast tables, one filled with a variety of breakfast foods and the other one empty, whereby the empty table must copy the filled table; or viewing one stove and one table, whereby the stove setting is copied to the table setting (van Asselen et al., 2008).

The categorical positions-only condition involves placing the same breakfast food (oatmeal) from the sectioned stove on the sectioned table in the right setting locations previously

displayed (van Asselen et al., 2008). The coordinate positions-only condition involves placing the same breakfast food (oatmeal) consumed during breakfast time from the unsectioned stove on the unsectioned table in the right setting locations previously displayed (van Asselen et al., 2008). The categorical object-to-position condition involves placing breakfast foods on marked sections of the table whereby the foods were previously displayed (van Asselen et al., 2008). The coordinate object-to-position condition involves placing breakfast foods on unmarked sections of the table whereby the foods were previously displayed (van Asselen et al., 2008).

When two control cues mutually overshadow each other, associative learning takes place (Kruschke, 2001). Ivan Pavlov believed associative learning emerges knowledge and used conditional responses (CRs) to study the brain functions and not to analyze all behaviors; U.S. psychologists welcomed this notion, however, posited that innate reflex behaviors (unconditional responses; UCRs) are evoked by UCSs emerging similar power to evoke reactions as the UCRs or acquiring a set of CSs that account for all our behaviors and experiences when new stimuli are paired UCS as a result of experiences (Malone, 1990). Neurobiologists aimed to acquire an understanding of (a) the plausibility of learning mechanisms to include how memory of temporal information (time) as conditional stimuli (CS) and unconditional stimuli (UCS) interval can be encoded in a signal case whereby memory is updated rapidly when the UCS change; (b) how information about a specific timeframe is stored by the nervous system; and (c) “how does the knowledge about the time affect the expression of behaviors” (Gallistel & Balsam, 2014, p. 137). Three temporal classes of memory used to determine the relationship between points in time or two intervals include immediate memory (few seconds), short-term memory (seconds to minutes), and long-term (permanent) memory (Malone, 1990; Purves et al., 2001).

Conditional learning may be expressed differently when intervals between the CS and US are increased (Gallistel & Balsam, 2014). Expression of learning (behaviors) changes as a result of formed relationships (manipulations) autoshaping [conditional response (looking at light/tasting of food) derived from delayed pairing of a UCS (cue/flash light on cue [object], food) with a CS (e.g., another cue/sight and smell of food/foreground cues)] whereby the time (seconds or minutes later) associated with the UCS or CS is extended for a longer interval, trace conditioning (CR derived from pairing an UCS with a CS whereby 10-15 min gaps are introduced between the UCS and the CS), and temporal pairing or simultaneous conditioning (CR does not emerge from paring the CS at the same time as or seconds before the onset of the UCS as a result of the biological clock being the interval not the US (Gallistel & Balsam, 2014; Malone, 1990). Trace conditioning hypothesis is referred to "the expectation concerning the duration of an upcoming foreperiod builds up from the memory of the duration of the foreperiod experienced just before. . . . [The foreperiod is referred to the delay between the warning cue (ready signal) and the imperative stimulus" (Ameqrane et al., 2014, p. 1). The estimation of probabilities about the event occurence (hazard rate) may progressively rise and override the influence of the memory trace when delays expire and targets become absent, thus, providing external validity that when areas of the hippocampus become suppressed, others become increased (Ameqrane et al., 2014; Frank et al., 2006).

Changes may take place in the spatial memory; however, changes may not take place in the background environment (Smith & Mizumori, 2006). In structure-function relationships, when systematic structures change, the functions of the structures change (Chen, 1998). When the main temporal parameter is changed, most time cells "re-time", and when the salient spatial cue or stimuli is changed, most place cells "remap" (MacDonald, Lepage, Eden, & Eichenbaum,

2012, Abstract section). The empty temporal gap or temporal order information, which are moments (discontiguous event) between key events exist, along with location and ongoing behaviors are encoded by "time cells" forming the robust hippocampal representation of sequence memories (MacDonald et al., 2012). Re-time, which involves forming qualitatively different representations when the firing rate is changed or activities are ceased, and remap, which result from firing patterns called place fields of the hippocampal neurons, are fundamental mechanisms resulting from the network parsing spatio-temporal context into a given unit (MacDonald et al., 2012; Smith & Mizumori, 2006).

Changes in the behavioral and mnemonic task demands and environmental stimuli, such as appearance and odor of foods, may stimulate changes in the spatial firing patterns (Smith & Mizumori, 2006). When the temporal lobe, positioned at the lower part of the brain, which stores the hippocampus and controls smelling (oifactory), becomes damaged, the object-location memory, semantic memory (recognition/identification), hearing, language, and retention of information may become impaired, and emotions (i.e., the limbic system), may become difficult to control, such as anger (Cancelliere, 2011; Cohen & Rein, 1992; McCormick, 2013; van Asselen et al., 2008). Premenstrual women with a marked decrease in cerebral blood flow in the temporal regions during the luteal period may experience elevated risk of cognitive decline associated with verbal, articulator, and fine motor tasks (Batra et al., 2003, p. 50; Edman, Edenbrandt, Fredén-Lindqvist, Nilsson, & Wallin, 2011; Maki et al., 2002; Protopopescu et al., 2008). When the corpus callosum, which connects the two halves of the physical brain, becomes damaged, expressing and establishing relationships and emotions may become difficult (Cancelliere, 2011).

"An item in working memory [non-memory task performance] can suppress hippocampal activity" (Reas et al., 2011). In regards to the different neurosystem and the influence on spatial memory, the conscious awareness (explicit) spatial memory operations involve general search efficiency related to WM, known as spatial WM where spatial information is stored for a short period of time (Oudman et al., 2011; Purves et al., 2001). "A special sort of (procedural) short-term memory is called working memory, which refers to the ability to hold information in mind long enough to carry out sequential actions" or manipulate the information in the face of distracting information (Greendale et al., 2011; Linck et al., 2014; Purves et al., 2001, Chapter 31). Unlike the storage-based slave system, the executive attentional system is linked to long-term memory (Linck et al., 2014). Implicit spatial memory, which results from repeated presentation or enhanced instructions (cues) that also derive procedural memory, is measured by implicit contextual learning, which is related to general search times on new items and not related to WM or the association between perception and motor responses or verbal material (Oudman et al., 2011).

When the motor (movement) and somatosensory systems located in the parietal lobe, which is positioned at top of the brain, becomes injured, the integration, processing, and analysis of sensory information (figures), constructive abilities (e.g., spatial organization/drawing), and expressions of ideas though language become affected (Cohen & Rein, 1992). Input on relations between objects sent to the frontal lobe from the parietal lobe maybe delayed impacting motor planning and eventually movement in the prefrontal cortex (Cohen & Rein, 1992). However, when the holonomic brain becomes injured, the brain and encoded memory from the flux do not become altered (AbZu, 2015). The quantum-informational holographic model of brain-conscious-universe interactions posit that the brain and universe, known as holonomic

information systems, are interconnected by a self-organizing nonlocal flux/waves of the universe (and not axons) that encode the memory (from spatial patterns) where the holonomic holographic neuron information is stored and is featured in each part of the universe (waves) as a whole, not as a representation, demonstrating that information is/can be transmitted faster than the speed of light (Di Biase, 2009).

> The hippocampal formation can encode relative spatial location [to form a spatial map of the surrounding], without reference to external cues [but to internal sensory proprioceptive information], by the integration of linear and angular self-motion (path integration) . . . In path integration, the information to be maintained and updated is not a set of discrete items (as are found in Hopfield-type attractor networks for discrete memories); rather, it is a continuous variable representing position or head direction. (McNaughton et al., 2006, pp. 663, 665; Sukumar et al., 2012)

Competition exists between the navigational commands driven by the Basal ganglia and hippocampus (Sukumar et al., 2012). "Navigation is a combination of goal-directed movements and wandering, exploratory movement" (Sukumar et al., 2012, p. 2). In regards to the indirect pathway, functions of Basal ganglia include "action selection, working memory, motor preparation, goal-oriented behavior, and sequence generation" (Sukumar et al., 2012, p. 2). The Basal ganglia (caudate) is associated with naviations using response strategies, and the Basal ganglia (putamen) is associated with navigational ability based on habits or prior learnings (Protopopescu et al., 2008).

> The Basal ganglia as a whole are broadly responsible for sensorimotor coordination, including response selection and initiation . . . The caudate nucleus contributes to behaviour through the excitation of correct action schemas and the selection of

> appropriate sub-goals based on an evaluation of action-outcomes; both processes fundamental to successful goal-directed action. This is in contrast to the putamen, which appears to subserve cognitive functions more limited to stimulus-response [S-R], or habit, learning . . . adaptive behaviour towards significant goals can be identified (motivation; ventral striatum [implicit associative area]), planned (cognition; caudate) and implemented (sensorimotor coordination; putamen) effectively. (Frank et al., 2006; Grahn, Parkinson, & Owen, 2008, Abstract section; Protopopescu et al., 2008)

Basal ganglia or parietal cortex learning result from the recruitment and coding of cue-based spatial navigation (uses egocentric/taxon/response strategies/self-to-object relations [learned repetitious implicit contextual temporal information] to navigate to locations), S-R (habit), or praxic forms of navigation whereby decisions on when to turn the body are determined when stimuli, such as landmarks, are sensed (Ameqrane et al., 2014; Bøyum, 2013; Oudman et al., 2011; Protopopescu et al., 2008; Sukumar et al., 2012). The S-R type/praxic forms of navigation use stored internal sensory proprioceptive information initially derived from visible targets to perform stereotyped body movements; whereas, spatial place-based navigation uses hippocampcal temporal information for path-integration (Ameqrane et al., 2014; Sukumar et al., 2012). When explicit spatial contextual information (coordinate) is unknown, information is obtained from view-sensitive cells--visual cues or spatial contexts--of the hippocampal cells as frames of references (Oudman et al., 2011; Sukumar et al., 2012).

When the frontal lobe of the physical brain, which is positioned at the front of the brain (prefrontal cortex) and is involved with motor controls, becomes damaged, pre-conditioned learned actions, learning of conditioned-tasks, self-awareness, initiative, decision-making, planning, problem solving, and maintaining goal orientation for a long period become altered

(Cancelliere, 2011; Cohen & Rein, 1992; McCormick, 2013). Preconditioned eating behaviors are formed as a result of a signal stimulated when a particular level of taste or satiation that drive intake or control for intake, a psychic reflux or conditional response, is not encountered (Booth, 2008; Jönsson, Granfeldt, Erlanson-Albertsson, Ahrén, & Lindeberg, 2010; Malone, 1990). In a study, nontasters consumed more cruciferous vegetables, which contain glucosinolate, maybe because the bitterness could not be tasted (Campbell et al., 2012). To taste bitterness in the compound glucosinolates is associated with the inherited variation of the amino acid gene, haplotype (TAS2R38) whereby the taster or nontaster determines the presence or level of bitterness (Campbell et al., 2012). Haplotype genes produce compound antigens whereby the alleles of the genes encode the antigens (Westhoff, 2010).

Mann and LaDuke (2006) stated, "A body that is anxious makes anxiety-ridden decisions that are most often self- and mutually destructive. A body that eats for taste is not a sane, rational, or strong body" (p. 44). S. Balasekar (personal communication, January 20, 2014) stated, in India, dishes are made with:

> . . . rice, vegetables, fish. . . especially fish curry made in mud pots or stove will be real tasty. . . the pots are placed over the holes through which the woods are inserted to make fire. . . this is still followed in villages [of India]. . . now completely preparing with modern style with gas [in the cities], steel utensils, but without taste and health. . . use ginger [which is an ingredient in curry] for insomnia.

Learning, thus, is associated with the five traditional senses/conditional stimuli: taste, touch, visual, hearing, and smell (Malone, 1990). The nerve (lemniscal) systems that extend past the psychological classification consist of touch and light mechanical stimulation, which include pain, pressure, warmth, and cold (Nafe & Kenshalo, 1962; Sherrick, 1996). Combination cues

(visual/tactile) and congruent cues (visual and visual) may produce similar reliable explicit and implicit sequence learning; thus, adding tactile stimuli to verbal or visual stimuli most likely will not strengthen verbal, motor, or visional sequence learning or representations (Abrahamse, van der Lubbe, & Verwey, 2009).

When the occipital lobe, which is positioned at the rear of the brain and controls visual, is damaged, the comprehension of visual stimuli that was formulated becomes affected (Cohen & Rein, 1992). Food porn is used to test self-discipline or the reactions to the sight of foods and food preparation techniques, such as gazing and vicariously consumptions (Dejmanee, 2015). Because "eye movements can work in concert with belief systems that underlie implicit attitudes," social signals from external influencers, such as heuristics (beliefs about foods), may cause a change in decision-making to increase or decrease consumption (Booth, 2008; Gigerenzer, 2001; Library Economic Liberty, 2012; Mele et al., 2014; p. 5; Wansink, 2010).

Sensory signals, which include taste, sight, hearing, and smell drive visual-spatial, speech, audio, or environmental stimuli/sensations when sensory signals activate somatic sensations, which include hunger, thirst, fatigue, movement, and pressures (Crespo-Garcia et al., 2010; Sense, 2016). Somatic symptoms include feeling full during intakes; somatic premenstrual symptoms include mastalgia, bloating, body aches, fatigue, and headaches (Booth, 2008; Jarvis & Morin, 2010). Because somatic signals that rely on sensory signal are hidden, normally most experience difficulties describing somatic symptoms (Moss-Morris & Petrie, 2003). Named words to describe somatic symptoms include disease, sick, fatigue, infection, nausea, dizzy, and aches (Moss-Morris & Petrie, 2003). Interoception cues are pscychoeduction, exposure-based, occult-based, mindfulness-based, or emotion-focused interventions aimed to achieve awareness of somatic physical symptoms or how the body felts and to identify the emotions felt in relation

to the condition (MacDonald, 2007). Aristotle, however, believed that psychological and biological factors are psychosomatic, that is inseparable (Malone, 1990). When the physical brain becomes injured or damaged, then thinking skills, memory, attention, and cooperation become altered either simultaneously, instantaneously, or subsequently resulting in the deterioration of academic performance and behaviors (Cancelliere, 2011; Malone, 1990).

Research has shown that when the hippocampus becomes damaged, the mind can still make transitive judgements and inferences because the associative mechanisms (cues, stimuli, probabilistic information, learning tasks) are independently of the hippocampus although the mechanisms interact with the explicit memory processes that depend on the hippocampus; thus, "hippocampal disengagement allows the implicit system (intuition) to have full reign on behavior" (Frank et al., 2006, p. 1). Transitive (pairwise) judgement are validated conclusions based on particular expressible learning derived from two seemingly unrelated concepts (perimenopause and food selection stimuli/perimenopause and academic progress) connected by auxiliary concepts (effects of natural remedies); whereas, intransitive judgement cannot be validated because particular learning is inexpressible because what was learned is unknown (e.g., expressions) or no particular learning actually emerged because what was known was already known (Bøyum, 2013; Tan et al., 2015). Cues and contextual considerations influence pure judgements/decisions derived from skilled implicit intuitive patterns, imperfect judgements/ decisions derived from heuristic implicit intuitive patterns or evaluations of cues stored in memory, or relational judgements/decisions derived from remembered stimuli or explicit awareness or evaluations of cues or contexts binded with a particular selection, forming conjunctive items of which have been studied together (Frank et al., 2006; Kahneman & Klein, 2009). Parity judgements are made based on implicit conditions, such as the quality of sound

and voices to include phoneme; whereas, magnitude judgements are made based on explicit conditions, such as the pitch heights/intensitive of sound/voices, are expressed in numerical format reflecting a best guess (Beecham et al., 2009; Merkle & Steyvers, 2011).

Through perpetual or continuous learning, conscious and unconscious judgements can be made to demonstrate a certain level of knowledge (Workman, 2010). Judgements may not be credible based on unconscious incompetence or conscious incompetence (Workman, 2010). Unconscious incompetence involves knowledge never known or aware of, which cannot be considered intransitive in nature because intransitive judgement is based on learning that cannot expressed or do not add to the knowledge base (Bøyum, 2013; Workman, 2010). Conscious incompetence is gained when awareness is made about matters unknown resulting in high stress; whereas, conscious competence is gain when knowledge comprehension results in skillsets that can be used to complete tasks (Workman, 2010). The advancement to unconscious competence involves automatically performing tasks without conscious thought resulting in minimal stress (Workman, 2010).

Disorders Impacting Brain Functions Associated with Perimenopause

In the adult hippocampus, the number of adult neurogenesis (new neurons) comprising of axons that carry nerve impulses, which determine how human behave and is associated with learning, memory, or depression, tends to decrease with age, stress, and sleep deprivation (McCormick, 2013; Wentz & Magavi, 2009). "Estrogens, [however,] have been shown to have a stimulatory effect on prefrontal-hippocampal connectivity enhance hippocampal synaptic plasticity, and may interface with cholinergic and serotonergic transmission to influence working memory and verbal cognition" (Berent-Spillson et al., 2012, p. E1691). The increase in cognitions across the menstrual cycle is featured in Table 2 (Maki et al., 2002; Protopopescu et

al., 2008). Thus, if the "transient deficits in processing speed during late perimenopause were not associated with depression, sleep disturbance, or vasomotor symptoms," then the decline in the functions of the hippocampus and the adult neurogenesis may be more associated with chronological aging rather than reproductive aging (Berent-Spillson et al., 2012, p. E1691).

Table 2

Cognition Increase Across the Menstrual Cycle

Premenstrual or late-luteal/ Follicular or proliferative phase (Low estrogen)	Luteal or secretory/midcycle/ Postmenstrual late-follicular phase (High estrogen)
Spatial tasks/ability	Verbal tasks
Deductive/abstract reasoning tasks	Articulatory tasks
Mental rotations	Fine motor tasks

"Perimenopause is characterized by changes in ovarian hormones, feedback relationships and menstrual cycle length; it ends at menopause or 1 year after the final menstrual flow" (Loreti et al., 2009, p. 558). The gonadotropin hormones (GnRH), which do not cause or eliminate hot flashes, derive from endocrine (gonadotrope/gonadotropic) cells or neurosecretory cells that tend to signal from and control the release of the thyroid-stimulating hormones (TSH), follicle-stimulating hormones (FSH, a glycoprotein), and luteinizing hormones (LH) from the anterior pituitary gland in the brain whereby the former is where ovarian follicles are developed and the latter whereby the follicles secrete estrogen (E_2); thus, the GnRH may "affect the central nervous system functions, such as mood, anxiety and behavior" (Chrousos, Torpy, & Gold, 1998; Nussey & Whitehead, 2001, Neuroendocrine Interactions section, para. 1-2; Shanafelt, Barton, Adjei, & Loprinzi, 2002; Zhao, 2015; Zhao & Mu, 2011). The predominant proportion of the FSH charge isoforms whereby serum FSH is more diverse in premenopausal women are heavily sialylated

glycoforms (Loreti et al., 2009). The glycoforms of the FSH hormone, thus, differ in branch synthesis, degree of branching, and sialic acid content (Loreti et al., 2009).

Symptoms resulting from the fluctuation of estrogen may signify other health conditions, and symptoms associated with disorders have been found to be similar to perimenopause symptoms (McCormick, 2013). "Perimenopausal syndrome is defined as a series of symptoms occurring during menopausal transition that require adjustment to respond to the loss of ovarian function" (Wang, 2011a, p. 15). "Estradiol exerts a negative, although indirect, effect on the activity of the gonadotropin-releasing hormone neuron" (Chrousos et al., 1998, pp. 230-231). Women with endocrine disorders experience stress, anxiety, eating disorders, mood swings or disturbances, feelings, and vulnerability to autoimmune and inflammatory disease, which follow estradiol (E_2) fluctuations, when oestrogen directly stimulates the peptide corticotropin-releasing hormone (CRH) gene expressions and the central noradrenergic functions, of which the two systems regulate the hypothalamic-pituitary-adrenal (HPA) axis that controls stress and regulates the female reproductive system (Chrousos et al., 1998). The hypothalamus produces CRHs, the anterior pituitary produces adrenocorticotropic hormones (ACTHs), and the adrenal cortex produces the cortisols (Chrousos et al., 1998; Nussey & Whitehead, 2001). The stress system, comprised of the HPA axis, arousal, and autonomic nervous systems, activates the CRH-ACTH-cortisol axis (Chrousos et al., 1998; Nussey & Whitehead, 2001).

Anxiety disorders are related by two emotional systems, fear (anxious anticipation) and panic (separation and suffocation signals), and characterized by avoidance, dissociation, specific worries, and feeling (MacDonald, 2007). "Anxiety is a generalized response to an unknown threat or internal conflict; whereas, fear is focused on known external danger" (Steimer, 2002, Section 3, para. 3). Fear of fear itself is an experiential avoidance whereby "automatic, phobic

patterns of disattention to contemporaneous somatic feelings of anxiety" are developed (MacDonald, 2007, p. 60). When the thalamus is activated by external cues, information is relayed to the cortex and viscera then recirculated to the cortex to generate emotional states (Steimer, 2002). In some cases, anxiety symptoms are unconscious known (occult) resulting in a deficit of interoception (mindful awareness of somatic experience; MacDonald, 2007).

Disorders to include organic mental disorders and comorbid psychiatric disorders continue to impact the functions of the brain to include the reasoning processes (Ross, Medow, Rowe, & Stewart, 2013). Organic mental disorders include delirium (acute confusion), dementia (Alzheimer, neurodegenerative disorder), Axis I (schizophrenia), alcohol amnestic, multiple sclerosis (MS), and obsessive compulsive behaviors (OCB), which are repetitive behaviors linked to bipolar, depression, and anxiety (Batra et al., 2003; Nakate, 2011). In regards to cognitive impairment associated with a major depression disorder (MDD; unipolar, melancholia depression), age rather than gender has a more profound effect on cognitive performances (Monzón, Gili, Vives, Serrano, & Bauza, 2010). Although women experience depression more so than men, melancholia depression leads to lifestyle and biochemical changes, such as "anxiety about the adequacy of self, dread for the future prospects of such a deficient self, insomnia, anorexia, loss of libido, and other manifestations compatible with a hyperfunctional stress system" (Chrousos et al., 1998, p. 238).

Sleep deprivation, fatigue, prolonged standing, physical dehydration, and feeling faint have been found to trigger brain fog (Ross et al., 2013). "Disturbances in sleep involve difficulties in getting to sleep, staying asleep, and in quality of sleep" (Griffin, 1990, Chapter 205, para. 14). Diagnosed sleep disorders include insomnia, sleep apnea, and restless leg syndrome (Ross et al., 2013).

Chronic fatigue syndrome (CFS) is characterized as the body being weak from unknown origin whereby patients less likely believe the illness results from self behavior or is as serious as other conditions; thus, prompting more psychological distress (Moss-Morris & Petrie, 2003). Patients who experience prolonged lightheadedness and fatigue may be a candidate of postural tachycardia syndrome (POTS), a chronic form of orthostatic intolerance (OI), which stimulates excessive heart palpitations (Ross et al., 2013). When the body is in the upright position, orthostatic (low blood pressure) tends to decrease the calf blood flow (Stewart, Karman, Montgomery, & McLeod, 2005). For perimenopausal women, while not affecting the heart rate (HR), the leg fluid flow improves when plantar vibration is applied (Stewart et al., 2005).

Although stress result in disorders, stress can result in positive changes, which include mobilizing of adaptive behaviors, peripheral functions, such as the flow of blood, and inhibiting costly disturbances associated with the vegetative functions (Chrousos et al., 1998; Griffin, 1990). Vegetative functions, which are concerned with the maintenance of life, such as reproduction, feeding, and growth, encompass "nutritional, metabolic, and endocrine functions including eating, sleeping, menstruation, bowel function, bladder activity, and sexual performance" (Chrousos et al., 1998; Griffin, 1990, Definition section). In a study that investigated the relationship between anxiety status and dietary diversity, although a cause and effect was not determine, some women aged 20-49 who attended a health center and had a high diet diversity score experienced less anxiety (Poorrezaeian et al., 2015).

> Healthy diet was found to be inversely associated with anxiety, with unhealthy and western dietary patterns, known to increase the risk of anxiety. Higher scores of healthy diet (greater intake of fruits, vegetables, whole grains and low-fat meat) were found to be associated with better mental health and lower anxiety. On the other hand, higher intake

> of processed foods, sweets, beverage, red meat and its products were found to have a positive association with mental disorders. (Poorrezaeian et al., 2015, p. 625)

"Dietary deficiency of omega-3 fatty acids in humans has been associated with increased risk of several mental disorders, including attention-deficit disorder, dyslexia, dementia, depression, bipolar disorder and schizophrenia" (Gómez-Pinilla, 2008, p. 6; McCormick, 2013). In elderly patients, duloxetine (Cymbalta®) is often administered and have proven to enhance learning and memory (McIntyre, 2014). In a study whereby a 52-year-old woman who had a 16-year history of schizoaffective disorder, the researchers eluded that menopausal symptoms can impact the outcome of treatment, such as transcranial magnetic stimulation (rTMS), a non-invasive technique used to treat MDD (Kelly, Gill, Clarke, Burton, & Galletly, 2012). In another study, a 39-year old mother of two who experienced fuzzy thinking and poor memory who was diagnosed with MDD and not perimenopause, however, was given psychotherapy for 6 months instead of the common conventional antidepressants; however, continued to experience difficulties working (McIntyre, 2014).

Thirty to 76% of women diagnosed with premenstrual dysphoric disorder (PMDD) experience depression (Batra et al., 2003). Symptoms associated with premenstrual are categorized as somatic (unconsicious/hidden; CFS), affective (conscious emotions), behavioral (reactions to stimuli; appetite changes), and cognitive (mental processes, sleep disturbances) complaints (Jarvis & Morin, 2010; MacDonald, 2007; Moss-Morris & Petrie, 2003). During the luteal or secretory phase (Days 14-28), women experience high estrogen; however, during premenstrual or late-luteal phase (1-5 days prior to the onset of menses; Days 24-28), women may experience low estrogen; during the follicular or proliferative phase (Day 1 of the menstrual cycle to Day 14), women experience low serum of 17β-estradiol (E_2), and during the

postmenstrual late-follicular phase (Days 10-12 following onset of menses), women may experience high-estrogen (Maki et al., 2002; Protopopescu et al., 2008). Women with PMDD have to further consider their history, as many mothers of women diagnosed experienced PMDD (Batra et al., 2003).

> PMDD is a severe form of PMS whereby somatic and emotional disturbances lead to distress. Luteal Phase Dysphoric Disorder (LLPDD), which is associated with the premenstrual phase, involves emotional symptoms, such as irritability, mood swings, anxiety, and depression. Irrational Anger (IA) is . . . associated with a deficiency in Vitamin B_{12} that causes depression. Vitamin B_{12} is a supplement that has been linked to nourishing the nervous system. During transitional phases, vitamin depletion may derive form consuming over-the-counter or prescription medications [i.e., aspirin/diuretics (Spironolactone for bloating)], interacting with environmental factors, and not consuming foods containing essential nutrients. (Batra et al., 2003; Nelson-Porter, 2014a)

The somatic and emotional disturbances associated with PMDD derive from biochemical phenomena in the brains triggered by normal ovarian functions of susceptible women (Batra et al., 2003). Although hormone replacement therapies (HRT, oestradiol) are prescribed to prevent heart disease, which increases with the use oral contraceptive and smoking; surgical removal, the suppression of gonadal hormones, contraceptives, such as depot medroxyprogesterone acetate (DMPA), prometrium, selective serotonin reuptake inhibitors (SSRIs), and HRT are methods used to relieve PMS, PMDD, and perimenopause symptoms (Batra et al., 2003; Collin et al., 2007; Jarvis & Morin, 2010; Loreti et al., 2009; Wang, 2011a). Cardiovascular (heart, myocardial infarction), hypertension, and dyslipidaemia have been found to increase after the

menopausal phases whereby during the perimenopause phase, high cardiovascular risk factors leads to high cardiovascular risk profiles (Collin et al., 2007; Greendale et al., 2011).

Although HRT suppresses heightened FSH and HRT administered with drospirenone, a synthetic progestin, relieves perimenopause symptoms accompanied by hypertension, SSRIs, however, have been found to be ineffective in approaching brain fog, and little evidence shows that dietary habits relieve PMDD (Batra et al., 2003; Brown, Henneman, & Desai, 2013; Collin et al., 2007; Ross et al., 2013; Zhao, 2015). Estrogen promotes the growth and health of nerve cells and increases the level and density of neurotransmitters to regulate moods; thus, improving the network and transmission between the brain cells (McCormick, 2013). If research show that no hormonal imbalances is associated with PMS and PMDD, researchers may inquiry if the effectiveness of HRT is associated with perimenopause rather than PMDD symptoms (Jarvis & Morin, 2010). Thus, approaches to related symptoms of disorders and perimenopause could render different results; however, although the approaches (e.g., the intake of cruciferous vegetables) could render similar results, the results may be based which intracellular mechanisms of each approach interacts with the molecules, chemicals, and receptors in various parts of the body (Buettner-Janusch, 2009; Campbell et al., 2012; Knight & Eden, 1996; Lam & Lam, 2014; Lampe et al., 2000; Pall & Levine, 2015).

Genetic Functions Associated Hormones and Memories

This section of the research presents the foundation of which natural remedies may be an approach to perimenopause symptoms that result from ovarian activities that modulate proteins and the hippocampal dependent memory impacting the learning processes (Boffelli, Zajchowski, Yang, & Lawn, 1999; Frick, 2013). Nutrients and dietary and environmental chemicals have been found to influence how the brain and ovarian functions (McCormick, 2013; vom Saal,

1995; Zhao & Mu, 2011). "Dietary factors can affect multiple brain processes by regulating neurotransmitter pathways, synaptic transmission, membrane fluidity and signal-transduction pathways" (Gómez-Pinilla, 2008, p. 6). In one study, 9 elder adults who were given "blueberry juice scored higher on memory tests than those receiving a placebo" (U.S. Highbush Blueberry Council, 2011, p. 2). Cabbage, a brassica vegetable, and soy contain phosphatidylserine, a primary source to decrease the loss of brain functions (Kidd, 1996; WebMed, 2015). Herbs, such as rosemary leaves and Sage, and "fruits are rich in antioxidants that help in lowering incidence of degenerative diseases such as . . . brain dysfunction and acceleration of the ageing process" (Arshiya, 2013, p. 265; D'Archivio et al., 2007; Rouse, 1998).

Hormones/DNA/RNA. The classical transmission process is regulated by hormones in the body, which are classified as protein and peptides, steroids (containing Vitamin D), tyrosine, tryptophan (serotonin), or fatty acids (Nussey & Whitehead, 2001). Pregnenolone, a steroid hormonal transmitter, works "to clarify thinking, promote concertation, and prevent memory loss" (McCormick, 2013, p. 6). A single tyrosine molecule, secreted by the adrenal medulla, yields the norepinephrine, a hormone and neurotransmitter; whereby, two or more joined tyrosine molecules form the thyroid hormones, homeostasis, and metabolism (Nussey & Whitehead, 2001). Tyrosine is metabolized from phenylalanine by the enzyme, phenylalanine hydroxylase, and when the enzyme is absent, the genetic disorder, phenylketonuria (PKU) arise accumulating phenylalanine leading to mental retardation (Norheim et al., 2012). "Tryptophan is the precursor of serotonin (5-hydroxytryptamine) and melatonin synthesis" (Nussey & Whitehead, 2001, para. 7).

Based on molecular level research, most protein and peptide hormones are transcribed from a single gene through the glycoprotein hormone subunits derived from various genes when

the introns (non-coded) are excised from the RNA leaving the exons (coded protein) of which oftentimes amino acids are formed (Nirenberg, 1968; Nussey & Whitehead, 2001). Genes in the body instruct or govern cell activities to produce protein and molecules (Feinstein & Eden, 2008). We have to note, agents within cell stimulate communications within a cell and with neighboring cells (Nussey & Whitehead, 2001).

A serious of glycoprotein and glycolipids are the blood group antigens that are located on the surface of human red blood cells (Elmissbah, 2013). Antigens may be produced by multiple alleles found in each gene based on the Wiener concept or by a series of linked genes based on the Fisher-Race concept (Heiken & Rasmuson, 2009). Alleles, the alternate forms of genes following mutation, form the genotype and distinguish the phenotype (Aki et al., 2014; Elmissbah, 2013). In plants, when polyphenols and polysaccharides are of good quality and bind to RNA, the isolation of plant RNA to study the gene expression becomes difficult although plant MicroRNAs (miRNAs) can regulate targeted human genes (Norheim et al., 2012; Vasanthaiah, Katam, & Sheikh, 2008). MicroRNAs are small non-coding RNA molecules that help in the reduction of cholesterol removal from plasma after binding to messenger RNAs (mRNAs; Norheim et al., 2012).

Human genes, which are sequences of DNA, do not code directly, but code for RNA (mRNA) or polypeptide that synthesizes proteins (Siegfried, 2013). "The production of new DNA molecule(s) from two parental DNA molecules or different segments of the same DNA molecule" known as recombination serves to repair broken or gapped DNA (Hardison, 2005, Chapter 8, para. 1). General recombination results from the crossover of alleles on parallel homologous chromosomes (Hardison, 2005). Nonhomologous recombination result from the crossover of alleles from different chromosomes, however, similar genes. Site-specific

recombination result from integration of dissimilar parental DNA molecules. Replicative recombination results in copied DNA encoded by transposable specific enzymes (Hardison, 2005). "Poly (ADP-ribose) polymerase (PARP)-1, a member of the PARP family of proteins, has initially been described as a DNA repair enzyme playing primarily as a regulatory protein controlling traffic of DNA repair proteins during base excision repair" (Kim et al., 2015, p. 2).

Genes assembled in different ways encode the red blood cell enzymes, which are grouped in systems: "ABO, Rh, MNSs, Kell, Duffy, Kidd, Lewis, Lutheran P, Diego, Yt, xg, Ii, Dom Brock, and Colton systems" (Elmissbah, 2013, p. 1; Heiken & Rasmuson, 2009). The ABO blood group based on the polymerase chain reaction (PCR) amplification of specific alleles (PASA) consists of positive and negative haemoglobin or antigen categorized as A, B, AB, and O blood types (Aki et al., 2014; American Red Cross, 2015; Udomah et al., 2015). The six ABO genotype are A/A, A/O, B/B, B/O, O/O, and A/B (Aki et al., 2014, p. 49). The PASA "allows for the simple and rapid detection of multiple single nucleotide polymorphism (SNP) sites on the ABO gene" (Aki et al., 2014, p. 50). The ABO genotypes are detected using serological tests in laboratories or molecular biology techniques whereby DNA is initially extracted from the blood and saliva and purified and distinguished based on the molecular size of the amplification of specific alleles product containing certain nucleotides or "the pyrophosphate generated during PCR" (Aki et al., 2014, p. 50; Yaku, Yukimaasa, Nakano, Sugimoto, & Oka, 2008, p. 4130).

The Rhesus (Rh) blood group, which follows the ABO blood group, consists of the main genes, RHD and RHCE, that carry the principal antigens: D, C, c, E, and e based on the Fisher-Race concept; whereby alleles of C produces c and alleles of E procedures e (Heiken & Rasmuson, 2009; Westhoff, 2010). "The Rh proteins exist in the red cell membrane as part of a

complex of proteins and glycoproteins . . . In D-negatives, the RhD polypeptide is not present in the Rh membrane complex" (Singleton et al., 2000, p. 17).

The Rh positive (D positive) carries the antigens DCcEe (R) in these formats: "Ce (R_1), 2 for cE (R_2), 0 for ce (R_0), and z for CE (Rz)" (Westhoff, 2010, p. 141). When the D gene is totally absent, the blood type RHCE is considered Rh negative (D negative) and carries the antigens in these formats accompanied by shorthand symbols (prime, double prime): CcEe (r), Ce (r'), cE (r"), or CE (r^y; Westhoff, 2010). However, in another study of African descents, D was present in some Rh negative Rh phenotypes resulting from having the exon 4 37 bp insert in the exon 4 and not the normal RHD exon 4 (Singleton et al., 2000). Unlike Caucasians, some Africans who are D-negative have an inactive RHD gene (Singleton et al., 2000). "The most common D-negative Rh haplotype in Africans is RHD⊎ with the ce allele of RHCE, although RHD⊎ might also be occasionally associated with ces. The 37 bp insert in exon 4 of RHDu is a duplication of a sequence . . . [that] introduces another potential splice site;" however, a second split/mRNA (messenger RNAs) decay would not produce a D-negative RHD⊎ (Singleton et al., 2000, p. 17). Following the Rh blood group, the Kell blood group system consists of but are not limited to the following antigens: high-frequency mutations [k, Kp^b (K4), Js^b] and low-frequency mutations [K, Kp^a (K3), Kp^c, Js^c] of which develop the most common phenotypes: K-k+ and Kp (a-b+; Bethesda, 2005; Bogui et al., 2014; Elmissbah, 2013).

DNA/hormones/estrogen. "Conventional tests for the identification of blood, saliva and semen are based on enzymatic and immunological reactions of cell specific enzymes and antigens, but many of these tests lack specificity" (Haas et al., 2014, p. 204). Because no specific markers have been identified for vaginal fluid for all women, bacteria and human tissue-specific transcripts were combined to identify if the fluid is vaginal fluid (Jakubowska,

Maciejewska, Pawłowski, Bielawski, 2013). To identify if fluid is vaginal fluid or blood is menstrual blood, the profile of certain mRNAs, which are markers that encode, can be matched with the mRNAs detected through multiplex PC derived from testing the vaginal secretion or menstrual blood (Jakubowska et al., 2013). Result from testing indicated that the mRNA that are specific to vaginal secretion or even saliva are indicated as the following markers: MUC4, which encodes vaginal mucus, HBD1, which encodes vaginal antimicrobial peptide, and MMP11, which cleave proteins (Jakubowska et al., 2013).

In a more recent study, analysis showed that MUC4 and HBD1 results should be interpreted carefully because of their cross-reactive potential with other body fluids (mainly saliva)" (Haas et al., 2014, p. 210). Most vaginal secretion triplexes (genes), such as MYOZ1, CYP2B7P1, MUC4, and Mesothelin (MSL), and menstrual blood triplexes, such as MMP7, MMP10, MMP11, MSX1 and LEFTY2, were detected as specific for positive identification of menstrual blood and vaginal secretion. Obtaining the reliability of the findings, analysts have to consider the type of swab and phenotypes (Haas et al., 2014; Singleton et al., 2000).

Salivary testing administered to view the profiles of estrogen and progesterone was an effective assay to substantiate that a relationship exists between *CYP17* polymorphism in the gene (genetic variation that controls the biosynthesis of steroid/sex hormones) and full cycle profiles/levels of 17β-E_2 among healthy premenopausal women (Diagnos-Techs, 2012; Jasienska et al., 2006). Estrogen is one of several hormones that interact with sex steroids and undergo conversions (Boffelli et al., 1999). Although the production ceases of anti-Mu¨llerian hormone (AMH), of which the increase reduces aromatase mRNA expression, is unknown, during this stage, the FSH follicles are released to produce E_2 (Pellatt, Rice, & Mason, 2010). Androstenedione is a weak steroid or androgen hormone that produces E_1 and E_2 during the

circulation processes (Monteiro et al., 2014). During the conversion of E_2 to E_1, the human genes *CYP1A1* and *CYP1B1* become involved in estrogen catabolism, whereas, the *CYP1A1 rs2606345* SNP may metabolize estrogen for secretion in perimenopausal and premenopausal women (Sowers, Wilson, Kardia, Chu, & McConnell, 2006). At high fecal concentration, E_1 is reduced to E_2 which is influenced by diets, antibiotics, and intestine flora (Gorbach, 1984).

Estrogen modulates the protein component that determines the plasma level of particles, to include the Lp(a), a lipoprotein that transports fat (Boffelli et al., 1999). Results based on cloning/sub cloning vectors revealed sex steroid hormones, such as gonadal, which interact with estrogen/receptors (ERs) that indirectly binds to the DNA [apo(a) gene expression] through the DHII element, regulate the concentration of Lp(a) plasma expression and apo(a) gene expression, however, differently (Boffelli et al., 1999). Estrogen response activities and DHII sites are eliminated by mutated DNA molecules validating an indirect association (Boffelli et al., 1999). Although the "sex steroid hormones and particular estrogen are known to have a lower Lp(a) levels," the plasminogen expression is not responsive to estrogen; however, the plasma level increases when administered HRT resulting in increased Lp(a) whereby the excess plays a role in vascular issues (Boffelli et al., 1999, p. 15569).

Dehydehydroepiandrosterone (DHEA), "the most abundant steroid hormone produced by the adrenal gland," which is a precursor to the estrogen hormone and begins to declines around age 25, may have a great influence on libido, improve dry eyes, vision, dizziness, mood, and emotional stability, and protect the brain against damage (Jackson-Mann, 2004; McCormick, 2012, p. 1; Nelson-Porter, 2014b). "The gonads and the adrenals express all the necessary enzymes to synthesize estrogens from cholesterol" (Monteiro et al., 2014, Estrogen section, para. 1). Adrenal gland impairment, an autoimmune disorder or HPA-axis disorder, may result in high

FSH when the hormones in the hypothalamus, such as the CRH, inhibit the secretion of GnRH-releasing hormones, which secrete the glucocorticoids that suppress the LH and the secretion of estrogen (Chrousos et al., 1998; Zhao, 2015).

The newly discovered adipocyte-derived peptide hormone leptin, which is higher in polycystic ovarian disease (PCOD), "interacts directly and indirectly with both the adrenal and gonadal axes, and its levels are higher in women than in men" (Chhabra, 2014, p. 4; Chrousos et al., 1998, p. 232). Although estrogen treatment increases leptin sensitivity in the brain of humans, ovariectomy tends to reduce the sensitivity (Monteiro et al., 2014). When adipocytes, specialized metabolic fat cells, produce leptin, an appetite-suppressing hormone, along with adipose tissue (AT) and store energy as fat in excess, the hormone adiponectin that causes insulin sensitivity are decreased resulting in a decrease in the sex hormone binding globulin (SHBG), which then produces higher free estrogen levels. Adipocytes activate metabolic stress initiating and sustaining the inflammation derived from harmful physical, chemical, or biological stimuli (Chhabra, 2014; Evans, 2008; Harvard T.H. Chan, 2015; Monteiro et al., 2014).

During mid-follicular phase of regularly menstruating menopausal women between the ages of 45-52 prior to the elevation of its immunological levels whereby early alterations happens in the hypothalamic-pituitary-ovarian (HPO) axis, the reduction in the number of recruited follicles and inhibition of oestrogens occur, and when present, internal functions, such as the high degree of sialylation and complexity of serum FSH oligosaccharides become altered, and external functions, such as moderately elevated E_2 or LH serum levels, the inhibin (Inh B) glycoprotein hormones, and inhibitory aromatase activity factor, such as AMH produced in the granulosa cells (GCs), become decreased (Loreti et al., 2009; Padmanabhan et al., 2001; Pellatt et al., 2010). The alteration in the HPO axis function, such as decreased Inh B and elevated E_2

serum levels, which are characteristics of the premenopause, may result in the change in the sensitivity of the gonadotrope (molecular microheterogeneity that secretes LH/FSH) to respond to the hormonal regulation of sialyltransferase expression resulting from age or the use of contraceptives (Chrousos et al., 1998; Loreti et al., 2009).

During the follicular phase of premenopausal women when the ovaries start to diminish, the aromatase activity may be stimulated as a result of monotropic increase in the FSH levels (Klein et al., 2004; Loreti et al., 2009). Aromatase, an enzyme found in estrogen producing cells that is controlled by the gonad and brain promotor, regulates oocyte maturation and catalyze (modify to increase effects) Androstenedione that transforms androgens into estrogens (de Cremoux This, Leclercq, & Jacquot, 2010; Monteiro et al., 2014; Zhao & Mu, 2011). "The follicular or proliferative phase extends from Day 1 (the first day of menstruation) to Day 14 . . . The follicular phase ends at the time of ovulation. The luteal or secretory phase generally extends from Days 14 to 28" (Maki et al., 2002, p. 519). During the luteal phase when the FSH or estrogen rises, the Inh levels decrease and the activin levels increase; although activin does not correlate with FSH levels (Klein et al., 2004; Maki et al., 2002).

Comparative to Inh B, AMH, another measure of the occurrence of ovulation senescence, inhibits FSH-stimulated follicle growth and reduces aromatase activity and the aromatase mRNA expression (Pellatt et al., 2010). Because AMH is a reliable measure of ovarian reserve and predictor of ovarian response, AMH, unlike the FSH receptor (FSHR) gene, is considered a marker for ovarian hyperstimulation syndrome (OHSS), a rare controlled ovarian stimulation condition (COS) whereby pregnant women with enlarged ovaries resulting from follicle stimulation experience multifollicular response encountered in gonadotropin stimulations resulting in possible fatal complication of ovarian stimulation human chorionic gonadotropin

(hCG; Fiedler & Ezcurra, 2012; Mahajan, 2013). OHSS have been mostly associated with mutated FSH receptors, polycystic ovarian syndrome (PCOS) or PCOD, and rising E_2 levels (Fiedler & Ezcurra, 2012; Mahajan, 2013). PCOS is characterized as enlarged ovaries with small collection of fluid (follicles) that emerge from the hypersensitivity of intra-ovarian-insulin-androgen, acidic pattern of circulating FSH, or AMH, which may lead to breast cancer-1 (AIB1) and estrogen-induced anovulatory follicles, which are "over-stimulated, proliferative endometrium, and endometrial hyperplasia" (Chhabra, 2014; Goncharenko et al., 2013; Padmanabhan et al., 2001; PCOS, 2016; Wang, 2011a, p. 15).

Endometrial hyperplasia becomes increased when taking estrogen alone. Prometrium containing progesterone is given with estrogen to treat secondary amenorrhea (AbbVie, 2013). More research is warranted on if natural or micronized progesterone derived from wild yam or soy is effective in approaching secondary amenorrhea and abnormal uterine bleeding (Hudson, 2011; Patel, Gadewar, Tahilyani, & Patel, 2012). Limited scholarly research also exists on estrogen dominance whereby normal or high levels of estrogen are accompanied by suppressed levels of progesterone resulting from environmental estrogens (Lawley Pharmaceuticals, 2010). Progesterone receptors (PRs) and ERs, which are found in the epithelial cells, are independent of the menstrual cycle (Goncharenko et al., 2013). Danazol, a synthetic steroid, as well as E_2 reduces some and perimenopausal and premenstrual symptoms by controlling the release of the GnRH that controls the release of glucocorticoids (Batra et al., 2003; Chrousos et al., 1998; Jarvis & Morin, 2010; Padmanabhan et al., 2001).

The follicular phase was not a focus because, "the onset of menses is an end-organ response to falling ovarian steroids and, as such, is a crude and inaccurate indicator of the beginning of the follicular phase" (Klein et al., 2004, p. 2980). Although women with PCOD

enter menopause later as compared with normal women are not estrogen-deficient, but are anovulatory and have hirsutism (excess hair growth in uncommon areas), perimenopausal women are difficult to diagnose as having PCOS because the irregular menses are difficult to measure for PCOS, which is often identified based on salivary testing (Chhabra, 2014; Goncharenko et al., 2013). "Identification of hormonal, functional and genetic markers of ovarian response will facilitate iCOS" (Fiedler & Ezcurra, 2012, p. 7). Determining the association between the Inh B or AMH and FSH to determine the peak of the FSH, ovulation function, senescence, gonadotropin, hormone receptor associated with endometrial hyperplasia, hyperfunctional stress system, or genetic markers of ovarian response thus, is highly not feasible for this study (Chrousos et al., 1998; Goncharenko et al., 2013; Klein et al., 2004).

During the perimenopausal transition phase, women mostly experience a decline in the normal ovarian functions (Prior, 1998). Comparing Caucasian and Asian women, research identified that when estrogen metabolism becomes slow, whereby metabolism is controlled by the effectiveness of liver enzyme (e.g., Cyp3A4) as a result of gene mutation, perimenopause symptoms, such as palpitations, feeling of anxiety, and VMS (hot flashes/night sweats) become more frequent (Deecher & Dorries, 2007; Prior, 2013; Wang & Prodoehl, 2011; Zhao, 2015).

> A hot flash can be described as a warm sensation that begins at the top of the head and progresses toward the feet . . . The physiologic mechanism whereby a hot flash occurs is thought to be an elevated body temperature leading to cutaneous vasodilation, which results in flushing, [anxiety, palpitation, red blotching of the skin] and [profuse] sweating in association with a subsequent decrease in temperature, chills, and potentially relief. (Goodman et al., 2011, p. 6; Shanafelt et al., 2002)

VMS and other symptoms emerge when the neuroendocrine system becomes impacted when the FSH contributes to the loss of ovarian follicular activity, as the secretion of estrogen level need to be high to reduce symptoms (Collin et al., 2007; Prior, 2013). When estrogen withdraws, an increase occurs in the release of norepinephrine and serotonin, which are neurotransmitters (Shanafelt et al., 2002). If norepinephrine lowers the thermoregulatory set point in the hypothalamus and triggers hot flashes, which activates heat loss mechanisms (sweats), and if serotonin receptors can either stimulate (2c) or mediate (2a) hot flashes, then nutrients associated with the proper activation of receptors and release of blood plasma that decrease and modulate norepinephrine or serotonin may be a focus to approach perimenopause because SSRIs has been effective with some and not all the symptoms (Ross et al.., 2013; Shanafelt et al., 2002; Wurtman, 1994).

The decline in the normal ovarian functions often results in possible irregular or excess uterine bleeding (Prior, 1998). Abnormal uterine bleeding (AUB) is classified as metrorrhagia, which is blood loss separate from expected menses, or menorrhagia, which is either increased duration or volume of blood loss or both (Livdans-Forret et al., 2007; Society of Obstetricians and Gynaecologists of Canada [SOGC], 2013a; Subhankar et al., 2011). Menses according to the Chinese are said to originate from the blood and start at the age of 14 (Wang, 2011b). Tiangui or Tiangui Zhi (evolving then arriving), the menstrual fluid transported to the uterus, is initiated by the maturation of the Kidney Qi whereby physiological functions take place under the transport power of Qihua (Qi) of the Kidney (Wang, 2011b). Yuan Qi is transport for the start of the menses (Wang, 2011b). Menorrhagia may be diagnosed by quantifying menstrual blood loss volume (MBLV) by documenting loss in a menstrual diary, using the alkaline-hematin-method by analyzing the blood from used sanitary napkins and soiled underwear, or by

charting the volume of perceived blood loss from used tampons and towels and during urination (Menorrhagia Research Group, 2011; Schumacher et al., 2012; SOGC, 2013b). Menstrual blood, however, is comprised of menstrual blood, peripheral blood, and vaginal secretions (Haas, Hanson, Anjos, Ballantyne, & Banemann, 2014).

Hypomenorrhea, which is light bleeding; amenorrhea, which is a condition characterized by the "absence or abnormal cessation of the menses;" anovulation, the "limited growth of ovarian follicles in the presence of low E_2 serum levels" whereby no ovaries are released; and dysfunctional anovulatory uterine bleeding, which is irregular or unpredictable bleeding may be indicators of the effects of stress (ASRM, 2008, p. S219; Chrousos, 1998; Jarvis & Morin, 2010; Livdans-Forret et al., 2007; Loreti et al., 2009; Prior, 1998; Subhankar et al., 2011; Wang, 2011a). The main symptoms of high FSH include vasomotor symptoms, insomnia, chronic fatigue (lethargy), short menstrual cycle with scanty bleeding, amenorrhea, menometrorrhagia, early ovulation, anovulation, lack of cervical mucus, infertility, and so forth (Zhao, 2015). Menometrorrhagia is dysfunctional uterine bleeding whereby the bleeding takes place at irregular intervals or heavy blood/menstrual flow is related to the intake of contraceptives (Jarvis & Morin, 2010; Livdans-Forret et al., 2007). Scholarly research is limited on how contraceptive injections, such as DMPA, cease the flow of the menstrual cycle and other perimenopause symptoms (Loreti et al., 2009).

"Polyps from the endometrium cause abnormal uterine bleeding, infertility, and pelvic pain" (Goncharenko et al., 2013, p. 4). Cycles that consist of heavy and prolonged bleeding result from high estrogen levels whereby clomiphene-induced ovulation (secretory) does not take place are often a result of anovulatory follicles where FSH serum/molecular microheterogeneity during the follicular phase of normal ovulatory cycles, in vitro FSH bioactivity, and sustained

increment of serum E_2 levels are absent as a result of changes in the sialic acid and complexity of the carbohydrate chain (Chhabra, 2014; Goncharenko et al., 2013; Loreti et al., 2009; Padmanabhan et al., 2001; Prior, 1998; Wang, 2011a). When an increase exists in circulating levels of E_2, an increase exists in acid FSH bioactivity accompanied by the prevalence of a decrease in acidic FSH isoforms (Loreti et al., 2009; Padmanabhan et al., 2001).

> Glandular cystic hyperplasia of the endometrium [which usually characterized by irregular proliferation of glandular and stromal components due to irregular activation of the receptor system of glands and stroma] occurs during anovulatory cycles, which tend to be longer than the normal menstrual cycle after prolonged persistence of follicles, most of which frequently occur in women 40-45 years [premature menopause] who are bleeding prior to amenorrhea for 1 and 2-5 months. (Goncharenko et al., p. 8)

Fibroid growth of the uterus often result from the fluctuation of estrogen during the perimenopausal phase, however, in some cases endometrium malignancy has not been identified in the peri- and premenopausal women (Peddadaa et al., 2008; Subhankar et al., 2011). Epithelial ovarian neoplasm and mature cystic teratoma are classes of ovarian teratomas, neoplasm, or tumors whereby mature cystic teratomas (e.g., dermoid cyst) affect women around the age of 30 (Outwater, Siegelman, & Hunt, 2001). Unlike blood clots (hemorrhagic cysts/lesions), mature cystic teratoma, which seems to derive from an undeveloped embryo consists of hair, teeth, skin, and 93% fat. Mature cystic teratoma very seldom causes abdominal pain or rupture (Outwater et al., 2001). Although fibroids, which are detected by surgical management techniques, mostly grow faster in African American women between the ages of 35-45, the growth of fibroids has not been systematically in White or African American women (Peddadaa et al., 2008; SOGC, 2013).

Other cervical exams that may benefit perimenopausal women include the human papillomavirus (HPV). Women unmarried, with lower-income and atypical squamous cells of undetermined significance (ASCUS) and low-grade squamous intraepithelial lesion (LSIL), and between the ages of 30-34 who may be characterized as perimenopausal have been found to have a higher infection rate than women who are experiencing menopause (Rositch, Silver, Burke, Viscidi, Chang, et al., 2012). More pathological confirmation and abnormal cytology results are needed to gain insight into relations between abnormalities and HPV infections in perimenopausal women.

DNA/system activators. When the pituitary gland, which produces and releases the FSH hormones, which secrete E_2, becomes injured or decrease in activity due to age, depression or life changes may occur, such as a disturbance in sexual functioning and food intakes, which are influenced by somatic unconscious physiological, sensory, and social signals (Berent-Spillson et al., 2012; Booth, 2008; Cancelliere, 2011; Loreti et al., 2009; Zhao, 2015). Understanding how cell signaling affects sexual functioning and food intakes may require understanding how memory processes within cells activate and function.

In regards to the mediating of the hippocampal memory consolidation, ERs "dimerise upon oestrogen binding, and then the hormone-ER complex binds to oestrogen response elements (EREs) on DNA to facilitate gene transcription" and activate signaling pathways (Frick, 2013, p. 1153; La Rosa, Pellegrini, Totta, Acconcia, & Marino, 2014; Maki et al., 2002). Systems and cellular consolidations of hippocampus-dependent or declarative memories benefit during slow wave sleep (SWS) rather during the period of REM sleep or waking activity when no new memories are formed (Mednick et al., 2011). The default network, which is "most active during passive resting states but can also be engaged by internally directed or personally relevant

thought," is thus associated with self-related cognition and may support some aspect of memory consolidation or recall; whereby the strength of the memory as well as difficult cognitive tasks influence or suppress the network (Harrison et al., 2011; Reas et al., 2011, p. 2). This reduced interference "renders memory trace less vulnerable to the negative effects of new encoding" (Mednick et al., 2011, p. 2). When SWS is not considered a means, brain opportunistically consolidates original encoded memories in the absence of the hippocampus encoding new memories (Mednick et al., 2011).

The hippocampus, thus, plays a critical role in the activation of the networks that code and retrieve memory (Reas et al., 2011). The regions of the hippocampus include the dentate gyrus, CA3, and CA1 whereby functional integration may occur (Reas et al., 2011). The gyrus and other regions "mediate the positive effect of semantic congruence on memory of episodic associations during successful memory encoding" (Crespo-Garcia et al., 2010, p. 1259). The dentate gyrus or CA3 specializes in encoding or pattern separation (e.g., spatial), and the inferior (subiculum) part of the CA1 specializes in the retrieval or pattern completion, and the anterior and posterior of the CA1 specializes in match or mismatch detection (Reas et al., 2011).

Many questions continue to emerge about the link between semantic memory and prefrontal cortex (Thompson-Schill, 2003). Understanding how the long-lasting memory episodic trace is bind with other memories and contexts through semantic encoding is relevant to understand the learning processes (Crespo-Garcia et al., 2010; Frick, 2013, p. 1153; Malone, 1990; Smith & Mizumori, 2006). Episodic memory, which takes place in the prefrontal cortex, centers on coding processes that occur when the time and place a specific event takes place (Smith & Mizumori, 2006). Content-specific (perceptional images/name-face/brand association) representations are reactivated during retrieval or bind into new episodic long-term memory

trace, which is supported by the hippocampal formation, by the signals in the prefrontal cortex of the brain (Crespo-Garcia et al., 2010). The subcomponents of episodic memory, such as the reactivation of the memory trace and associative re-encoding, are involved in retrieval sub-process whereby the retrieval processes stimulated by sensations and events are often studied in isolation rather and in alliances (Crespo-Garcia et al., 2010; Reas et al., 2011). Functional regional and structural integrations or relationships control the bindings of new associations whereby name-unknown face association is determined by the degree of connectivity (Crespo-Garcia et al., 2010).

> MTL neurons are intimately involved in one's ability to reactivate internal memories of events from one's past. The neural code representing human experience as it is processed by MTL circuitry is selective and invariant, represents consciously perceived external information, yet can be internally generated and modulated, and reactivated during imagery or free recall. (Suthan & Fried, 2012, p. 434)

Research formerly revealed that no distinction exists between semantic and episodic memory systems (McKoon et al., 1986). The declarative semantic memory does not rely on the hippocampus as the episodic memory, "spatial memory, novel object recognition, social recognition, inhibitory avoidance and trace eyeblink conditioning [tone paired with air to cornea]" (Frick, 2013, p. 1153). Semantic retrieval, which does not rely on the prefrontal cortex for selection mechanism, consists of a large organized distributed network of semantic representations to include "extensive regions of ventral (form and color knowledge) and lateral (motion knowledge) temporal cortex [nonperceptual (e.g., verbal) conceptual knowledge], parietal cortex ([real-life] size knowledge), and premotor cortex manipulation knowledge" (Thompson-Schill, 2003, p. 288). Visual semantics are associated with visual imagery; for

example, a small white potato and mango are the same size; functional semantics are associated motor imagery and knowledge of action; for example, oatmeal goes with breakfast, not lunch (Thompson-Schill, 2003). The output of the connectivity or the functional coupling during encoding and retrieval is modulated when semantic congruence enhances the signals in the prefrontal and parietal cortices of the medial temporal lobe (MTL; Crespo-Garcia et al., 2010).

Social contexts are associated with perceptual illusion, which are obligatory involving visual and interpretation of visuals to understand the significance of the visual, and semantic processes, which are conditional behaviors and interpretations that involve statements and interpretation of the statements in social situations that emerge or clarify social meaning (Iban˜ez & Manes, 2012; Nessler, n.d.; Thompson-Schill, 2003). Semantic congruent (e.g., face-location associations/recognition) whereby stimuli, items, or information paired with its contexts strengthens the memory trace for the specific item; semantic incongruent whereby stimuli are isolated from or are non-relevant to its contexts or neutral, whereby non-semantic noise is deemed as unacceptable, are less likely to benefit episodic memory (Crespo-Garcia et al., 2010). Explicit as well as implicit contextual information/cues are not variable that affects particular processes, but are intrinsic part of the cognitive processes that activates previous experiences and allows coordination between internal (previous experiences) and external (specific observed phenomena) cognitive processes stimulating an effect that enables an understanding of the specific significance of externals, such as an object, emotion/attitude, language, statement, situation, and social cues (Iban˜ez & Manes, 2012).

Although declarative memory to include semantic and episodic memory processing are of the conscious mind, this multifaceted trial primarily focused on the role of the subconscious mind in choice behavior in relations to general knowledge and awareness about natural remedies

to approach perimenopause symptoms. Research as suggested that empirical knowledge is needed to verify the actuality of an a priori knowledge (Tahko, 2011). "Semantically, a context can be viewed as a collection of local models of the same portion of a situation;" whereas, non-declarative implicit memory (intuition) is the collection of local models derived from propositions about a state of affairs that are either believed or not believed (Bouquet & Warglien, 1999, p. 2; Toplak & Stanovich, 2002). "Many intuitive hunches can be attributed to factors such as forgotten expertise, subliminal cues, and unconscious somatic influences" (Radin & Schlitz, 2005, p. 85).

Here, we may further note the relationship between a posteriori and a priori knowledge (Tahko, 2011). "When a subject encounters a known context, the hippocampal context code is expressed and the appropriate memories and behaviors are primed" (Smith & Mizumori, 2006, p. 3). The hippocampus is associated with priming (triggering), in that during unique context processing, foreground/background cues from learning and memory become activated to manipulate context-appropriate primed memories and rational behaviors; the Basal ganglia is associated with priming, which derives from the sensory cortex, in that the striatum of the Basal ganglia is recruited for the implicit probabilistic learning process whereby an elementary reinforcement value is assigned to each set of stored cues whereby the reference class become activated then noticed (primed) stimulating nonrational behaviors (Bøyum, 2013; Di Biase, 2009; Dougherty et al., 2008; Frank et al., 2006; Smith & Mizumori, 2006). In reference to Take the Best (TTB) or Take the Least (TTL), the binary classifier places a value on individual cues whereby inferences about the cues can be made (Dougherty et al., 2008; Duan, Keerthi, Chu, Shevade, & Poo, 2003; Gigerenzer, 1997).

The recognition-primed decision (RPD) strategy is based on the ability to implement appropriate options derived from progressive deepening or to modify or change options if not appropriate or could not be implemented easily. Progressive deepening is a skilled intuitive cue-based measure that involves mentally stimulating and evaluating if an option works in a particular situation whereby most likely promising solutions emerge (Kahneman & Klein, 2009). Priming result after seeing a list of items (targets; reference or starting points) and identifying the object from a degraded or faint list to show that the unconscious cognitive process, where most learning take place, influence how one responds to the environment (Loftus & Klinger, 1992). Priming, anchoring, and adjustments, thus, are implicit behaviors or effects resulting from the estimates/deductions derived about targets (contexts) or the values placed on the targets that have tangible or intangible resources (Quigley, 2013).

- Conceptual implicit priming whereby generating studied remedies from a list by drawing on the semantics or meaning associated with the remedies or the effects of the remedies studied are superior during the midluteal phase. Semantic implicit priming follows lexical implicit memory (i.e., word-stem completion), which "controls for the possibility of response bias when measuring interpretive efforts," whereby memory is based on the activation of the orthography during descriptive explanatory processes; for example, about the purpose or the effects of the remedies that were masked; that is, excluded from the list of studied remedies (Cermak, Mather, & Hill, 1997; Maki et al., 2002; Moss-Morris & Petrie, 2003, p. 205; Taft et al., 2008). Semantic explicit priming follows word-stem completion whereby memory is based on the activation of the orthography during descriptive

presentation of information processes about the purpoe or effects of listed studied remedies (Cermak et al., 1997; Valde´s, Catenab, & Marı´-Beffa, 2005).

- Verbal repetition priming, which involves presenting the same stimuli at a later date; motor sequence learning, procedural learning, and perceptual priming are influenced by spared implicit memory (Oudman et al., 2011; Postma et al., 2008).
- Perceptional implicit priming whereby identifying remedies in comparison to other remedies by drawing on the deductive physical characteristics of the remedies is greater during the follicular phase (Maki et al., 2002).
- Affective priming, which is suboptimal (less conscious), results in emotions activated by evolutionary stimuli, such as sad/happy images and sounds (not emotional words), which are engraved in the brain whereby the presentation of images/sounds has become weaker (Phaf & Kan, 2007).
- Automatic Stroop priming that triggers emotional interferences has not been found under suboptimal emotional conditions as contributing processes extend beyond experimentally using or long-term practice using general emotional/fear/threat words (e.g., general anxiety disorder [GAD]) that relate to particular concerns than the optimal (fully conscious) condition, such as semantic priming processes; however, attentional selectivity triggers interferences in optimal emotional conditions using optimal concern-specific emotional word presentations/threat words (e.g., disease-related/eating disorder/high cardiovascular risk) derived from competitive resources; slow disengagement process/effects, whereby anxiety prompts difficulties in disengaging from the fear stimuli after attention is directed towards the emotional meaning of the fear words, exist in emotional optical

conditions and classic Stroop; whereas, fast interference effects are only evident in classic Stroop where colours and fear meaning of optical words presentation lie in the same dimension. Threaten words, even masked/blocked, correlate with high anxiety than neutral words (Phaf & Kan, 2007).

Emotions are grounded in somatic signals that are received and regulated by the amygdala and insular cortices whereby the latter serves as convergence points for emotional and cognitive and the integration of internal and external milieus (Iban˜ez & Manes, 2012; MacDonald, 2007). "The insula integrates modality-specific feeling states and uncertainty with individual preferences and contextual information to produce a global feeling state" (Iban˜ez & Manes, 2012, p. 1358). The hidden somatic signals, which controls movement and rely on sensory signals, are activated from different somatic tissues whereby the mutation of regulatory pathways, such as insulin/insulin-like growth factor (IGF) and transforming growth factor (TGF)-β signal transduction pathways (e.g., AMH), may improve oocyte quality by balancing the somatic and reproductive needs (Booth, 2008; Ellis & Wei, 2010; Pellatt et al., 2010).

Priming, thus, plays a role in systematic activations associated with the functions of estrogen (E_2). The localization of E_2 of the hippocampus (ERβ) primes the hippocampal neurons to be further activated by the exogenous E_2 (Chamniansawat & Chongthammakun, 2012). When the secretion of the hippocampal E_2 continuously enhances the ERβ expression, a gene expression of estrogen receptor, memory, and the long-term potentiation (LTP) enhancement stimulated by synapses are strengthened (Chamniansawat & Chongthammakun, 2012). Forms of synaptic plasticity, such as LTP (retain new information) and long-term depression (LTD; cease new information), are generated by activated networks of neural activities that play a critical role in learning and responding to brain damage because the synapses or neurons have the ability to

modify their structures and functions (Abraham, 2008). When the ability of synapses or neurons to generate synaptic plasticity or maintain a learning-ready state becomes altered, in addition to other molecules that regulate proper balance, metaplasticity occurs to regulate the physiological and biochemical state of the synapses or neurons to cease excitotoxity or extreme levels of LTP (Abraham, 2008). Exogenous E_2 from the gonadal, however, indirectly up-regulate or strengthen memory consolidation and the ability of synaptic plasticity to discriminate events and store information (Abraham, 2008; Chamniansawat & Chongthammakun, 2012).

Impairment/pathogen/inflammation/natural inhibitors. During resting-states of goal-directed behaviors, some elaborative memory retrieval (tasked induced cued recall conditioning), which may overlap with non-memory task performance (WM**)**, deactivates network areas in selective medial temporal regions (Reas et al., 2011). Spatial WM, procedural short-term memory, and Basal ganglia/parietal cortex learning rather than implicit spatial memory, thus, can suppress the hippocampal activity (Greendale et al., 2011; Oudman et al., 2011; Purves et al., 2001; Reas et al., 2011; Sukumar et al., 2012). The impairment of contextual (e.g., semantic), cued fear conditioning, and spatial working memories result from the negative regulators of hippocampal synaptic plasticity and memory formation, such as histone deacetylase (HDAC2); as "perception, episodic memory [verbal memory processes], visuospatial abilities, and praxias are intact or relatively well preserved" (Frick, 2013; Iban˜ez & Manes, 2012, p. 1356).

In the absence of the dorsal hippocampus (DH), normal fear memories, which are highly permanent and differ from long-term contextual fear memories, thus, decay overtime (Zelikowsky, Bissiere, & Fanselow, 2012). For the long-term contextual fear memories to become permanent, the DH, however, must be intact while conditional training (reinforcing stimuli) is performed (Zelikowsky et al., 2012). Some form of protein synthesis, thus, promotes

memory consolidation (plasticity persistence); while other forms reverse memeory when acting as a metaplasticity mechanism (Abraham, 2008).

Histone modification and DNA methylation are “necessary for long-term memory formation and the modulatory influences of hormones on memory” (Frick, 2013, p. 1152). The means or proteins of which DNA is structured/supercoiled around and plays a role in regulating memory formation is known as histone modification, and the process of which methyl is added to the residues on the DNA to regulate the transcriptional access to DNA and hippocampal memory consolidation, which may change the chemical structure of histones and functions of the DNA to include activation and inactivation DNA processes, is methylation (Frick, 2013). Histone modifiers influence the DNA structure by regulating the transcription to access of DNA without changing the genetic code or primary sequences is known as epigenetic (Frick, 2013).

Learning of and E_2 in the hippocampus increase methylation proteins of histone (H3) in the hippocampus (Frick, 2013). The modulatory factor, $E_{2,}$ regulates epigenetic codes/ alterations, which assist E_2 to enhance and govern the hippocampal dependent NOR memory and contextual fear conditioning (Frick, 2013). NOR differs from spatial memory in that NOR requires less hippocampal tissue to perform tasks than spatial memory; thus, when impairment caused by lesions impact the hippocampus above 70%, the NOR performance becomes affected, and above 50%, the spatial memory becomes affected (Broadbent, Squire, & Clark, 2004). Thus, “epigenetic alterations are critically important for controlling the gene expression associated with normal learning, memory, and environmental experience” (Frick, 2013, p. 1152).

Systematic perpetual evolutionary learning encompasses spatiotemporal input/output pattern transductions (genetic transfer) performed by cytoskeletal neurons with intraneuronal dynamics and controlled by reference neurons with interneuronal dynamics whereby the

dynamics are self-organizing (Chen, 1998). The time-ordered events of systematic learning involve primary events and associated events whereby one series of event are removed or activated when the other series are removed or activated (Chen, 1998). For example, when a strong spatial component exists, perceptual priming for picture-fragment completion becomes impaired (Oudman et al., 2011). Gradual changes, thus, are necessary in certain system structures to advance untrained repertoire to working repertoire (Chen, 1998; Frank et al., 2006; Workman, 2010).

The transcription of genes is also altered when fatty acids (FAs) or their derivatives and phospholipids interact with nuclear receptor proteins that bind to certain promoter of DNA (Norheim et al., 2012). Oxidative deterioration of polyunsaturated fatty acids (PUFA) known as lipid peroxidation, is propagated by the characteristic "free radical chain reaction" whereby lipids are reacted with free radicals (Dauqan et al., 2011; Hybertson, Gao, Bose, & McCord, 2011). Free or oxygen radical produced by biological systems are superoxide $O_2\bullet^-$ (Hybertson et al., 2011). During the free radical processes, when electrons are taken from intracellular bodies, the structures of the bodies changes (Dauqan et al., 2011). Different from ROS, free radicals of which few are oxidant further contribute to the production of diseases and the aging processes, which effect molecule oxygen causing ROS (Dauqan et al. 2011; Hybertson et al., 2011).

"The glucocorticoid vulnerability hypothesis proposes that chronic stress alters the hippocampus by elevating levels of glucocorticoids, which in turn extends the time period during which the hippocampus is susceptible to damage from various sources" (Owen, Hayward, Koenig, Steffens, Payne, 2011, p. 3). Glucocorticoid, such as cortisol, is a stress steroid hormone secreted by the adrenal axis that modulates immune functions and the regulation of nutrient supply, however, suppresses the CRH, ACTH, and gonadal axis as a result of immune

cells releasing the ACTH (Chrousos et al., 1998; Nussey & Whitehead, 2001). Although glucocorticoid inhibits the release of estrogen, estrogen downregulates the steroid hormone from binding in the anterior pituitary, hypothalamus, and hippocampus while increasing the HPA activity (Chrousos et al., 1998; Nussey & Whitehead, 2001).

Antiestrogens, such as tamoxifen and dioxin, that stimulate biological responses to include environmental chemicals that effect the transcription of DNA and processing of RNA, initiated by the chemicals blocking the estrogen from binding to the ERs; thus impacting the estrogen within the cells (Norheim et al., 2012; vom Saal, 1995). "Environmental insults including diet, smoking, air pollution, life style, infection and medication leads to dysfunction of immune response" (Taha & Blaise, 2014, p. 513). The endocrine disruptors (EDs), known as xenoestrogens, include "the plastic-derived food contaminant bisphenol A (BPA) and the plant-derived flavonoid naringenin (Nar) differently interfere with ERa-mediated signalling driving cancer cells to different functional outcomes" (La Rosa et al., 2014, p. 1).

The human body consists of an internal microbial ecosystem of diverse symbiotic microorganisms and parasites, which assist in "the protection against pathogens, nutrient processing, stimulation of angiogenesis, modulation of intestinal immune response and regulation of host fat storage" (Vitali et al., 2010, p. 2). Small quantities of toxic antigens, which are activators (e.g., proteins, peptides, hormones, antibody), when bind with antibodies can be detected and quantified using the enzyme immunoassay (EIA) or enzyme-linked immunosorbent assay (ELISA; Gan & Patel, 2013). An immunoblot assay separates antigens or proteins to probe for the specificity inherent in antigen-antibody recognition (Gallagher & Chakavarti, 2008). Antigens are thus associated with each antibody, which is secreted by B cells (Heiken & Rasmuson, 2009; Westhoff, 2010). In reference to the Rh blood group, anti-ce, anti-ce^{s}, anti-Ce,

anti-CE, anti-cE, and anti-DC are antibodies that demonstrate antigens by carrying away foreign antigens that can result in cell death (Heiken & Rasmuson, 2009).

When pathogenic insults are present, memory B cells carrying autoantibodies along the mucous lining (mucosal associated lymphoid tissue [MALT]) are to trigger to respond rapidly to stimuli based on remembering previous encounters with the pathogens, such as viruses or protozoa (Tangye & Tarlinton, 2009). Although "autoantibodies to components of the RNA interference and mRNA processing pathway represents an additional unique subset of autoantibodies to a family of macromolecuales characterized as protein complexes," research is warranted on the association between autoantibodies and mRNA in regards to comparing the processes of the biological clocks/somantic triggers (Santiago, Eystathioy, Bhanji, & Fritzler, 2007, p. 61). Genetic information to include instructions stored in the genetic memory, which resides in specific nucleus acid of molecules of the DNA, is triggered when the reading mechanism select a molecule relative to the prior selections whereby the enzymes, proteins, and amino acids translated from the mRNA become initiated and terminated (Nirenberg, 1968; Nussey & Whitehead, 2001).

"The ability of naıve B [Ag-inexperienced] cells to differentiate into memory [binded Ag-specific Ig/IgM+CD27+] and PC [plasma cell] underlies the success of most--if not all--vaccines currently in use," and in this case, the compounds found in natural remedies represent the vaccines (Tangye & Tarlinton, 2009, p. 2065). Memory cells, which differ from innate-type B cells and do not rely on the Ag protein or T-cells for continuous exposure and do not encapsulate bacteria but serve as a secondary immune response (Nussey, & Whitehead, 2001; Tangye & Tarlinton, 2009). "Upon primary activation by Ag, $CD8^{+}$ T cells follow a program of proliferation and differentiation into effectors that control the infection" (Cush, Anderson,

Ravneberg, Weslow-Schmidt, & Flaño, 2007, para. 1). Peripheral white blood cell count (WBC), which includes neutrophil counts, is a measure used to identify infection and acute inflammation and have been found to be lower in Blacks than Whites in America, United Kingdom, and Africa (Bain, Seed, & Godsland, 1984; Nalls, Wilson, Patterson, Tandon, & Zmuda, 2008). Although no specific reasons were provided for the lessors, economic status and high fat count may be factors (Bain et al., 1984).

Histone deacetylase (HDAC1/HDAC2) knockout, HDAC inhibitor (HDACi), or activator of p300/CBP HATs inactivate the epigenetic enzymes HDAC1 and HDAC2 reversing hippocampal memory deficits to include cognitive dysfunction associated with aging and neurodegenerative disease (Frick, 2013). "Postmenopausal estrogen supplementation has been associated with greater hippocampal size" (Protopopescu et al., 2008, p. 985). Selective inhibition of HDAC2 abort the expression of estrogen and progesterone receptors increasing the sensitivity of breast cancer cells to tamoxifen and to topoisomerase inhibitor induced apoptosis (Jurkin et al., 2011).

From literature-based discoveries, weak evidence shows an association exists between endogenous premenopausal oestrogens (E_2) and breast cancer risk; young women are rarely diagnosed with breast cancer or research/meta-analysis has been limited on this disease (Walker, Bratton, & Frost, 2011). Carcinogenic 4-OH, 16a-OH, and less harmful 2-OH metabolite pathways for E_2 are reported to be associated with breast cancer risk (Harmon et al., 2014). Steroid hormones evoke receptor down-regulation; BPA like E_2 induces the 26S proteasome-dependent ERa degradation, a protein bound to E_2; whereas, Nar although increases the ERa protein, Nar induces accumulations that block receptors ceasing the breakdown of proteins during the treatment of the breast cancer cell, MCF-7(La Rosa et al., 2014). Although the intake

of total fat is correlated with breast cancer, doubling of circulating E_2 possibly increases the risk of breast cancer by 10% in premenopausal women (Gorbach, 1984; Walker et al., 2011).

Although HDACi induce free radicals and apoptosis, HDACi here in most cases suppress and aborted the cells in the intrinsic or extrinsic pathways where tumor cells are created (Ouaïssi et al., 2011; West & Johnstone, 2014). Suberoylanilide hydroxamic acid (SAHA) has shown to decrease lipopolysaccharide (LPS)-induced TNF-α and IFN-y mRNA, but has not shown to increase cytokines (Leoni et al., 2002). Anti-inflammatory cytokines (e.g., p38/MAPK) as mediators regulate (homeostasis) the anti-microbial and anti-tumoral defenses, while proinflammatory cytokines regulate the toxic ROS (e.g., singlet oxygen, hydrogen peroxide, peroxynitrite) or metabolic disturbances that cause the depletion of antioxidant pools and emergence of oxidative stress (Hybertson et al., 2011; Karaoulanis et al., 2012; La Rosa et al., 2014; Schroecksnadel, Fischer, Schennach, Weiss, & Fuchs, 2007). HDAC1/HDAC2 knockout or gene target and HDACi (e.g., MS-275, trichostatin A [TSA], vorinostat, romidepsin, hydroxamic acids), are also "sufficient to reduce tumor growth in vivo" although in some cases proliferation has been known to increase (Jurkin et al., 2011; West & Johnstone, 2014, p. 35). Chemical technologies, such as ester-HDACi hybrid, which consist of HDACi and esterase-sensitive motif, hydrolyzed by human monocytes and macrophages, are being used for cancer, the inhibition of HDAC-regulated inflammatory cytokines, and the treatment of inflammatory diseases (West & Johnstone, 2014).

"NF-E2-related factor 2 (Nrf2) encodes for antioxidant and general cytoprotection genes, while NF-κB regulates the expression of pro-inflammatory genes" (Bellezza, Mierla, & Minelli, 2010, Abstract section). Although the Nrf2 expression is controlled by DNA methylation and histone modifications, the Nrf2 antioxidant responsive element (Nrf2-ARE) pathway resulting

from Nrf2 binding with ARE is activated when activities are produced by anti-inflammatory or anti-carcinogenic phyto-chemicals (Bellezza et al., 2010; Lee et al., 2012).

> Nrf2 is referred to as the "master regulator" of the antioxidant response, modulating the expression of hundreds of genes, including not only the familiar antioxidant enzymes, but large numbers of genes that control seemingly disparate processes such as immune and inflammatory responses, tissue remodeling and fibrosis, carcinogenesis and metastasis, and even cognitive dysfunction and addictive behavior. [Acetylation–deacetylation of Nrf2 determines its nuclear translocation, its ability to promote transcription, and its egress from the nucleus to terminate its transcriptional activity]. Thus, the dysregulation of Nrf2-regulated genes [whereby the acetylation is decreased by Sirtuin 1 (SIRT1) and can be suppressed/knockdown by the protein, Keap1] provides a logical explanation for the connections, both direct and indirect, between observable oxidative stress and perhaps 200 human diseases involving these various physiological processes, each reflecting a network involving many gene products. (Hybertson et al., 2011, pp. 234, 240)

Through the ARE and the dissociation of Keap1, the Nrf2 controls over 200 genes that are responsible for protein homeostasis, antioxidants, and detoxification, although Keap1 may prevent Nrf2 from accessing the ARE-containing promotors in the nucleus (Hybertson et al., 2011; Smith et al., 2015). With age as Nrf2 protein levels degrade or weaken, the detoxification of potential carcinogens become low, however, possibly not as a result of the dysregulation of Nrf2 transcription by aged miR-146a but as a result of the age-related lesion in Nrf2 proteostasis and inducibility (Smith et al., 2015). Anethole trithione (A3T), a bile-secretion drug is used to treat dry mouth in elder adults, has been found to cause Nrf2 to accumulate significantly in cells in young not elder animals (Hamada et al., 1999; Smith et al., 2015). Superoxide dismutases

(SOD) are enzymes known as anti-inflammatories, which are similar to antioxidant gene output (catalase, GSH peroxidases) that act like various proteins (e.g., *Orgotein*, *Ontosein*, *Palosein*) aimed to decrease markers associated with free/oxygen radicals (Hybertson et al., 2011).

Natural healthcare scientists continue to attempt to find the primary immune response or the remedies that ensure the primary immune response triggers simultaneously when pathogens invade the living machine! Encoded antioxidant and anti-inflammatory proteins have been upregulated by Protandim, a natural phytochemical Nrf2 activator dietary supplement (Hybertson et al., 2011). Dietary phytochemicals can block or reverse epigenetic alterations and decrease the total HDAC activity by scavenging for free radicals and also generating stress sensors or signals that trigger the activation of the Nrf2-Keap1 complex (Lee et al., 2012). This oxidative stress sensor aims to induce cellular defense mechanisms and slow the degradation of Nrf2 (Hybertson et al., 2011; Lee et al., 2012).

Research is limited on the association between methylation status and the tumor suppressor gene (Zhu et al., 2003). The methyl-deficient diet, a gene-diet, may increase the risk of cancer because of the decreased or change in intakes of folate found in fruits and vegetables and methionine found in fish, poultry, and dairy products (Zhu et al., 2003). Unlike the E_1 and E_2 that have tumorigenic activities, the estrogen (E_3) metabolites, which appear in the bile, feces, and as free hormones, however, do not cause cancer (Gorbach, 1984). In the intestines, E_3 is degraded by the intestinal flora and either returned to liver or form free E_3 (Gorbach, 1984).

The ‘microbiome’, the collective genome of the human microbiota, which has nearly 150 times the number of genes represented in the human genome, however allows for a wide range of metabolic functions, such as indigestible carbohydrate, energy, amino acid, valuable short-chain FAs, and vitamins biosynthesis and metabolism (Maccaferri, Biagi, & Brigidi, 2011; Norheim et

al., 2012). A fecal sample whereby DNA is obtained has been used to access the overall structure and survival of gut microbiome (Vitali et al., 2010). The metabolic assessment profile has been used to screen for excess harmful bacteria, insufficient digestive enzymes, and adverse food reactions by measuring the total bile acids (Biohealth Laboratory, 2016). The human gastrointestinal (GI) tract contains mostly bacteria as well as archaea, protozoa, and fungi (Norheim et al., 2012). Metabolomics involves assessing metabolites in a cellular system, metaproteomics involves identifying microbial proteins, and metatranscriptomics sequences mRNAs from a complex microbial ecosystem to assess gene expressions within a certain revealing responses to environmental fluctuations (Maccaferri et al., 2011).

> The concept of molecular nutrition research is-'Science concerned with the effect of nutrients and foods/food components on whole body physiology and health status at a molecular and cellular level' . . . The concept of nutrigenomics has often been focused on the effects of nutrients and other food constituents on gene expression . . . The influence of genetic variation on absorption, metabolism, elimination or biological effects of nutrients have also traditionally been included in the concept of nutrigenomics to optimize nutrition according to the subject's genotype. (Norheim et al., 2012, p. 1900)

Studying the various types of nutrients (see Table 3) can be very challenging (Norheim et al., 2012). Food studies consisting of *in vitro* and animals have been more common than with human subjects, and the results may not be applicable to humans (Norheim et al., 2012). The more diverse the diet, the greater positive impact the microbiomes will have on pathogens. Adult habitual diets have formed less productive personalized GI microbiome (Heiman & Greenway, 2016). The carbohydrate-active enzymes in the intestinal microbiota allows for the metabolism of polysaccharides. Carbs transformed into fatty acid by the microbiota as well as

diets high in polysaccharides cease hunger activation and appetite; whereby, diverse diets are less hindrance (Heiman & Greenway, 2016; Maccaferri et al., 2011). Prebiotics, such as Acidophilus, probiotics, such as Activia®, and synbiotics enhance the absorption of nutrients, minerals, and vitamins, regulates the bowel functions, and may play a role in changes the metabolic phenotypes (Vitali et al., 2010).

Table 3

Functions of Nutrients

Nutrients/Diets (*omics)*	Functions
Genomics	Interact with genes and alter functional outcomes like dietary treatment of phenylketonuria
Epigenomics	Induce epigenetic changes like fatty acids promote methylation of the PGC-1α promoter
Transcriptomics	Influence gene expression as ligands for nuclear hormone receptors
Proteomics	Post-translationally modify proteins, e.g., protein-energy malnutrition leads to post-translational modifications of transthyretin
Metabolomics	May change the metabolomic signature in the blood, e.g., carotenoids are biomarkers of fruit and vegetable intake

Note. Adopted from "Molecular Nutrition Research-The Modern Way of Performing Nutritional Science," by F. Norheim et al., 2010, *Nutrients*, 4, pp. 1898-1944. Permission to reprint from the author, 2016.

In a study assessing the association between special diet statuses and supplement use, findings from 1306 first year students pursing a degree in food and nutrition, however, showed that more health conscious individuals consume micronutrients, and "that supplement users are already consuming diets aligned with public health guidelines" used in Australia (Wiltgren et al., 2015, p. 1104). Limitations of food studies include inaccurate, under, and over-reporting of the variations in the types of foods from various regions (Norheim et al., 2012). Causality may be strengthened from the various experiments supported by observational and social sciences research, because "no epidemiological study can alone provide an absolute answer about the effect of the exposure on the outcome" (Norheim et al., 2012, p. 1909).

Behaviors/Effects Associated with Natural Remedies

Conventional medications have been primary choices to approach perimenopause symptoms because of increased manufacturing and distribution (Mann et al., 2004; PhRMA, 2007). Unlike conventional medications, natural remedies do not include synthetic ingredients (Nelson-Porter, 2015a). Non-best behaviors to select an approach survive when those behaviors are rationalized or the best behavior is not a heritable behavior (Dekel & Scotchmer, 1991). Nutritional effects have been documented to be transmitted to offspring by influencing hereditary events, which include kidney yin deficiency and genetic variation that causes variation in sex hormones (Gómez-Pinilla, 2008; Jasienska et al., 2006; Zhao, 2015).

> The Kidney is the base of the axis on which these physiological functions are formed. It is the prerequisite for female development and maintenance of reproductive function; the Kidney stores the congenital essence, including Yin and Yang . . . the strength of the Kidney decides the arrival, maturation or exhaustion of Tian Gui, and if the Chong Meridians are open and flourishing. Therefore the Kidney is the organ most related to reproduction. The Kidney Yin and Yang are the material and power for a woman's reproductive development and must remain harmonized and flourishing in order to maintain normal physiological functioning. (Fang, 2011, pp. 10-11)

Although functional medicines are based on the unique genotype (heterozygote or homozygote) and phenotype descriptors (AACE Nutrition Guidelines Task Force; 2003; Jasienska et al., 2006), dimension of behaviour (phenotype) has yet to be captured by economic theories; this inference by economist researchers was a typical biological explanation founded on principles offered by Pavlov (Bossaerts & Murawski, 2015). In regards to the dopamine that stimulates the switch between direct and indirect pathways, Pavlow stated, "Levadopa (L-dopa),

a drug designed to increase levels of the neurotransmitter dopamine in the brain, has unintended effects on economic choice;" meaning "it does not explain conjectured effects on parameters of existing choice models" (Bossaerts & Murawski, 2015, p. 39). Thus, this observational clinical trial aimed to explain the effects of natural choices.

Dietary factors have been found to affect multiple brain processes and pathways; however, when selections of natural remedies are considered intuitive, adaptability to external stimuli becomes difficult (Gómez-Pinilla, 2008; Jan van de Kaa, 2010; Loftus & Klinger, 1992; Skinner, 1985). Society, religion, culture, environmental cues, such as the amount, size, and packaging of food items in an assortment and consumptions by others stimulate sensory, social, or somatic signals that influence selections and consumption norms (Booth, 2008; Gómez-Pinilla, 2008; Thompson & Subar, 2013; Wansink, 2010). Inertia, life structural barriers, or the lack of the support structure--the choice architecture, furthermore, refrain individuals from choice changes (Wansink, 2010). "The most common nutritional problems affecting a large population in Africa are protein energy deficiency (PED), iron [Fe] deficiency anemia (IDA), iodine deficiency disorders (IDD)," Vitamins A and zinc (Zn) deficiencies (Global Panel, 2015; Kinabo, 2001, p. 104). In certain Africa regions, the selection and consumption of foods are influenced by factors that affect crop production, such as population movement, epidemics, deterring pasture production, rain falls, dry spells, and deficits (World Food Programme, 2015). The excess intake or lack of intake results in malnutrition and disease characterized by cellular imbalances (Kinabo, 2001).

Within African nations, although spices are abundant, "cereals (including rice, maize, and wheat) and livestock products (dairy and meat)" are not because of limited import from other nations (Rakotoarisoa et al., 2012, p. 3). The Zn contained in cereal contributes to overall health

to include strengthening the immune system by protecting and maintain the structural ability the membrane of the cells (Cakmak, 2008). The structural ability of the membrane allows for the necessary release of nutrients (carbohydrates/amino acides) to attract pathogens (Cakmak, 2008). In the yam family, cassava and taro, which are high in carbohydrates, are used as substitutes for cereals in many African nations (Rakotoarisoa et al., 2012).

Cereal/wheat whole grains contain limited Zn when grown in Zn-deficient soils (Cakmak, 2008). Zinc deficiency has been found to be responsible for learning disabilities and result in increased DNA damage and cancer. Although grain contains Zn, the phytic acid (phytate) in the grain decreases the utilization (bioactivity) of Zn by the digestive system (Cakmak, 2008). Through biofortification, the increase of Fe, Zn, and beta-carotene in soils, allows for the increase of vitamins and minerals in roots, whereby the Zn result in a decrease of phosphorus (P) in the root and thus phytic acid in the grains (Cakmak, 2008; Global Panel, 2015). Agronomic biofortification, a strategy, which involves distributing seeds, such as beans and rice, and roots, such as orange flesh sweet potato and yellow or golden cassava that have accumulate Fe, Zn, and beta-carotene through plant cellular transports, ensures the success of genetic biofortification, which involves the cross-breeding of plants (Cakmak, 2008; Global Panel, 2015).

When dietary substances are scare or not convenient, micronutrients are consumed (Wiltgren et al., 2015). The excess intake of micronutrients has also been reported to pose a negative health risk (Kinabo, 2001; Wiltgren et al., 2015). Prescribing micronutrients and explaining the benefits of natural remedies, thus, may influence choice and have stimulated choice changes (Wiltgren et al., 2015). In comparison to conventional medication prescribed, “the aggressiveness of [natural] treatment interventions should match the severity of the

symptoms" although obtaining the amount of food intakes can be difficult (Shanafelt et al., 2002, p. 1214; Wansink, 2010).

Vitamins/nutraceuticals/phytochemicals. Fair- to good-quality trials that evaluated dietary supplements, including multivitamins, Vitamins B, C, and E, and omega-3 fatty acids to determine the effects of vitamins on mild cognitive impairment or mild-to-moderate dementia found none of the supplements improved cognitive function (Guallar, Stranges, Mulrow, Appel, & Miller, 2013). Cognitive impairment has been referred to as brain fog; however, brain fog may be better termed as a cognitive complaint, which is similar to mental fatigue resulting in forgetfulness (see Table 4 for descriptors; Ross et al., 2013; Smith & Mizumori, 2006). Absent-minded forgetting or mind wandering or disengagement occurs when the internally generated thought and the associated neural processes are anticorrelated, decoupled, perceptional disrupted, or mentally shifted from the conscious thought from concurrent perception input during stimulus-independent thought (SIT; Schooler et al., 2011). While wandering, the consciousness supports cognitions with limited associations to external situations, which leads to a dampening in the processing of environmental stimuli and allows the mind to focus in detail on internal train of thoughts, on information unrelated to the current situation forming the centerpiece of conscious thought, or on the mental consideration of goals other than those in the present (Schooler et al., 2011). In regards to the Basal ganglia or parietal cortex Indirect Pathways, wandering/searching movements are necessary for spatial navigation (Sukumar et al., 2012).

Although cognitive complaints in perimenopausal women may be contributed to perimenopause anxiety and depression symptoms, factors to consider pertaining to mental fatigue and navigation may include the memory-mood links associated with "the tasks, variations in the tasks, and motivation level of individuals to complete the tasks" (Greendale et al., 2011;

Nelson-Porter, 2014b, p. 3; Sukumar et al., 2012). Because IV saline has been found to improve brain fog, scientific research may be needed on the effects of vitamin injections to reduce perimenopause symptoms to include brain fog and amenorrhea (Fowomola, 2010; Jarvis & Morin, 2010; Loreti et al., 2009; Ross et al., 2013). The consumption of vitamins, thus, may be essential to approach cognitive complaints rather than cognitive impairments (Ross et al., 2013).

Table 4

Descriptors of Brain Fog

Most commonly reported descriptors (relate to impaired cognition and performance on cognitive tasks)	Least commonly reported descriptors (indicative of general fatigue, anxiety, and depression)
Forgetful	Thoughts moving too quickly
Difficulty focusing	Detached
Cloudy	Lost
Difficulty communicating	Sleepy
or finding the right words	Annoying

Increased mortality have been shown in a result of many clinical trials totaling 10 of thousands participants randomly assigned to consume β-carotene, Vitamin E, and possibly high doses of Vitamin A (Guallar et al., 2013; Reboul, 2013). Although large doses of B_6 (pyroxidine) stimulate nerve disorders, the deficiency of folate, which is a water soluble B vitamin (found in chicken breast, fish, liver, broccoli, brown rice, potatoes, fortified cereals, bananas, peanuts) leads to "neurological disorders, such as depression and cognitive impairment" (Batra et al., 2003; Freedenberg, 2009; Gómez-Pinilla, 2008, p. 9; NIH, 2012b). "Some alkaloids for example potato alkaloid (solanine) cause gastrointestinal upsets and neurological disorders, especially when taken in excess of 20 mg/100 g sample" (Fowomola, 2010, p. 475).

In a study of premenopausal women most experiencing a normal menstrual cycle, certain vegetables and fruits tend to change the activity of CYP1A2 (Lampe et al., 2000). Cytochrome P450 1A2 (CYP1A2) is a biotransformation enzyme that metabolizes xenobiotics, which are harmful plant-based or man-made chemicals. Lipophilic xenobiotics must be converted from its parent compound to safely metabolize (Lampe et al., 2000). Certain dietary constituents in the apiaceous group were found to inhibit CYP1A2 activity and in the brassica group were found to increase CYP1A2 activity (Lampe et al., 2000). The apiaceous vegetables include carrots, dill, celery, and parsley, as well as grapefruit; allium vegetables include onions, garlic, and leaks; brassica vegetables or cruciferous vegetables include broccoli, cabbage, and Brussel sprouts; and basil-vegetable free include basils (Lam & Lam, 2014; Lampe et al., 2000; Taggart, 2004).

> Health-promoting nutrients and other factors act, at least in part by raising Nrf2 [an antioxidant and cytoprotective activator] including: many phenolic antioxidants; gamma- and delta-tocopherols and tocotrienols; long chain omega-3 fatty acids DHA and EPA; many carotenoids of which lycopene may be the most active; isothiocyanates from cruciferous vegetables; sulfur compounds from allium vegetables; terpenoids. (Pall & Levine, 2015, Abstract section)

"Research indicating that an excessive intake of calories [i.e., from *trans* and saturated fats] might negate the positive effects of certain diets suggests that there is an undefined line between abundance of foods and neural health" (Gómez-Pinilla, 2008, p. 12). In a study of 496 women aged 25-44 from stated *premenopausal* African women who underwent nutrition transition from more traditional foods were found to have high body fat (Hattingh, Walsh, Veldman, Bester, & Oguntibeju, 2008). Estrogens have been found to assist in metabolism control by influencing the leptin expression (appetite, energy to burn fat) and immune processes

(Jönsson et al., 2010; Mayo Clinic, 2015; Monteiro et al., 2014; Störk et al., 2004). In reference to leptin, when the body does not break down the compounds in foods to produce energy, metabolic stress occurs and initiates inflammatory responses (Chhabra, 2014; Harvard T.H. Chan, 2015). The six-transmembrane protein of prostate 2 (STAMP-2) modulates leptin and inflammatory responses in macrophages to prevent aberrant responses from nutrients that triggers inflammation (Monteiro et al., 2014).

In regards to anti-inflammatory nutrition "essential fatty acids are the most powerful modulators of NF-κB. In particular, the omega-6 fatty acid arachidonic acid (AA) activates NF-κB; whereas, the omega-3 fatty acid eicosapentaenoic acid (EPA) does not" (Sears, 2012; para. 7). Chicken, eggs, beef, sausage, and fish are high in omega-6 fatty acid arachidonic acid (National Cancer Institute [NCI], 2014). Docosahexaenoic acid (DHA), another n-3, and EPA can be found in fish (wild, cold-water), chicken, shrimp, eggs, and tuna (Evans, 2008; European Food Safety Authority (EFSA), 2010; NCI, 2014). Omega-3 (n-3) polyunsaturated fatty acids (PUFAs), which also reduce depression associated with several disorders, are found in broccoli, spinach, flaxseeds, walnuts, baked salmon, and cantaloupe (Freedenberg, 2009).

> Consumption of fruits, vegetables and other foods and beverages including apples, berries, broccoli, Brussels sprouts, cauliflower, onions, herbs, cocoa, tea and red wine provides an important source of Nrf2 [and maybe proanthocyanidins, a polyflavan] and has been found as having many therapeutic effects via induction of key enzymes involved in cellular antioxidant/anti-inflammatory network. Many of these same enzymes also appear to play a key role in maintenance and redox recycling of essential Vit A, C, and E. (Beecher, 2004; Kassim et al., 2009; Pall & Levine, 2015; Taha & Blaise, 2014, p. 517)

Alpha lipoic acid, which enhances the inositol effects, “is a fatty acid that plays a leading role in the cellular energetic metabolism exerting antioxidant activities on free radicals promoting glucose cellular intake, taking part in fat catabolism on the Krebs cycle” (Capasso et al., 2013, p. 2). Myo-inositol, an inositol, which is a sugar alcohol, is a polyalcohol help with repairing the nerve functions (Clements & Darnell, 1980). Grapefruit, oranges, bran flakes, green beans, and Brussel sprouts are high in myo-inositol (Clements & Darnell, 1980).

Vitamins E, α-tocopherol, and C (ascorbic acid, gooseberries, known as Amla) have been found to suppress neopterin production and tryptophan degradation, which lead to inflammation (Kumar et al., 2012; Schroecksnadel et al., 2007; Shylaja et al., 2015). Serum levels of Vitamin E found in vegetable oils, nuts (almonds, pecans, walnuts, flax and sunflower seeds), green leafy vegetables, and fortified cereals improve poor memory performance in older women (Gómez-Pinilla, 2008; Thomas & Gebhardt, 2006). The supplement, phosphatidylserine, found in cabbage and soy, is a primary source to decrease the loss of brain functions (Kidd, 1996; Knight & Eden, 1996; WebMed, 2015).

Although plantar vibration have been found to improve lower body muscle activities that increase blood flow, in addition to Vitamins E and C (grape juice) reducing inflammation, pineapples containing the enzyme Bromelain tends to relax muscles and reduce inflammation (Kelly, 1996; Schroecksnadel et al., 2007; Stewart et al., 2005). The reduction is stress coping abilities result from chronic inflammation, which is associated with age related diseases, whereby toxic molecules are released activating pain receptors (Chevalier, Sinatra, Oschman, Sokal, & Sokal, 2012). In a clinical trial of 80 postmenopausal women, Femarella (DT56a), a new ER modulator (SERM) derived from soy, relieved menopausal symptoms: arthralgia (joint

pain), myalgia (muscle pain), vasomotor, headaches, and insomnia, but no mentioning of hemidystonia (LeDoux, 2009; Yoles et al., 2004).

"A woman who is both menopausal and has PCOD needs to follow a strict exercise regimen and follow a diet that is lower in carbohydrates," because insulin resistance is a characteristic of PCOD (Chhabra, 2014, p. 5). Specific regional diets differ, such as Nordic and Paleolithic nutritional diets may be analogous to Western diets (Eaton, Eaton III, & Konner, 1997). Different foods associated with Western diets, however, may share the same name as other foods from various nations (Thompson & Subar, 2013). Research, however, has proposed favorable health benefits of various diet (Wang, García-Bailo, Nielsen, El-Sohemy, 2014, p. 1).

Many low-carb diets have been reported to be ineffective in weight loss because weight loss is not only depended on the consumption of diets but other dietary factors; thus, the reduction in the total intake of energy has to be considered (Cheuvront, 2004; Gardner et al., 2007). "Simple carbohydrates include sugars found naturally in foods such as fruits, vegetables, milk, and milk products. They also include sugars added during food processing and refining. Complex carbohydrates include whole grain breads and cereals, starchy vegetables and legumes" (MedlinePlus, 2015, para. 2).

> The diversity of dietary components reveals that the LM-485 diet is a vegetarian diet comprised primarily of ground corn, dehulled soybean meal, ground oats, wheat middlings, dehydrated alfalfa meal, soybean oil and corn gluten meal. The 7002 diet is more diverse containing animal products and less fermentable carbohydrate (ground corn, porcine meat and bone meal, dehulled soybean meal, wheat middlings, ground wheat, ground oats, dehydrated alfalfa meal, brewers dried yeast, cane molasses, porcine fat, dried whey and casein). Thus, it is possible that LM-485 diet drives a microbial

> community supporting higher levels of SCFAs [short chain fatty acids] than does the 7002 diet. (Heiman & Greenway, 2016, p. 3)

Using a cohort of peri- and premenopausal women aged 25-50 tested the outcome of the various diets, after a 75% attendance of a 1-hour diet class for 8 weeks (Gardner et al., 2007). The various diets primarily measured the carb, energy, protein, fat, and saturated fat contents (Gardner et al., 2007). The Ornish and LEAN diets are high in carbs (Gardner et al., 2007). The Ornish diet, which consists of whole foods, plant-based protein, fruits, vegetables, unrefined grains, and legumes, has been proposed to reduce aging at the cellular level by lengthening the telomere, which is the region that protects the ends of chromosomes (Lomangino, 2013). The zone diet, which is low in carbs, aims to maintain hormone balance by reducing the insulin-to-glucagon hormone ratios (Cheuvront, 2004; Gardner et al., 2007). The ketogenic diet limits carbohydrates whereby the body relies on ketones for fuel (McDonald, 1998).

The Gluten-free diet, which include fish, fruits, nuts, cereals, such as rice, buckwheat, and teosinte, exclude all foods, such as wheat, barley, and rye, and medications, which contain gluten (Saturni, Ferretti, & Bacchetti, 2010). The Ayurveda Kapha diet favors warm foods, such as grains (corn, buckwheat, and rye), fruits except for banana and avocadoes, and mostly vegetables and hot beverages, such as organic skim milk and teas (Amrita Veda, n.d.). The various foods and beverages are listed by constitutional types representing the stages of life: Vatika, Pittaja, and Kaphaja (The Ayurvedic Institute, 2008). The guidelines state if foods should be consumed raw, cooked, dry, ripped, and so forth (The Ayurvedic Institute, 2008). In reference to group identities, raw has been associated with nature, while cooked has been associated with culture that has been shaped by laws (Avakian & Haber, 2005). Unlike the vegetarian diet, the pescatarian diet, which is similar to omnivores, consists of red meats,

poultry, fish, diary, vegetable, and fruit intakes resulting in lower plasma levels of oestrogens (Harmon et al., 2014). "Vegetarian women have an increase in fecal output, which leads to an increase in excretion of fecal estrogen [E_3] and a decrease in concentration of plasma estrogen [E_1, E_2]" (Gorbach, 1994, p. S88; Harmon et al., 2014).

> Based on the 'Blood-Type'diet theory, group O is considered the ancestral blood group in humans so their optimal diet should resemble the high animal protein diets typical of the hunter-gatherer era. In contrast, those with group A should thrive on a vegetarian diet as this blood group was believed to have evolved when humans settled down into agrarian societies. Following the same rationale, individuals with blood group B are considered to benefit from consumption of dairy products because this blood group was believed to originate in nomadic tribes. Finally, individuals with an AB blood group are believed to benefit from a diet that is intermediate to those proposed for group A and group B. (Wang et al., 2014, p. 1)

The historical Inuit diet, originated in the artic region, which is associated with an high omega-3 fatty acids intakes, consists of caribou, red char (arctic char), seal meat (ringed, misiraq), walrus meat and liver, seal fat and skin, white whale blubber/fat of whale (mallu), whale (mal/u, beluga) meat, fish (lake whitefish), other seafood (salmon, trout, herring), geese, swans, muskox, and mutton, and berries (Blanchet, Dewailly, Chaumette et al., 2002). The Inuit diet was low in Vitamins (A, C, & D) because of the lack of vegetable and fruit intakes (Blanchet et al., 2002). The New Nordic Diet in comparison to the Danish diet consists of more foods from the plants, sea and lakes, and wild countryside to include higher intake of herbs, vegetables (legumes, leafs, such as cabbages, roots, such as beets, carrots, potatoes, and onions), fruit (berries), whole grains, seafood (arctic fish, shellfish, seaweed), and nuts (Jensen & Poulsen,

2013). Wild is defined as being difficult to locate (Aryal, Berg, & Ogle, 2009). In the Danish book, *Spis Dig Fra*, women consume a dish made of oatmeal and dates for premenopause symptoms (L. F. Larsen, social media communication, January 13, 2016).

The macrobiotic diet, which denotes a "way of long life," and seems to be similar to the New Nordic Diet, is claimed to be based on the principles of yin and yang (James, 2004). Although the macrobiotic diet include soups made of sea vegetables, such as seaweeds, the nutritional value has been reported to consist of an adequate supply of nutrients, such as Fe, Vitamins B_{12} and D, and calcium leading to low energy and protein (James, 2004). However, although the fiber of seaweed and sea lettuce occurs largely without digestion in the gut, these vegetables have been found to be high in Fe, cooper, and calcium (MacArtain, Gill, Brooks, Campbell, & Rowland, 2007).

"The Mediterranean-like diet based on whole grains [cereals], low-fat dairy products, fish, fruit and vegetables" increases the consumption of more energy from the fat content; whereas, "based on lean meat, fish, fruits, vegetables, root vegetables, eggs and nuts," the Paleolithic diets of the Stone Age consist of wild games and plant foods mostly comprised of protein and fiber (Eaton et al., 1997; Jönsson et al., 2010, p. 1). Uncultivated foods of specific regional diets include roots, leaves, leafy greens, fruits, wild fruits, nuts, and tubers, all of which are "high in fiber relative to energy" (Aryal et al., 2009; Eaton et al., 1997, p. 213). Folk medicines were derived from uncultivated foods to approach ailments, such as headaches and swellings (Aryal et al., 2009). Although yacon and ahipa, function as 'fruits' and are eaten raw, other botanical tubers, such as oca, ulluco, mashua, arracacha, mauka, and achira are cooked to easily digest (Hermann & Heller, 1997). Blanching is a method of preserving the flavor and color more so than the nutrients by boiling and cooling the foods prior to freezing (Reyes De

Corcuera, Cavalieri, & Powers, 2004). Scholarly research is limited on the functions of certain fruits, such as butternut squash.

Paleolithic diet was deprived of carbohydrate having more satiating per calorie and may have lacked retinol (Vitamin A; Eaton et al., 1997). Carrots, red yam (sweet potatoes), and cantaloupe contain provitamin A (β-carotene), which is converted to Vitamin A once consumed (Tang, 2010). Golden or yellow rice, which accumulate provitamin A, has been modified and can be bioengineered to cope with impaired vision that may lead to blindness (Global Panel, 2015; Schaub, Al-Babili, Drake, & Beyer, 2005). Associated with anti-aging and antioxidant effects, "Chinese medicine considers L. barbarum berries [goji, exotic fruits] to have the ability to maintain the function of eyes and strengthen the activity of liver, kidneys, and lungs via boosting and balancing 'Yin' and 'Yang' in the body" (Cheng et al., 2015, p. 34). In addition to improving eyesight, raspberry anthocyanins (flavonoid) enhance cognitive brain functions and inhibit malignant cell growth (Kassim et al., 2009).

To normalize estrogen production and prevent fibroids, endometriosis, and breast cancer, more women are seeking natural approaches, such as taking herbs, such as curcumin (Evans, (2008). Studies on the relations between high serum oestrogen levels and meat intake and breast cancer have been inconsistent (Harmon et al., 2014). The pescatarian diet, thus, has not been proven as a diet that reduces breast cancer (Harmon et al., 2014). Although more research is needed to validate that phytoestrogen (PE) is not considered toxic, more research is warranted to determine if PE provides protection against proliferative endometrium as PE (genistein with quercetin) has been found to provide protection against cellular proliferation leading to breast and ovarian cancer; isoflavones (genistein, coumestrol) has been found to inhibit tumor formation, which may include anatomical abnormalities, such as polyps or fibroids

(Goncharenko et al., 2013; Knight & Eden, 1996; Subhankar et al., 2011; Wang, 2011a; Zhao & Mu, 2011). If PARP inhibitors can be used to treat breast and ovarian cancer, because a connection has been found between PARP and ER-stimulated growth of cancerous cells, then researchers may consider if PE acts as a modulator or modulate PARP, which regulates the expression of a scaffold protein, PDZK1, by controlling the expression of the IGF-1 receptor (IGF-1R, insulin; Kim et al., 2015; Zhao & Mu, 2011).

The function of traditional nutrients differs from phytochemicals, which are non-nutritional compounds from natural plants that produce chemical reactions in the body used to prevent diseases (National Onion Association, 2011). "Phytoestrogens are a family of diverse polyphenolic compounds derived from nature plant that structurally or functionally mimic" in the mammalian reproductive system the circulating estrogen (E_2), the sex steroid production released by both FSH and LH (vom Saal, 1995; Zhao & Mu, 2011, Abstract section, p. 1). PEs, which are stored in fatty tissues, are released in the blood stream rapidly metabolizing producing aromatase inhibitory effects or estrogenic effects depended on their estrogen receptor (ER) agonist activity (de Cremoux et al., 2010; vom Saal, 1995). Mostly studied in animals, PEs have been reported to control oocyte (immature egg cell) generation during the modulation of steroidogenic enzymes and aromatase regulates oocyte maturation producing E_2; whereas, mostly studied in animals and humans, dietary isoflavones, as class of E_2, have been reported to reduce progesterone (P_4) in the ovary by inhibiting the generation of aromatase (Zhao & Mu, 2011). In premenopausal women, if the doubling of circulating E_2 possibly increases the risk of breast cancer by 10% (Gorbach, 1984; Walker et al., 2011), we may research the association between the compounds in dietary isoflavones and (a) the aromatase inhibitor, AMH, which reduces the aromatase mRNA expression and activities, (b) anastrozole, which inhibits aromatase and suppresses ERβ, or (c)

phosphatases, which triggers the activation of *N*-methyl-d-aspartate receptors (NMDAR) subtype of Glutamate receptors (GLuR), which trigger metaplasticity and LTP induction in perimenopausal women experiencing cognition issues and are at high risk for cancer (Abraham, 2008; Chamniansawat & Chongthammakun, 2012; Itoh, Sakta, Watanabe, Aikawa, & Fujii, 2008; La Rosa et al., 2014; Pellatt et al., 2010; Zhao & Mu, 2011). The results may be applied to the effects of PEs and isoflavones on the mutation in the activities of IGF and TGF-β pathways, which balance somatic and reproductive needs improving oocyte quality (Ellis & Wei, 2010).

In regards to PE metabolism, the dietary habits, ethnic origins, gut microflora population are factors that have to be considered (de Cremoux et al., 2010). Phytoestrogen, which is found in soy and cruciferous vegetables (beans), has a low affinity for binding ER; whereas, E_2 has a high affinity (Atkinson et al., 2004; Goncharenko et al., 2013; Subhankar et al., 2011; Zhao & Mu, 2011). Because the high chemical structure of PE has been found to relieve hot flashes, maybe because of bitterness, women experiencing hot flashes are not consuming ample amount of cruciferous vegetables (Campbell et al., 2012; Knight & Eden, 1996; Lam & Lam, 2014).

Phytochemicals found in cruciferous vegetables and citrus restore tumor suppressor genes and reduce intracellular ROS production (Lee et al., 2012). In addition to storing the antioxidant Vitamins, A, C, and E, calcium (Ca), and magnesium (Mg), mangoes, known as the superfruit, are rich in a variety of phytochemicals (Fowomola, 2010). Avocados contain phytochemicals, "such as lutein, phenolic antioxidants, and phytosterols (Fulgoni, Dreher, & Davenport, 2013, p. 2). Lutein, a nonprovitamin A carotenoids, is found fruit and vegetables, such as in lettuce and cooked spinach, although Vitamin A is animal-based (Reboul, 2013). Phytosterols, used to lower cholesterol level, are found in corn, Brussel sprouts, onions, bananas, broccoli, almonds, and wild blue berries (Raju, Babu, Kumar, & Rajashekar, 2013). Flavonoid is one of three

families of compounds contained in onions that act as an antioxidant (National Onion Association, 2011). Scientific studies associated with the anti-oxidative compounds of onions, such as bioflavonoid (quercetin), as well as alpha lipoic acid seem to focus on the impact of cancer prevention and bone health to include bone turnover or remodeling, which is highly associated with menopause and post-menopause rather than peri- or premenopause (Capasso et al., 2013; National Onion Association, 2011; Prior, 1998; Sowers et al., 2003; Taggart, 2004).

More scientific research, however, is warranted on the extent of which bioflavonoids (formally known as Vitamin P) impact perimenopause symptoms, such as abnormal bleeding and fluid or water retention, because as indicated phytoestrogen (PE) has a low affinity for binding ERs (Atkinson et al., 2004; Goncharenko et al., 2013; Subhankar et al., 2011; Zhao & Mu, 2011). Isoflavone, such as found in red clover, reduces elevated plasminogen activator inhibitor type 1 (PAI-1), an inhibitor released in response to inflammatory reaction that assists with fibrin clot stability in a small sample of perimenopausal women (Atkinson et al., 2004; de Cremoux et al., 2010; Mayo Clinic, 2015). Here, we may hypothesize if heavy bleeding as a result of endometrium continue to sustain or increase, then a relationship may exists between endometrium and elevated PAI-1 during the menopausal phases, and administering isoflavone may not be the most appropriate remedy for menopausal women who experience AUB, but the consumption of Fe, Vitamin C (Amla), Vitamin K, and Ca, which is essential of the clotting of blood, may be recommended (Atkinson et al., 2004; Fowomola, 2010; Goncharenko et al., 2013; HubPages, 2009; Kumar et al., 2012; Peddadaa et al., 2008; Rutanen, Hurskainen, Finne, & Nokelainen, 2000; SOGC, 2013; Subhankar et al., 2011). "GnRH-induced hypoestrogenism results in endometrial thinning usually to the point of amenorrhea" (SOGC, 2013b, p. 712).

Repeated dosages of Vitamin K found in fruits and vegetables, such as Romaine lettuce, help the blood clots property (Fulgoni et al., 2013; HubPages, 2009; SOGC, 2013b). Vitamin K as well as vitamin E is contained in olive oil, however, not avocado oil (Mayo Clinic, 2014). Cabbage, which contains Vitamins C, K, and B_6 and minerals, also increases the activity of CYP1A2 (Lampe et al., 2000; NIH, 2012a).

Minerals/metals. Heavy metals, such as mercury, lead, and aluminum found in foods, free radicals (e.g., smoking, pollutants), chronic emotional stress, and nutritional deficiencies affect the chemical synaptic transmission in the brain and the peripheral and central nervous system disrupting brain and cellular calcium levels that significantly affect the body to properly absorb nutrients found in remedies to include lithium, Mg, Zn, Fe, and Vitamins $B_{1\text{-}12}$ causing depression and mood swings (Kidd, 1996; Roth, 2006; Windham, n.d.). Fruits growing in Bangladesh have been contaminated with calcium carbide to ripen the fruits (Hossain, Akhtar, & Anwar, 2015). While Mg as well as Vitamin D is needed to ensure the absorption of Ca, low-Ca as well as low-manganese (Mn) diets during the premenstrual phases result in increased pain, water retention, and poor concentration (Collin et al., 2007; Itoh et al., 2008). Vitamin D, which is found in tuna fish, salmon, sardines, and milk, prevents depression (Freedenberg, 2009).

Magnesium, which is high in fish, broccoli, and spinach, also has been found to be beneficial for bloating, fluid retention, and dehydration as well as breast tenderness and negative mood states (Collin et al., 2007; Freedenberg, 2009). Whether menopausal women experience dehydration from not replenishing fluids and fluid retention from reproductive surgery, low Na (an electrolyte), the enabling by Mg, HRT, or drospirenone derived from spironolactone, has been found effective in approaching the conditions (Batra et al., 2003; Stachenfeld, 2014; Sterns, Nigwekar, & Hix, 2009). Based on this investigator's observation, during the time of bloating

and overactive bladder, the body experiences pressure in the lower abdominal area and frequent urination although less urine is expelled during each restroom visit. Literature-based discovery reported migraine headache is also associated with the Mg deficiency (Weeber et al., 2001).

Hypotonic fluids (saline) and desmopressin (hormone) acetate (DDAVP) have been administered to reduce hyponatremia (low Na resulting in cell swelling due to excessive consumption of water) and prevent brain damage (Sterns et al., 2009). The nine amino acid residues that make up the vasopressin regulate water balance, appetite, body temperature, and sleep. Vasopressin, also called antidiuretic hormone, is a peptide synthesized in the hypothalamus that affects blood volume (McKee & McKee, 2008). "Water is found in saliva to 99%, in blood to 80%, and to 75% in muscles" (Jensen, 1983, p. 153).

"The ubiquitous presence of Mn in a variety of foods accounts for the fact that Mn deficiency in the adult is practically nonexistent" (Roth, 2006, Manganese Homeostasis section, para. 2). The dietary intake of Mn derives from "cereal, vegetables, fruits, nuts, spices and beverages such as wine, tea and coffee" (Roth, 2006, Manganese Homeostasis section, para. 2). "Pineapples are rich in manganese, a trace mineral that is needed for body to build bone and connective tissues . . . Pineapple is an excellent cerebral toner; it combats loss of memory, sadness and melancholy" (Hossain et al., 2015, p. 86).

Feeding and fasting cycles regulate the liver, which contains the STAMP-2, which "modulates nutrient-induced inflammatory responses" (Harvard T.H. Chan, 2015, para. 3). However, when exposed to Mn (e.g., free radical) transported through the air from work sites, intoxication result in "reduced response speed, intellectual deficits, mood changes, and compulsive behaviors in the initial stages of the disorder to more prominent and irreversible extrapyramidal dysfunction" (Roth, 2006, Abstract section). Wild blueberries as well as

blackberries, cherries, grapes, kiwi, and strawberries are high in antioxidants aimed to approach free radicals causing oxidative stress/damage; alpha lipoic acid, an antioxidant, found in liver, spinach, broccoli, and potatoes influence cognitive functions (Gómez-Pinilla, 2008; Prior, 2008).

When much Mn enters the bloodstream from the air prior to making contact with the liver, maintaining normal homeostatic becomes difficult (Roth, 2006). Mn (ion Mn^{2+}), which mimics Ca (ion Ca^{2+}) and is transported via the mouth through diets instead of via air through the mucocilliary escalator, may enter the bloodstream through the gastrointestinal tract (intestines) and the brain through the blood brain barrier, such as Ca channels (Itoh et al., 2008). Manganese is involved in the biosynthesis of choline, which is not considered an essential nutrient (Coomer, 2014; Zeisel et al., 1991). A deficiency of Mn may result in a deficiency of choline, and when the human body becomes deprived of choline, the signs include liver dysfunction and memory disorder (Coomer, 2014; Zeisel et al., 1991).

Although the *adult* liver does not produce estrogen and has been reported to control the estrogen (E_3) metabolism via the liver enzyme (i.e., Cyp3A4), the liver metabolizes the integration of glucose and fatty acid, regulates Mn levels, and attempts to influence the amount of Mn transported to the brain (Booth, 2008; Gorbach, 1984; Itoh et al., 2008; Monteiro et al., 2014; Prior, 2013; Roth, 2006). When Mn enables the sodium (Na) exporters, the permeability transition pore (PTP) and loss of mitrochodrial function become activated accumulating calcium that may result in brain injury (Roth, 2006). Based on literature-based discovery and experimental field data, the active ingredients (omega-3 fatty acids) in fish oil may be further researched to determine how the agents act within the flow of blood or platelets and how choline approach damaged arteries as a result of accumulation (Coomer, 2014; Weeber, Klein, & de Jong-van den Berg, 2001).

Herbal remedies/other techniques. Based in prior research on the effectiveness of herbal as well as homeopathic remedies to approach perimenopause symptoms, open source scientific research on their interactions and effectiveness at the cellular level (antidiuretic, glycoprotein, and gonadal hormones, and tyrosine molecules) is limited (Batra et al., 2003; D'Archivio et al., 2007; Monteiro et al., 2014; Sharad et al., 2011). Cocoa, coffee, teas, and spices are abundant in many African nations; and the coffee and teas contain polyphenols serving as an antioxidant, which protect cells constitutes from oxidative damage (D'Archivio et al., 2007; Rakotoarisoa et al., 2012). A clinical trial of 65 perimenopausal women who were administered a serum test (assay) found that serum levels cytokines did not differ between depressed and normal female participants (Karaoulanis et al., 2012). Based on findings, if perimenopausal depression is associated with hot flashes, and proinflammatory cytokines is not associated with perimenopausal depression, then proinflammatory cytokines may or may not be associated with hot flashes (cause or elimination of; Karaoulanis et al., 2012). If increased levels of estrogens influence the inflammatory processes, and proinflammatory cytokines influence the release of gonads, which assist with synthesizing estrogens from cholesterol, then cytokines may have an association with hot flashes, but not a cause-effect relationship with hot flashes (Karaoulanis et al., 2012; Nussey & Whitehead, 2001; Monteiro et al., 2014, Estrogen section, para. 1; Shanafelt et al., 2002; Störk et al., 2004). Hot flashes linked with perimenopausal depression, thus, may not need to be treated or approached as would depression linked with proinflammatory cytokines (Karaoulanis et al., 2012).

Herbal and homeopathic remedies have always been a part of cultural appropriations to approach menopausal symptoms (Nicolazzzo, 2009; Sharad et al., 2011; Thiel, 2012). Polyphenols and polyflavans found in fruits (red grapes), vegetables, and herbs prevent oxidative

damages, and Ginkgo, a fossil that contains flavonols, one of the groups of polyphenols, are actual polyflavans, which approach the homeostasis of oxidative stress and learning and memory impairment because of its neuromodulartory properties (Beecher, 2004; D'Archivio et al., 2007; Gómez-Pinilla, 2008; Rouse, 1998). Soy, which contains DT56a and isoflavone (daidzein, apigenin, prunectin) and is found in peas and red clover (herb), tends to relieve menopausal symptoms and oxidative stress (Knight & Eden, 1996; LeDoux, 2009; Yoles et al., 2004).

To approach neuronal damages resulting from the decline of gonadal hormones whereby activation patterns are altered, natural formulas have been manufactured and can be purchased via the Internet (see Table 5; Deecher & Dorries, 2007). In addition to Ginkgo and horse chestnut seed (Aesculus glabra) as herbals consumed to improve circulation, to include the lower extremities, many extracts (green/black tea) and herbs (Padma 28, Xiao Yao San) also suppress depressive moods (Rouse, 1998; Schroecksnadel et al., 2007; Wang & Prodoehl, 2011; Yeung et al., 2014). The formation of teas is categorized as tinctures, infusions, decoctions, and so forth (Nicolazzzo, 2009). Caffeine is an alkaloid, natural compound, stimulating alertness and improving performances related to tasks requiring sustained attention over an extended period of time (Wentz & Magavi, 2009).

Table 5

Natural Formulas for Cognition

Blends	Approach benefit	Sources
Bacopa / Brahmi Powder	Mental clarity	Satveda, n.d.
BrainEssence™	Short-term memory; problem solving	Pure Essence Laboratories, 2015
Deep Thought	Mental clarity	Dr. Ron's Ultra-Pure, 2015
Mind-Max	Memory, cognitive performance	The Health Help, 2011
Nutrimind	Levels of neurotransmitter	Whatifnutrition, 2015
Power Thought	Cognition	Bluebonnet Nutrition, 2009

In addition to Vitamins C (Amla) with P, in Germany, the leaves and flowers of Sage are brewed into a tea and made into a pill, which are consumed to assist with approaching VMS and estrogen loss as well as fatigue, nervous exhaustion, and memory and cognition improvement (Bruno, 2002; Foster & Johnson, 2006). Injectable magnesium sulfate has been used to approach heart arrhythmias and chronic fatigue syndrome (Fowomola, 2010). Although Vitamin E, which has a mild effect on hot flashes, has been found to improve poor memory performance in older women, herbal remedies to include black cohosh and Chinese remedies are effective in approaching hot flashes (Gómez-Pinilla, 2008; Shanafelt et al., 2002; Wang & Prodoehl, 2011). Zuo Gui Yin, a Chinese medication, is used to nourish the Kidney Qi, which is responsible for the heat associated with hot flashes (Wang & Prodoehl, 2011). Like Sage, Eleuthero, an adaptogenic or homeostasis herb, improves learning and memory (Foster & Johnson, 2006). In a study of 64 participants between the ages of 40-65, Brahmi monniera, which was found to have no effects on memories and psychological states, but on "a significant effect on a task requiring the retention of new information: the recall of unrelated word pairs after a short delay," which may was mediated by hippocampal antioxidant actions (Roodenrys et al., 2002).

No Internet sources show the number of conventional medications sold to treat symptoms to include depression or cognitive complaints or impairments. Drospirenone has been found to decrease VMS and negative moods; venlafaxine and fluoxetine, which are SSRIs, have been found to decrease hot flashes, but not severe VMS or perimenopausal depression that result from VMS (Batra et al., 2003; Brown et al., 2013; Karaoulanis et al., 2012; Shanafelt et al., 2002). A study on the positive effects of piracetam, a drug aimed to enhance memory and intellectual capabilities, have been found inconclusive (Flicker & Evans, 2015). The compound properties of piracetam (2-oxopyrrolidineacetic acid derivative), one of several smart drugs known as

nootropics, have been tested and found effecting in improving learning and memory and the flow of information, resistance of physical injuries (Gouliaev & Senning, 1994).

Release of substances in remedies. The formation of natural remedies to include herbal formulas, such as the Jit-Tra-Rom (JTR) aromatic and Liu Wei Di Huang (LWDH), vitamins, and minerals in the form of extracts, tinctures, concentrated powders, and tablets, giving broader insight into processes aimed to approach the natural physiological processes, such as regulating the menses to normal (Jearasakulpol et al., 2015; Löbenberg & Steinke, 2006; Montoni, Saingam, Suksaeree, Sakunpak, 2014; Zhao, 2015). Many extracts are formulated to approach the aging process by removing components from fruits using alcohol (Cheng et al., 2015).

Polyherbal formulas have been made to approach kidney deficiency in women because the deficiency has been found to relate to a menopause disorder when the normal physiological functioning of the kidney becomes damaged, injured, and compromised by disease (Fang, 2011; Jearasakulpol et al., 2015). Concentrated powder formulas used to approach perimenopause symptoms that may be linked to the kidney, liver, or blood stasis include False Unicorn, Life Root, Schisandra, Chai Hu, Huang Lian E Jiao Tang, Shan Yao, Tu Si Zi, Yi Mu Cao, Zi Bei Chi, Ziziphus, and Zuo Gui Wan (Hoffmann, 2007; Kronenberg & Fugh-Berman, 2002; Wang & Prodoehl, 2011; Zhao, 2015). The tablet, JTR aromatic powder, consists of 40 herbs to include the jasmine flower chrysanthemum flower aim to avoid exacerbation of symptom of kidney disease (Montoni et al., 2014).

The active ingredients, which should be compatible to natural remedies, can only be absorbed if the ingredients are released into solution from the dosage/tablet form (Löbenberg & Steinke, 2006). The form of tablets are based on the angle of repose (unslumped stacked power following dilution techniques using a mortar/pestle), bulk of density (uncompact volume), tapped

density (compacted volume), compressibility index and Hausner ratio (ability to settle/compress; Jearasakulpol et al., 2015; Montoni et al., 2014). After compression, other physical properties are established: weight variation (content uniformity by milligrams [mg]), friability (percentage will crumble/break), thickness, hardness (breaking strength), disintegration time (DT), marker/molecule content (active chemical ingredients used to calculate dosage presented on labels: polyestrogen, polyphenol, PE) plus microbial and heavy metal contamination, and quality parameters (usability, dissolvability; Jearasakulpol et al., 2015; Lam & Lam, 2014; Montoni et al., 2014). Natural polymers, which include banana powder and mucilage, are non-toxic extractions used as binders, diluent, and dissolvent used to increment the release rate and decrement the dissolution and disintegration time (Alam, Parvez, & Sharma, 2014).

The disintegration and dissolution of tablets and absorption of active ingredients in natural remedies into the body are either immediate or time-released (Löbenberg & Steinke, 2006). Disintegrants "promote the breakup of the tablet and capsule 'slugs' into more small fragments in an aqueous environment thereby incrementing the available surface area and promoting a more rapid release of the drug substance" (Alam et al., 2014, Introduction section, para. 1). Tablets are formed to fully disintegrate but some do not fully disintegrate, all units do not disintegrate, but pass the test, and some controlled release dosage form do not disintegrate in a timed manner; that is, within 30 min to 1.5 hr (Löbenberg & Steinke, 2006). Tablets that are not expected to totally disintegrate during the duration of the disintegration testing are classified as time-released (Löbenberg & Steinke, 2006).

Following testing and passing safety requirements, some medications receive a drug identification number (DIN; Löbenberg & Steinke, 2006). The labeling processes governed by the "Physician Labeling Rule" (PLR) established by the FDA further assist prescribers and

providers clearly understand the safety of the medications and which medications to prescribe to specific individuals (FDA, 2015b; Pinkerton, 2012). Regardless of the remedies, the acceptance of the nature of the impact of remedies has been minimal; thus, a clinical trial was warranted to increase capability and learning leverages whereby conclusions were based on the experiences of academic learners who are experiencing perimenopause symptoms (Hagel, 2011; Mann et al., 2004; Richerson & Henrich, 2012).

Conclusion

The results of the literature presented in Chapter 2 follows the literature-based discovery paradigm, which may be used to compliment meta-analysis and metasyntheses research. Meta-analysis involves bringing data from a number of quantitative studies together to create a single estimate of the effects of a treatment; whereby, metasyntheses involves merging the findings of qualitative research (Cooke et al., 2012; Ravindran & Shankar, 2015; The University of Sheffield, 2016). Although no specific standard for searching for the literature was used, this literature-based discovery encompassed literature that presented meta-analyses and metasyntheses (Kostoff, 2007). The process did not follow the systematic review process, because the aim of the literature-based discovery was not to answer the central research questions, but emerge relationships between the two forms of reviews to produce a novel virtual clinical trial whereby the results would answer the central research questions and emerge a future virtual platform to conduct clinical trials (Cooke et al., 2012; Kostoff, 2007).

Much literature reflects the functioning of the brain and the estrogen and their association with learning (Luo et al., 2013; Malone, 1990; McCormick, 2013; Monteiro et al., 2014; Parnell, 2007). For example, left-handedness, which is controlled by the motor context of the parietal lobe of the brain, when injured, the integration, processing, and analysis of sensory information,

constructive abilities, and expressions of ideas become impacted resulting in language suppression in writing, eating, and drinking, depression, confusion, reduced social interactions and problems and so forth (Cohen & Rein, 1992; Masud & Ajmal, 2012). It is apparent that the ACT*ION of knowledge is further impacted by perimenopause symptoms, which signify other various conditions and disorders, to include MDD, LLPDD, and PMDD because the functions of the brain become altered when estrogen withdraws (Batra et al., 2003; Collin et al., 2007; McCormick, 2013; Monzón et al., 2010; Nelson-Porter, 2014a). Regardless of the condition or disorder, when injury or pathogens interfere with the regular functioning of cells, triggers cause the body to experience cognitive complaints, such as brain fog, which may result in cognitive impairments (Ross et al., 2013; Schroecksnadel et al., 2007; Tangye & Tarlinton, 2009).

Because estrogen produced in the ovaries, epigenetic alterations, and the adult neurogenesis (new neurons) found in the adult hippocampus, which determines how human behave, are associative mechanisms of learning, memory, or depression, which tends to decrease with age, stress, or sleep deprivation, we as medical scientists might gain a better understanding how adult cells (neurogenesis/active estrogens) that depend on the episodic (mental searching/ re-encoding) and declarative explicit memory (specific knowledge/relational judgement) might be regenerated and conjugated during the perimenopausal aging phase to avoid further cognitive complaints, disorders, and impairments, specifically focusing on verbal cognitive functions at the regional (behavioral, neuroanatomical) not the executive level (e.g., memory systems; Berent-Spillson et al., 2012; Frank et al., 2006, Frick, 2013; McCormick, 2013; Monteiro et al., 2014; Smith & Mizumori, 2006; Wentz & Magavi, 2009). For this research, the universe (i.e., brain waves) was not assessed and the hippocampal of the participants were neither assumed to be engaged or disengaged unless cognitive impairment, chronic stress or cognitive complaint, to

include brain fog, were indicated in the selection process (Di Biase, 2009; Ross et al., 2013; Smith & Mizumori, 2006). The main focus of this research project was to discover if the perimenopausl women selection of natural remedies resulted from processing of: non-declarative (intuition) memory, implicit memory that rely on non-declarative memory (e.g., Basal ganglia/parietal cortex learning [caudate/cue-based spatial navigation to the location using WM and response strategies or putamen or implicit spatial memory (enhanced/repeated instructions/habits measured by implicit contextual learning related to general search times on new items)]), probabilistic learning (set of cues derived from referenced inferences stored in long-term memory) that rely on implicit spatial memory (putamen), or problem strategies (fast and frugal heuristics [System I] based on cues with positive criterian values, or aspiration levels based on intuitively appealing responses) compared to explicit spatial memory related to general search efficiency related to WM or declarative semantic memory based on contextual memory about the general knowledge of concepts (Ameqrane et al., 2014; Bøyum, 2013; Dougherty et al., 2008; Gigerenzer, 2001; Gigerenzer et al., 1991; Frank et al., 2006; Mednick et al., 2011; Mercier & Sperber, 2009; Oudman et al., 2011; Owen et al., 2011; Reas et al., 2011; Smith & Mizumori, 2006; Zelikowsky et al., 2012). The outcome of assessing implicit and semantic knowledge in this trial showed the noval analysis of the relationship between a priori and a posteriori knowledge (Tahko, 2011). "Surprisingly, the straightforward prediction that memories formed in the absence of the hippocampus lack permanence has never been tested" (Zelikowsky et al., 2012, p. 3396).

It was fair to state, more research that discusses perimenopause symptoms may focus on comparing the effects of nutrition on tryptophan and tyrosine in regards to decreasing and modulating norepinephrine, because SSRIs, although effective in approaching mild hot flashes,

have not been effective in approaching brain fog or severe hot flashes (Karaoulanis et al., 2012; Ross et al.., 2013; Shanafelt et al., 2002; Wurtman, 1994). Because SSRIs have not been effective in approaching severe hot flashes, and if proinflammatory cytokines may or may not have a direct association with hot flashes or severe VMS resulting in perimenopausal depression, then this further give rise that cellular inflammation maybe a symptom rather than a precursor to estrogen modulation or fluctuation (Karaoulanis et al., 2012; Sears, 2012). Although the surgical removal or suppression of gonadal hormones, SSRIs, and HRT have been found to relieve PMDD symptoms, such as depression and hypersomnia, and research shows no hormonal imbalances is associated with PMS and PMDD, thus, the effectiveness of HRT is associated with perimenopause rather than PMDD symptoms, giving rise to the uniqueness of these conditions (Batra et al., 2003; Collin et al., 2007; Jarvis & Morin, 2010).

Research is limited on if cellular inflammation that cause chronic disease is a symptom of perimenopause; thus, establishing if cellular inflammation (HDAC, cytokines) is symptom rather than a precursor to or cause of estrogen modulation or fluctuation because proinflammatory cytokines do not have a direct association with causing or eliminating hot flashes or severe VMS that result in perimenopausal depression (Karaoulanis et al., 2012; Monteiro et al., 2014; Sears, 2012; Stachenfeld, 2014; Sterns et al., 2009; Störk et al., 2004). There is an association between (a) SSRIs and inflammation because the tryptophan can be considered a precursor of SSRIs and inflammation results from tryptophan degradation and (b) inflammation and the active ingredients found in Vitamins C, E, synthesis of cholesterol and Vitamin D, or the enzyme Bromelain because these remedies have been found to reduce inflammation (Kelly, 1996; Nussey & Whitehead, 2001; Schroecksnadel et al., 2007; Stewart et al., 2005).

Research is further limited on if general inflammation of cells that derive from excessive fluid and has been found to result in brain damage is a symptom of perimenopause (Sears, 2012; Stachenfeld, 2014; Sterns et al., 2009). Fluid retention derived from reproductive surgery, low Na, or the enabling by Mg have been found to be a symptom of perimenopause; however, bloating and fluid retention, which most likely signify that inflammation needs to be viewed from the cellular level (Sears, 2012; Stachenfeld, 2014; Sterns et al., 2009). Much medical research discusses inflammation, however, does not distinguish if the inflammation, for example, associated with swelling and pain is considered classical, overt, or cellular inflammation (Harvard T.H. Chan, 2015; Collins et al., 2007; Sears, 2012). It may be fair to state the nine amino acid residues that make up the vasopressin that regulate water balance, appetite, body temperature, and sleep contain some compounds similar to Mg, hypotonic fluids, DDAVP, or HRT, which have been administered to reduce bloating, hyponatremia, fluid retention, or dehydration (Collin et al., 2007; McKee & McKee, 2008; Nussey & Whitehead, 2001; Stachenfeld, 2014; Sterns et al., 2009). If the results validate that dietary habits and herbal formulas relieve PMDD and perimenopause symptoms, the need for prescription SSRIs and HRTs may no longer be necessary (Batra et al., 2003; Collin et al., 2007; Jarvis & Morin, 2010; Zhao, 2015). Research has been proposed that hot flashes linked with perimenopausal depression may not need to be treated or approached as would depression linked with proinflammatory cytokines; thus, fluid retention and excess fluid categorized as general inflammation may not need to be treated as cellular inflammation as different forms of active ingredients would be warranted unless the inflammation was found to a symptom of estrogen fluctuation (Nussey & Whitehead, 2001; Karaoulanis et al., 2012; Monteiro et al., 2014, Estrogen section, para. 1; Shanafelt et al., 2002; Störk et al., 2004).

Assuming that if the body maintains an adequate supply of Vitamin D (D2 or D3 to be determined), the steroid hormones and estrogen levels will resume normal functioning and the increased pain, water retention, and poor concentration experienced during the premenstrual phases will be relieved given that an adequate supply of Mg and Mn are present (Collin et al., 2007; Itoh et al., 2008; Nussey & Whitehead, 2001). Many women in African nations who are not consuming cereal lack a significant amount of Mn if not consuming teas, coffee, and spices (Rakotoarisoa et al., 2012; Roth, 2006; Sakta et al., 2008). Possible through strengthening the Androstenedione and aromatase though the synthesis of Vitamin D, omega-3 fatty acid, Mg, and Mn intakes, healing of all dimensions associated with producing and regulating estrogen may be effective because the disease at the cellular level to include degenerative diseases, such as atherosclerotic vascular, cardiovascular, inflammation, accelerated aging, and so forth (Arshiya, 2013; Collin et al., 2007; Monteiro et al., 2014; Nussey & Whitehead, 2001; Sakta et al., 2008; Sears, 2012; Wang, 2011a). Because the functions of compounds found in natural remedies seem to have similar functions as the exons found in amino acids, the effects of custom-made BHTs and biofortified crops or bioengineered foods, such as soy, yams (cassava), corn, rice, potatoes, and peanuts, on perimenopause symptoms may warrant more discussions to compare with the effects of natural remedies that have not been chemically altered (Bakshi, 2003; Cakmak, 2008; Fernandez-Cornejo et al., 2014; Freedenberg, 2009; Global Panel, 2015; NIH, 2012b; McKee & McKee, 2008; Pinkerton, 2012; Schaub et al., 2005).

Based on associations concerning the impact of active ingredients synthesized in various natural remedies, understanding the impact at the cellular level as well as the molecular level is essential to gain a broader, but, specific knowledge base about interactions of the compounds to approach hormonal issues, such as perimenopause symptoms (D'Archivio et al., 2007;

McCormick, 2013). Based on the limitations surrounding conducting research at the cellular or molecular level, that is conducting experimental epidemiology research, this research aims to gain more of an understanding of the effects based on the beliefs and memory of a cohort of African American women about their experiences and perceptions of their health conditions (Maddux & Yuki, 2006; Norheim et al., 2012; PhRMA, 2007). The lack of access to research and the limitations to conducting research in developing nations on the effects of natural remedies, which give rise to socioeconomic factors, however, seems to be contributed to government restrictions (Manuh, 1998; Rakotoarisoa et al., 2012; Sharad et al., 2011).

In the case of favorable outcomes, the compounds associated with the selected remedies may undergo more trials to approach perimenopause symptoms that impact of the ACT*ION of knowledge experienced by African American compared to African women. Proposing that n-3 fatty acids or other natural remedies may increase or restore the normal functioning of adult neurogenesis (Freedenberg, 2009; Gómez-Pinilla, 2008; McCormick, 2013) is insufficient until researchers further consider if the compounds of natural remedies that are said to either activate or regulate cells or hormones are further studied in regards to their effects on hormones and enzymes that contribute the natural menopausal experiences. New natural compounds to include functional medicines in the form of tablets and liquids continue to be formulated to maintain and regulate the normal functioning of the cells (AACE Nutrition Guidelines Task Force; 2003; Collin et al., 2007; Montoni et al., 2014; PhRMA, 2007; Rouse, 1998; Yoles et al., 2004).

However, in the case of unfavorable outcomes, based on if women who experience perimenopause symptoms to include women who have not been diagnosed as menopausal via hormonal panels, continue to experience the same symptoms after consuming conventional treatments or natural remedies to approach symptoms, rendering genetic testing becomes more

necessary because the relationship between polymorphism and full cycle profiles of 17β-E_2 may be an indicator that the right natural approaches will be more conductive at the molecular levels (E_1, E_2, E_3) rather cellular level to approach sex hormonal symptoms (Bethesda, 2005; Buettner-Janusch, 2009; Diagnos-Techs, 2012; Elmissbah, 2013; Gorbach, 1984; Jasienska et al., 2006; Kelly et al., 2012; Luo et al., 2013; McIntyre, 2014; Wei, 2011). For example, the discovery of a natural remedy may be necessary to approach the negative alteration of the hippocampus and the impairment of implicit spatial memory to de-elevate the levels of glucocorticoid, reduce chronic stress, the LTP enhancement, stabilize E_2 that governs the hippocampal dependent memory, and reverse other damages derived from various sources (Chamniansawat & Chongthammakun, 2012; Chrousos et al., 1998; Frick, 2013, Owen et al., 2011; Nussey & Whitehead, 2001). Although the hippocampal memory system is essential for long-term memory and spatial place-based navigation using explicit spatial contextual coordinate information to mediate conscious competence, suppressive systems of the hippocampus are essential for WM and cue-based spatial navigation to mediate unconscious competence (Ameqrane et al., 2014; Oudman et al., 2011; Sukumar et al., 2012; Workman, 2010). Natural remedies to approach impaired spatial WM, procedural short-term memory, and Basal ganglia/parietal cortices and cognitive complaints may enhance the integration, processing, and analysis of sensory information, verbal and perceptual priming, constructive abilities, expressions of ideas though language, and motivation to complete tasks (Cohen & Rein, 1992; Nelson-Porter, 2014b; Postma et al., 2008; Ross et al., 2013). Although some herbs have no effects on memories, psychological states, or the rate of acquisition of information, retroactive interference, whereby new subsequent learning interferes with previously learned information, may become a tested phenomenon during trials where learners consume and record the effects of remedies consumed in short, however, same intervals

to regenerated/reactivate historical knowledge to include information encoded in the internal representations of space derived from wondering movements to conjugated with new learning acquired in a short period of time and compare to the effects of same remedies consumed at increased intervals during conditional trace learning whereby previously learned stimuli trigger an auto/innate response to not only derive at possible awareness but determine the connectivity degree of the networks (Booth, 2008; Crespo-Garcia et al., 2010; Gallistel & Balsam, 2014; Mednick et al., 2011; Reas et al., 2011; Roodenrys et al., 2002; Sukumar et al., 2012).

Chapter 3: Methodology: Instrument and Validity Measures

The purpose of this novel mixed methods clinical trial was to identify selections of natural remedies and assess which remedies (independent/experimental variables) positively approach perimenopause symptoms (intervening variables) that negatively impact the acquisition, comprehension, and transmission (ACT*ION) of knowledge (dependent/response variable) by evaluating the effects of the selection processes and choices based on if improved memories or beliefs about the outcome are implicit ITIs or TIs about the influences of higher education processes, learning, and practices (Dougherty et al., 2008; Gigerenzer, 1997; Wansink, 2010). Various symptoms of perimenopause (termed in India "rajonivrutti") include but are not limited to vasomotor symptoms, insomnia, fatigue, stress, mood swings, depression, poor concentration/ memory, headaches, dry eyes, muscle spasms, heart palpitations, UTI, vaginal dryness, cycle changes, breast tenderness, bloating, and visible distension (Collin et al., 2007; Goodman et al., 2011; Greendale et al., 2011; "Perimenopause Symptoms," n.d.; Setorglo et al., 2012; Shylaja et al., 2015). This *in vivo* clinical trial revealed remedies have anti-perimenopausal activities (PhRMA, 2007; Roche, 2013). Contributions based on integrative analysis were presented whereby healthcare practitioners and scientists may understand the results (Curry et al., 2009).

Research Method and Design

The mixed methods approach was appropriate because the qualitative preliminary data, descriptive quantitative outcome data, and qualitative outcome data were integrated to gain a better understanding of a unique population (Curry et al., 2009). Matched prospective trials involved studies designed in advance than determined retrospectively; that is, after the evidence has been reported (Slavin, 2008). The preliminary qualitative research did not aim to present the

perception on what African women thought about natural remedies, but aimed to set the tone to transcended memories, beliefs, and experiences to discover the reality about their experiences as perimenopausal women and learners (Kafle, 2011). The results of the preliminary findings did not unveil the level of difficulties perimenopausal women experienced with the learning processes because the greater society has yet to realize the effects of perimenopause and natural remedies on the learning process (e.g., hermeneutic; Kafle, 2011; Linnekin & Broad Leib, 2014; McCormick, 2013; Sommer, 1992).

The female African American participants in this trial currently experience one or more symptoms associated with perimenopause and are 20-40 years of age. The women in the trial were enrolled in a minimum of two courses whereby team participation was required in one course. Although random assignment studies tend to be small sample size of and focus on the exemplary implementation of experimental treatments, this virtual observational trial emerged limitations in finding qualified participants, however, provided meaningful and reliable learner health information (McFadden, 1973; Slavin, 2008).

Because the interventions of the cohort were not controlled by the PI, the study was considered observational (Norheim et al., 2012; Siminoff, 2013). The quantitative field data obtained during the clinical trial provided descriptive selections of natural remedies. Cognitive behavior or adaptive skills also include traveling to find natural remedies and recognizing the flavor of natural remedies through learning and memory (Gómez-Pinilla, 2008). The descriptive outcome data from the clinical trial assisted with transcending memories and beliefs about the outcome of their choice and selection, which led to the discovery about the effects of natural remedies to approach perimenopause symptoms that impact the acquisition and transmission of knowledge (Kafle, 2011; Roche, 2013; Rubio et al., 2010).

Research Questions

Central research questions based on a problem are inquires that guide a study (Leedy, 1997). The following two central research questions guided this study. Central Research Question 1 aims to elicit responses on how hormonal imbalances impact the ACT*ION of knowledge in higher education settings. Few studies have shown the interruption of the brain functioning by physical and biological stressors resulting from hormonal imbalances lead to memory loss, poor concentration, confusion, slower choice RT (e.g, naming each individual word in Stroop task/remedy in a clinical trial), and vertigo and weakness caused by a heavy flow (McCormick, 2013; Prior, 1998; Sommer, 1992). Many young African women are absent from the classroom when having a heavy flow and have no or limited sanitary products (Taylor, 2011). During premenopause, cognitive symptoms include difficulty concentrating and sleep disturbance, and behavioral symptoms include appetite increase or decrease, reduced activity interests, and social withdraw (Jarvis & Morin, 2010).

RQ_1. How do hormonal imbalances impact the acquisition, comprehension, and transmission of knowledge?

ASQ_1. What higher education policies or processes consider the negative impact of perimenopause symptoms on the ACT*ION of knowledge? Explain.

ASQ_2. What higher education subjects are difficult to comprehend while experiencing perimenopause symptoms?

ASQ_3. During active learning in higher education team projects, explain how your perimenopause symptoms impact social interactions whereby behavior changes cannot be established.

RQ_2. Which economic beliefs guide food selections to approach hormonal imbalances?

ASQ_4. Are selections to approach hormonal imbalances based on rationalism?

ASQ_5. Are selections to approach hormonal imbalances based on behaviorism?

Central Research Question 2 aims to elicit responses that may assist in determining which economic beliefs guide natural remedy selections that may approach hormonal imbalances. The selection of each remedy may help identify what drives the participants' preferences and values, whether it is the markets, price, or personal finance whereby female learners and academia may assist educational institutions with building learning leverage to achieve greater knowledge and performance (Hagel, 2011; Linnekin & Broad Leib, 2014; Zeckhauser, 1986). African women may be able to establish capability leverage after applying the results from the trial and outcome research derived from the African women who participated in the study and are experiencing similar economic or health disparities (ACOG, 2015; Hagel, 2011; Salas, 2004). The Associated Sub questions are inquires based on factors associated with the primary problem.

Instrumentation and Data Collection Methodology

The concurrent triangulation mixed methods design was used so determine if the inferences drawn from the data either conformed or collaborated with one another (Cameron, 2009). The sequential descriptive mixed methods strategy was not appropriate because all data collection instruments had been pre-designed; the quantitative instrument guiding the second phase of the study was not designed based on the results of the qualitative instrument (Cameron, 2009). The concurrent strategy involved collecting qualitative preliminary data, descriptive quantitative outcome data, and qualitative outcome data.

Data collection involved using three-part pilot-tested self-designed instrument or case report form (CRF) to obtain qualitative and descriptive quantitative data based on simple rather than complex choices (Appendixes A-C; Bellary, Binny Krishnankutty, & Latha, 2014;

Deshpande et al., 2011; Fehr & Rangel, 2011). Electronic instructions accompanied the instrument (see Appendix D). Section I of the CRF represents a cognitive self-assessment that involves learning, comprehension, and interactions. The perceptions about the environment were likely based on needs, recall, and experiences (Jan van de Kaa, 2010).

Section II of the CRF reflects behavior economic, the foundation for this research projected, which involves making decisions based on intuition or impulse which can be applied to specific areas rather than rational theories and not a conscious choice that involves measuring cost and comfort, which can be applied to general/universal areas (Gigerenzer, 2001; Jan van de Kaa, 2010; Posner, 1997). Bounded rationality encompasses decisions that are only made based on cognitive limitations, such as the information presented through observation of the behaviors in a laboratory or field instead of through modeling the implications mathematically for aggregate behavior, which follows comprehensive rationality (Jones, 1999; Posner, 1997). Transcranial ion techniques such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) were not used because the trial did not focus on the neural activity in the cortex of the brain that may derive preferences (Fehr & Rangel, 2011).

Approaching the underlying cause of each perimenopause symptom (attribute) is a decision strategy that may elucidate approaching perimenopause holistically (Maddux & Yuki, 2006). Testing a various number of natural remedies to approach specific symptoms may give rise to cultural acceptance of functional medicines (AACE Nutrition Guidelines Task Force; 2003; Jasienska et al., 2006; Linnekin & Broad Leib, 2014; Maddux & Yuki, 2006; Wansink, 2010). Although energy medicines provide a decisive impact to regulate the flow of the body's energies and organizing fields on gene expression, and controlling the growth of cells, this medicines was listed to not only prompt awareness but determine if an association can be found

between energy medicines an reduced perimenopause symptoms (Feinstein & Eden, 2008). Acupressure, accupoint tapping, brain wave activities (Alpha, Beta, Delta, Theta), and neuro linguistic programming (NLP) are example of energy medicines (Zimmerman, n.d.). Earthing, a process that involve grounding the body by walking outside or connecting to the earth without footwear whereby the electrons from the earth neutralize ROS and thereby reduce inflammation was not required but was inquired about to establish if the process can be association with the reduction in pain, blood clots, sleep disturbances, anxiety, heart palpitations, and inflammation (Chevalier et al., 2012).

In Section II, framing, a mental function that involves weighing the simple choices within each category based on aspiration levels to determine which may meet the objective, is evident by the categories and subcategories in the CRF (Jan van de Kaa, 2010). The mental function based on the clinical and condition management pathways involves assessing the symptoms and the characteristics of an expected outcome, and determining the best outcome measures prior to making a simple choice, known as judgement, was further evident (Jan van de Kaa, 2010; The University of Sheffield, 2016). Concurrent judgement involves deciding which remedy was most appropriate to relieve symptoms based on real world events, such as clinical trials (Deshpande et al., 2011). The degree at which the selected remedies are believed to relieve symptom is deemed as a predictive judgement, which is based on theory, is evident in Section III of the CRF (Deshpande et al., 2011). Once a judgement had been made about the appropriate remedy, the participants recorded their choice on the CRF (Thompson & Subar, 2013).

Section III of the CRF reflects the evaluation-and-choice mental function, which involves the qualitative evaluation of the outcome of the choices that met the criteria based on improved memory and beliefs (Jan van de Kaa, 2010). This sequential choice behaviour strategy of the

clinical pathway aimed to coordinate the decomposed functions by analyzing if the constructed preferences selected, adjusted, or disregarded based on interpersonal or intrapersonal reasons resulted in cognitive consistency measured by improved memory or adjustments in beliefs and values (Jan van de Kaa, 2010). The perceptions and beliefs about the effects of natural remedies, however, may differ across cultures (Maddux & Yuki, 2006).

The instrument was partially tested by a 33 year old African American woman pursuing an Associate's degree in nursing. The instrument was fully reviewed by a 25-year old African American woman who continues to experience bloating before her cycle and spasm in her left foot, known as hemidystonia, during her menstrual cycle (B. Nelson, personal communication, August 27, 2015). Hemidystonia, which differs from arthralgia and myalgia, is associated with spasms experienced on one side of the body (LeDoux, 2009). The results of the pilot clinical review showed that women may have difficulties understanding the terminologies and conditions listed if the conditions have not been diagnosed. The outcome research, which examined the perceived effects of the natural remedies on the symptoms associated with perimenopause, aimed to evaluate the quality of instrument and selections that may impact learning capabilities (Curry et al., 2009). Because the three forms of data collaborated with one another during the interpretation phase, the actual study commenced as planned.

Human subject protection. The HIPAA privacy and security rules require that personal name and any other identifiers of participants be eliminated from the results (Duda et al., 2014; FDA, 2015a). Participants were fairly selected based on the criteria and provided an informed consent form to sign, which included the benefits of the study and an assessment of the risks (see Appendix E; Rice, 2013). Destruction of non-published materials related to the study will follow

the 2005 European Commission Directive in that the materials will be destroyed in 20 years of reporting (Duda et al., 2014; FDA, 2015a; Verheugen, 2015).

Sampling and data collection process. Over a period of 6 months, several African American women were asked verbally or electronically to participate in this clinical trial. Black women have been said to experience PMS more regularly than women of other races and African American women in the United States share similar DNA and economic and health disparities as women in Africa, thus, African American women participated in this clinical trial (ACOG, 2015; Batra et al., 2003; PhRMA, 2007; Prior, 2013; Salas, 2004). Although a brief period of intuitive distraction by physicians has been found to be more for diagnostic classifications, using both conscious and unconscious processes was most effective to qualify the women (De Vries et al., 2010; Stolper et al., 2010). The prescreening process was characterized as using both methods.

Based on claims that Black women experience PMS more so than others, we must further note, "there has been no genome-wide association study (GWAS) or generalization study published to date on AM [age at menarche, which between the ages of 12 and 15] or ANM [age at natural menopause] with an African American cohort" (Prior, 1998; Shylaja et al., 2015; Spencer et al., 2013, p. 2). The GWAS involves mapping genes for complex traits by assessing the association between the difference in the SNPs and phenotypic trait resulting from genetic polymorphisms (Norheim et al., 2012). Biologists have proposed that humans are biologically different by average frequencies of a few polymorphic genes and not by clusters of genes or heritable traits; thus, race should not be used as a proxy for medical approaches (Roots, 2013).

> A gene X that regulates drug metabolism can vary with a gene Y on a sex chromosome, but there is no race chromosome or race gene Y for X to vary with. As a result, doctors have a reason to study sex differences but not racial differences in drug response and a

> reason to use sex but not race as a proxy for response when deciding how best to treat an individual patient. Sex has more explanatory and predictive power in the clinic because there are genes for sex and good reasons to believe that the genes for sex and some genes for drug metabolism are concordant. (Roots, 2013, p. 1181)

Because Black women in the United States and in Africa are descents, the women genetically differ by just 10%-15%; although the blood type O+ dominates and Blacks have high O+, A+, and B+ blood types, determining percentage of the blood types of women in Africa would involve constructing a geographical gradient of increasing and decreasing frequency of genes to form a comparative analysis (American Red Cross, 2015; Buettner-Janusch, 2009; NCHPEG, 2015; Udomah et al., 2015). When studying the human evolutionary relationship using the Rh blood group in Africa, the Rh-negative type (5%) was found to be the much less common (Westhoff, 2010). One study covering four North African regions showed DCec as the highest of the Rh phenotypes followed by Dce; however, another study in Cote d'Ivoire located in West Africa showed Dce (R_0r, R^0r) as the highest Rh positive phenotype and dce/dce (rr) as the Rh negative phenotype (Bogui et al., 2014; Halima et al., 2015). The D antigen in some Rh negative Rh phenotypes were identified in a study of 82 D-negative Black African descents although the "frequencies of the 3 genotypes were different in African Americans and mixed-race South Africans" than in South Africans (Singleton et al., 2015, p. 16).

Another report showed African Americans have the highest R_0 haplotype/Rh positive in the Dce (44%) and the highest r haplotype/Rh negative in the Ce (26%) category (Udomah et al., 2015; Westhoff, 2010). Although D^u and C^w, C^u, C^x, E^w, E^u, e^s, and e^i, which all are other alleles in the Rh loci, are not common in Caucasian population, the most probable genotype found in Caucasian Americans was Dce/ce (R_0r; Heiken & Rasmuson, 2009; Westhoff, 2010).

Pertaining to the Kell blood group, the frequencies of phenotypes K-k+, K+k-, K+k+, Kp (a-b+), and Js (a-b+) have been detected in Caucasian and African Americans, and Kp (a+b+), Kp (a-b+), Kp (a+b-), and null have been detected in the Sudanese tribe of which Kp (a-b+) had the highest frequency (Bethesda, 2005; Elmissbah, 2013).

> Kell blood group antigen Kp^a was most frequent in Sudanese population (99.8%), in compared with American population the frequencies of Kp^a (4%), and Kp^b (100%) antigens were in agreement with their frequencies in White and Black American. The frequency of Js^b antigen was close to White American (99%), but higher than Black American (80%). Kp (a-b+) phenotype was detected in high frequency (93%), which was near to White (98%), and Black Americans (99%). (Elmissbah, 2013, p. 2)

In addition to comparing the phenotypes of African Americans, considering how genetics influences taste is essential to gain more insight into the similarities in the DNA of African descents. Medical researchers to date have yet to understand the genetic basis of complex traits and how diseases emerge as a result of the complexities (Campbell et al., 2012).

> Non-Africans have two main haplotypes, the taster PAV and nontaster AVI haplotypes, which together account for 99% of sampled chromosomes. In contrast, among Africans, in addition to the high-frequency PAV and AVI haplotypes, we also found the ‘‘intermediate’’ AAI haplotype at moderate to high frequency (between 14% and 23%) and the ‘‘intermediate’’ AAV haplotype at lower frequency (~1% and 2.5% in West Central and East Africa, respectively) . . . The AAI and AAV clades were located intermediately between the divergent PAV and AVI haplotype clades. The absence of reticulations among haplotypes in these networks suggests that little recombination has occurred in the coding exon of TAS2R38. (Campbell et al., 2012, p. 1144)

Taste stimulation in additional to hormonal status has the capabilities to modify salvia production (Chiappin, Antonelli, Gatti, & De Palo, 2007). Salivary testing can be used to obtain not from the 99% of water in saliva but from 1% of the biological fluids (saliva/serum) excreted from oral cells to analyze the gene expressions/DNA for forensic identification and biomarker profiling of estrogen and progesterone or non-steroids and protein polypeptide or for the concentration of strong or weak ions (e.g., K+, Mg2+, Ca2), protein compounds, fatty acids, and E_2 (Chiappin et al., 2007; Diagnos-Techs, 2012; Jasienska et al., 2006; Jensen, 1983). Buccal swab testing involves processing salivary or vaginal secretions with lysis mix to bind with beads whereby DNA will be extracted after washing the beads (ThermoFisher Technical Support Representative, personal communication, January 4, 2016). Serum and urine testing have been found to be inadequate to test for the intracycle variation in E_2 levels (Chiappin et al., 2007; Jasienska et al., 2006).

In a study salivary testing premenopausal healthy women, the results substantiated that a relationship exists between polymorphism and full cycle profiles of 17β-E_2 (Jasienska et al., 2006). Jasienska et al.'s (2006) study was conducted during the duration of one entire menstrual cycle and the "E_2 values from 18 consecutive days of each cycle aligned on day 0 were used in analyses" were recorded (p. 2132). Perimenopausal women were not considered because the female participants aged 24-36 who were not taking steroids were diagnosed as premenopausal healthy women (Jasienska et al., 2006). "A typical menstrual cycle is 28 to 30 days and the body temperature is biphasic, elevating on day 14 to day 15. . . It is important to note, however, that it is not only the current cycle that determines egg quality; the regularity of the previous cycles also play a role in the quality of the current egg" (Wei, 2011, p. 7). Thus, for this study, although gene expressions were not conducted because of cost and limited access to assays, women were

informed to conduct Stages I, II, and III of the actual clinical trial for a period of 7 days and to start with consumption starting the day prior to or the first day of the flow of their menstrual cycle or immediately if no menstrual cycle flows (Jasienska et al., 2006; Thompson & Subar, 2013; Wang, 2011b).

Race was reflective in this clinical trial because differences in the intelligence quotient (IQ) have been identified to have some genetic component based on race, which is hereditary (50% genetic-50% environmental; Rushton & Jensen, 2005). Because salivary testing, such as hormonal and Buccal swab testing (PGx) to obtain DNA, was difficult to obtain, age was reflective of the perimenopausal condition/symptoms because during the last reproductive years, the activity of the HPA axis when altered changes the sensitivity of the gonadotrope (Loreti et al., 2009). African American women, thus, between the ages of 20-40 experiencing perimenopause and enrolled in a minimum of two higher education courses, whereby one course involves team participation, were emailed the three-part CRF. Age-related memory defects may cause disrupted default network connectivity and encoding and retrieval of memory, whereas, the self-focused spontaneous cognition or mind wandering disrupts the successful execution of many demanding cognitive tasks (Harrison et al., 2011; Reas et al., 2011).

Cognitive complaints (brain fog) and cognitive impairments as well as chronic stress; thus, were factors in the selection process to attempt to identify if the hippocampal of the African American women was possibly engaged or not engaged and whether scientific research can emerge supporting how genetic factors instead of stereotypes, stigmas, and neurogenesis influence learning capabilities using race and reproductive age as confounding factors compared to race and chronological age as confounding factors (Berent-Spillson et al., 2012; Owen et al., 2011; McCormick, 2013; Ross et al., 2013; Rushton & Jensen, 2005; Schroecksnadel et al.,

2007; Smith & Mizumori, 2006; Tangye & Tarlinton, 2009; Wentz & Magavi, 2009; Zelikowsky et al., 2012). If a longer response times (i.e., classification and recall time) and less response fluency (verbal expressions) are associated with greater deactivation of the hippocampus; then a decline in articulation (verbal skills) and slower choice RT, which involves making simple decisions (e.g., identifying, selecting and consuming a natural remedy to approach a symptom, which is situational stimuli) if evident in hormonal women furthermore may be an indicator that their hippocampus and default network are disengaged (Berent-Spillson et al., 2012; Maki et al., 2002; Moss-Morris & Petrie, 2003; Reas et al., 2011; Sommer, 1992). During the midluteal phase when estrogen is high, estrogens stimulate the prefrontal-hippocampal connectivity enhancing verbal articulation and verbal cognition (Berent-Spillson et al., 2012; Maki et al., 2002). Patients who experience CFS or other mood disorders may experience slower RT when encountering distractors (e.g., Stroop tasks; Moss-Morris & Petrie, 2003).

If the conditioning protocols that involved pairing the CS with an UCS took place and if the hippocampus is disengaged, then learning most likely have occurred prior to the CR (i.e., selection/consumption decisions), however, learning may be expressed differently (Gallistel & Balsam, 2014). The speed of learning may be measured based on the ratio of the time between US's (cycle time) and the CS-US interval duration (trial time), which the brain tissue encodes this experiential fact (Gallistel & Balsam, 2014, p. 137).

Stage II of this clinical trial involved the recording of the polygenic, phenotypes, symptoms, and intake of natural medicines for 1 week. Polygenic constitutes the outward expressions of phenotype, such as skin, hair, and eye colors, such as bluish, brownish, and greenish, have not been a meaningful way to assess human variation (Jackson-Mann, 2004; Lewis, Jurmain, & Kilgore, 2012). The women who partook in this race-aged based clinical trial

was asked to document their symptoms and the medical history of their maternal parent to note inheritable menopausal conditions; as physicians usually respond based on ancestry information (De Vries et al., 2010; Roots, 2013).

Self-reported patients with CFS, depression, and chronic pain who believe that their condition is physical in nature have biases when processing information through attentional or memory (Moss-Morris & Petrie, 2003). Research showed that patients with CFS self-report somatic symptoms or level of disability in an interpretive catastrophic or over-generalized biased manner and not in an attentional informational process biased manner (Moss-Morris & Petrie, 2003). Because some illness-related self-reports have failed to tell the origin of their thoughts that leads to beliefs resulting in negative reportings, distorted beliefs, and maintained pathogenic cognition, during the pre-screening processes, the participants were asked if their annual physicals, pap, and blood works were completed (Moss-Morris & Petrie, 2003).

No members from the female cohort were suggested which interventions to select and consume during the trial. Deliberate reasons were the foundation for each choice listed, thus, deliberate analysis and intuition were used by the PI during the analytical processes (De Vries et al., 2010). "Knowing the patient's narrative and its interpretation by an experienced GP [general practitioners] can help trainees and medical students to understand both aspects of diagnostic reasoning and enable them to refine their knowledge base" (Stolper et al., 2010, p. 201).

Seven days were essential because patients have been found to do well after taking medications (SSRI) for PMDD after 1 week with no negative side effects (Batra et al., 2003). To attempt to ensure participants did not cross contaminated, participants were instructed to record current conventional medications and natural supplements, continue taking prescribed medications, and read the label of remedies selected prior to consumption. "Studies indicate that

fewer than half of patients with cancer actually tell their physicians they are using some form of complementary or alternative medicine" (Siminoff, 2013, p. 4). Prior to the study, the participants were informed that the cost of purchasing their natural remedies and medical examinations were the responsibilities of the participants. Once each participant completed each individual section of the instrument, the data were forwarded to the primary trial investigator.

Data monitoring plan. The safety of the participant was most important and required carefully consideration. Adverse effects and the recommendations to adverse effects were documented to ensure the safety of each participant. Adverse effects to foods, herbs, and vitamins, and homeopathic remedies may derive from fillers (substitutes) and exposure to highly toxic contaminants (Nelson-Porter, 2015a). "Precautions are more associated with the source materials rather than the treatment processes, in that the maximum amount of alcohol has been mandated by the FDA" (Nelson-Porter, 2015a, p. 17).

Participants who are allergic to unknown foods were advised to refrain from selecting that food. An independent clinical trial sponsor (CTS), data safety monitoring board (DSMB), clinical research associate (CRAs) from a contract research organizations (CROs), or endpoint adjudication committee (EAC) were not contracted to monitor the progress, safety, or risks of this research or the data, because the trial was conducted virtually and using natural remedies are not governed by the FDA (Inc Research, 2015; WorldCare Clinical, 2015). The CTSs include members of government or regulatory agencies who delegate, monitor, and evaluate the processes, toxicologies, and technologies surrounding trials because of profound interests in advancing regulatory science, which involves understanding regional and cultural sciences through the development of "new tools, standards, and approaches to assess the safety, efficacy,

quality, and performance of FDA-regulated products" (FDA, 2012, 2011, p. 5; WorldCare Clinical, 2015). The PI of this novel clinical trial will serve in these roles.

A DSMB who are assigned by the CTS develops monitoring plans to monitors the outcome of mostly high risk or vulnerable populations and validity of the trial (Duda et al., 2014; FDA, 2015a; Verheugen, 2015). Risk-based monitoring involves devising specific plans to ensure the data collection protocols and safety of the patient are not at risk (WorldCare Clinical, 2015). Information risk management (IRM) involves documenting the digital process (Inc Research, 2015). To detect risks, adverse reporting was sectioned in the research instrument for participants to record effects and a daily phone call was conducted to each participant to encourage each followed the reporting process concerning the intakes (see Appendix F; Thompson & Subar, 2013). Mitigation plans are devised for risks that cannot be avoided (Inc Research, 2015; WorldCare Clinical, 2015).

If adverse effects caused reactions were reported by the participants, the PI evaluated, closely monitored progress, and either advised the participant to discontinue the food(s) selected, commence with the trial at a later time, or discontinue the trial altogether (Rancich et al., 2005). General pain, weakness, skin conditions, neurological and psychological conditions, such as anxiety and sleep disturbance, digestive conditions, asthma, allergy, and female genitalia complaints are various direct adverse effects (Stub, Kristoffersen, Alraek, & Musal, 2015). Direct effects could start day 1 and last past the duration of the trial. No indirect effects that may have been caused by the PI were reported (Stub et al., 2015). Although some symptoms that already experience may temporarily worsen, homeopathic aggravation also includes positive reactions expected from the intakes (Stub et al., 2015).

The project manager is a target monitor who handles the risks; whereas, the central monitors are usually off-site representatives who perform ongoing physical remote data reviews to include safety data (Inc Research, 2015). The CRAs are onsite monitors who conduct medicine accountability, view source documentations, and transcribe the data into the CRF. In regards to the data collection protocols, the data can be electronically captured, which is referred by as EDC. The source document verification/review (SDV/R) involves looking up sources although the SDV needs to be reduced (Inc Research, 2015). Making note or prejudgements about the data can be recorded in the charter, CRF, eCRF, or local standard operation procedures (SOPs) rather than in the actual protocol because changing the protocol would be more difficult because the sponsor or IRB has to approve changes to the protocol (Bellary et al., 2014; Inc Research, 2015; WorldCare Clinical, 2015).

Triggered monitoring involves review initiated by data triggers (Inc Research, 2015). On demand, members of the EAC conduct blind assessments of clinical data to view and document what events occurred (WorldCare Clinical, 2015). The goal of members of the EAC is to create regulations that eliminate bias by developing a source document, charter document, which belong to the core lab, and manual. All non-disclosure agreements (NDAs) do not have endpoint adjudication (WorldCare Clinical, 2015). Reviews are essential to adjudicate the triggers that are clinical relevant. Consensus review may lead to group think; thus, lead internal reviewers (IRs) rotate with others to avoid group think. The FDA calls for a BICR for complex quantification whereby each reviewer look at the data independently (WorldCare Clinical, 2015). Time to review data is critical because of budgets (Inc Research, 2015; WorldCare Clinical, 2015).

Data Analysis Methodologies

Data analysis is a reproductive process of emerging common themes from data collected (Curry et al., 2009; Leedy, 1997). Data collected from the qualitative preliminary data and outcome data were analyzed to emerge descriptive textual theme supported by direct quotes to give voice to the findings (Leedy, 1997). No software (e.g., HyperResearch™) will be used to organize and categorized the data; the PI for this novel clinical trial read an analyzed based on her own expertise as a scholar, qualitative analyst, and Naturopathic Doctor (ND).

If learning improved based on beliefs rather than calculated predicted behaviors, then behavior economics become well supported (Booth, 2008; Jan van de Kaa, 2010). Probit, angular, and Softmax, are analytical methods that could be considered. Although the outcome is based on overall responses from the intake of natural remedies, probit analysis would not be effective because the effects of certain amounts of concentration/potency of dosage on the cells (bioassay) is not the primary focus of this study, which could be considered a limitation in this study although obtaining the amount of consumption, which stems from low-involvement decisions, would have been difficult (Throne, Weaver, & Baker, 1995; Wansink, 2010). Research (Batra et al., 2003; Collin et al., 2007; Freedenberg, 2009; Kidd, 1996; Windham, n.d), although limited, has already reported that natural remedies and changing dietary habits have been some pro-effects in approaching perimenopause symptoms or the fluctuation of estrogen.

Angular analysis would have been appropriate if data from visuals derived from computer and imaging systems, such as functional magnetic resonance imaging (fMRI), Positron Emission Tomography (PET) and single photon emission computed tomography (SPECT), were computed (Batra et al., 2003; Bossaerts & Murawski, 2015; Kidd, 1996; Klucharev, 2014; Soon, Allefeld, Bogler, Heinzle, & Haynes, 2014; Turner, 2001). This study might have benefited

from Softmax if classifying the selected natural remedies into multiple categories was primary; however, if the results or specifics of this study are tested in larger clinical trials, then Softmax might be highly considered, as the binary classifiers may derive a medical solution or remedy that can be marketed to consumers (Bossaerts & Murawski, 2015; Duan et al., 2003; PhRMA, 2007). For example, when a choice is classified as TTB or TTL, then classification may be mapped to a binary classifier as displayed in Winner-Takes-All or Max-Wins (Dougherty et al., 2008; Duan et al., 2003).

The demand function will not derive from standard consumption model/conventional consumer analysis, such as utility-maximization, or the regret minimized regret (RRM) as the amount of consumption is not under investigation, but from logit analysis (De Bekker-Grob & Chorus, 2013; McFadden, 1973). Logit analysis involves establishing the probability a remedy will be selected from a certain population or a subset of population, such as the second-tied subgrouped nominal variables (McFadden, 1973) listed under the meal groups: breakfast, lunch, and dinner. The behaviors (physical actions/reactions) are the actual selection processes from the same measured categorical attributes/contexts/independent variables/nominal descriptive variables, which are randomly listed and categorized as a subgroup or subcategory (vectors of qualifiers; models; meat *vs* fruits); however, not ranked and not consisting of equal nutritional values, such as *meats* include baked chicken breast, baked turkey, beef liver, fish, and tuna, and fruits *include* bananas, blueberries, cantaloupes, grapes, guava, papaya, and pineapples, and so forth (Berg, 2003; Bouquet & Warglien, 1999; Gigerenzer, 2001; Loftus & Klinger, 1992; McFadden, 1973; Thompson & Subar, 2013). Although meal replacements, known as medical foods, contain various vitamins, these prepackaged products were not used in this trial because

the intake might have decreased the consumption of vitamins that can be derived from natural fruits and vegetables (Krasny, 2004).

Based on the principle of compatibility, the groups and subgroups (contexts) have structured relations (Bouquet & Warglien, 1999; Deshpande et al., 2011). Intentionally designed health-affecting options, however, differ from randomly constructed health-affecting options in that choice architects, which are often PIs, construct the choices to support an assumption or belief about a particular subject matter (Quigley, 2013). In addition to participant-centered care resulting in increased adherence, participants selecting from few choices have been found to return greater adherence (Siminoff, 2013; Wansink, 2010). In a preliminary study of 2374 participants, unexpectedly the study found that giving too much choice latitude reduced adherence; that is, a small percentage does not substitute a choice when permitted (Wansink, 2010). Because the categories reflect the four food groups consisting of similar type options, each option is medically associated with a symptom of perimenopause, and adherence seems visible, this trial may seem to be intentionally designed with health-affecting options that participant would select to approach specific perimenopause symptoms (Quigley, 2013). No participants were informed to select a particular choice option or given health information about any choice option prior to the start of the trial, thus, the health-affecting options were considered randomly constructed not to influence choice, but to note the fast and frugal heuristic problem strategies and aspiration levels and the perceived beliefs about the effects obtain from the active ingredients in the selections whereby a remedy may emerge to approach perimenopause or specific perimenopause symptoms (Gigerenzer, 2001; Quigley, 2013).

Cognitive judgement/decision-making. “In a conditional logit model, a [*observed*] choice among alternatives is treated as a function of the characteristics of the alternatives;

whereas, in a generalized logit model, the choice is a function of the characteristics of the individual making the choice" (So & Kuhfeld, 2010, p. 666). Note, observation stems from observing a copy of the alternative (presentation) not the actually alternative (representation) because stimuli changes perceptions (Berg, 2003; Skinner, 1985). The universal objects, selections or natural remedies (*X*), which consist of perceived attributes (*s*) of the vectors of qualifiers (*S*) rather than attributes (*x*) of alternative qualifiers (*B*) represent some stimuli that triggered the behaviors of the cohort of perimenopausal women (McFadden, 1973). Qualitative ("lumpy") qualifiers were the actual foods or remedies listed in this trial that have been found to be effective in approaching perimenopause symptoms or the fluctuation of estrogen (Batra et al., 2003; Freedenberg, 2009; Collin et al., 2007; Kidd, 1996; Windham, n.d).

Although research suggested that behaviors (selections) are best to be described by the function $x**(\theta)$, this descriptive study involved describing the behavior based on the models of cognition instead of statistical measures (Berg, 2003). Preceding the analysis of the descriptive quantitative outcome data based on the actual selection, findings showed that the selections derived from fast and frugal heuristics, aspiration levels, and learning processes that rely on or are related to various memory systems (Gigerenzer, 2001; Mercier & Sperber, 2009; Oudman et al., 2011). Description of the reasoning (underlying) processes are based on behaviors that are close to being optimal and produced by proximal mechanisms to include heuristics, habits, or forms of social imitation (Gigerenzer, 2001).

Heuristics are tips or cues are classified as being restrictive, flexible, or oppositional (Wansink, 2010). "Cues have the following three properties: They are strongly associated to the target, they are distinctive, and they are consistent across encoding and retrieval" (Tullis & Benjamin, 2015, p. 2). Anchoring or priming heuristics are subconscious cues that influence

behaviors (Quigley, 2013). Availability heuristic involves classifications based on how easily events or the purpose of objects can be recollected; whereas, representative heuristic involves classifications based on familiarity and stereotypes (Quigley, 2013).

Habits are non-associative automatic responses or unconditional reflexes generated from repeated behaviors that require less thoughts when activated by cues (situations) in the environment; whereas, intuition is an automatic, effortlessly judgement that does not warrant justification or explicit awareness or evaluation of cues (Jan van de Kaa, 2010; Kahneman & Klein, 2009; Lally, Van Jaarsveld, Potts, & Wardle, 2010; Malone, 1990). Based on the RPD model, *skilled or expert intuition* is recognition derived from validated, practical cues whereby answers are generated from memory stored data (Kahneman & Klein, 2009). Heuristic intuition (e.g., imperfect solution), which is associated with tacit knowledge and less reliable than skilled intuition, does not reflect the TMM; as heuristic does not derive from experience (disjunctive reasoning tasks/strategies) but from operations of memory (e.g., the appending process to space/mental blackboard/stored cues) of which the thoughts (mental models) do not have a tangible resource (e.g., Bouquet & Warglien, 1999; Bøyum, 2013; Kahneman & Klein, 2009; Toplak & Stanovich, 2002).

Although "neuroscience by itself is incapable of explaining the control of ingestion, because the internal and external systems are what the brain is required to organize," neuroscience mental models attempt to explain "how the human brain learns new information while not overwriting previously stored memories" (Booth, 2008, p. 3; Mednick et al., 2011, Introduction section, p. 1). Non-declarative or implicit memories, which include non-conscious memories, such as sensorimotor skills, perceptual skills, habits, priming, and so forth, are independent of the hippocampus (Maki et al., 2002; Mednick et al., 2011). Declarative or

explicit memories, which includes conscious memories of events, places, and general knowledge, are dependent on the hippocampus and usually consists of *decreased forgetting* after a post-encoding period of non-REM (nREM) sleep (Mednick et al., 2011). In the study, "When the Memory Fails, Intuition Reigns," the results supported that when the initial binding of items studied together occurs, the hippocampus becomes activated more formulating a recall database, and the manipulation of the premises support rational choices; however, when individual items not studied together recombine flexibly, associations that are ingrained habitually over multiple experiences drive intuition (Frank et al., 2006). The concept of LMM concept, which posits that solutions derive from the direct memory, reasoning processes, and logical operations and not inferences based on cues providing a partial truth-functional evaluation contrasts with probabilistic mental model (PMM; Bouquet & Warglien, 1999; Dougherty et al., 2008). Regarding the LMM, solutions can only be searched within the target context derived from input contexts that have been constructed based on reason, which is an outcome based on long-term reflections (Bouquet & Warglien, 1999; Gigerenzer et al., 1991). The context, however, must be organized to perform disjunctive reasoning task (Bouquet & Warglien, 1999). Disjunctive reasoning skill is the device use for generating "the tendency to consider all possible states of the world when deciding among options or when choosing a problem solution in a reasoning task" (Bouquet & Warglien, 1999; Toplak & Stanovich, 2002, p. 197).

Unless the participants studied health science or natural health, it would have been unrealistic for participants to select based on having to compute the value of each choice variables, such as the amount and speed of consumption, instructed consumptions, and measurement of the consumption and integration rates (Gigerenzer, 2001). Participants had the opportunity to search for information that gives reasons (references, cues) to choose a particular

remedy (i.e., fast and frugal heuristics) or search information and select the first particular remedy after searching other alternatives that meet or exceeded their aspiration levels, known as *satisficing* (Gigerenzer, 2001). Thus, when considering and applying the fast and frugal heuristics the PMM concepts as well may be applied to behavior healthcare research project, citing that internal cues (e.g., toxic antigens, pathogens) that trigger memory (e.g., memory B cells) serving as a validation measure (e.g, secondary immune response) to respond rapidly to cues (stimuli) based on a sequential search of past cues (e.g., remembering previous encounters with internal cues) may led to the development of behavioral decision-making models in the healthcare sectors (Dougherty et al., 2008; Tangye & Tarlinton, 2009).

The concept posited by PMM posits that set of cues derive from the related inferences stored in memory, originally drawn from the interplay between the structures of tasks and known environmental or group structures formed the bases of confidence (any choice is correct) and frequency (based on the number of correct choices) judgements; whereas, fast and frugal heuristics, reflective of PMM, posit that cues are found and selected based on predictor positive values that meet a criteria (Dougherty et al., 2008; Gigerenzer, Hoffrage, & Kleinbfilting, 1991). The one dimension of PMM, spontaneous confidence, which derives from probabilistic information (targets/cues/indirect inferences) from a known natural environment (i.e., structure stored in long-term memory, becomes activated when LMM (100% confidence) fails to activate (Gigerenzer et al., 1991). When beliefs are justified based on a priori (non- experimental /basics) or a posteriori (experimental) beliefs, confidence becomes evident (Gigerenzer et al., 1991; Thurow, 2006). PMM, thus, "assumes that inference about a criterion variable is based on cues that are probabilistically related to the criterion variable" (Dougherty et al., 2008, p. 200). Overconfidence, which involves making conceptual distinctions between confidence and

frequency of confidence of each belief and is not based on deficient cognition or motivation processes, tends to change when beliefs change; thus, overconfidence can disappear or invert at will (Thurow, 2006).

The TTB, which is also a basic algorithm of the PMM framework, implements the following based on contexts or having a limited memory buffer and maximizing (Bouquet & Warglien, 1999; Dougherty et al., 2008; Gigerenzer, 1997; Yu & Huang, 2014):

1. *Limited search*. The stopping rule, which involves using only a few predictor (cue) value inferences because of the sudden termination, is reflective of the fast and frugal concept; however, sudden termination in reference to satisficing is derived from the first cue that satisfies the searcher.

2. *One-reason decision making*. The inference is made by one predictor only and cannot/will not be reversed because of any higher ranking predictor.

3. *Step-by-step procedure*. The recognition principle whereby the recognized cue are found and selected based on the highest ranking value of the predictors from step-by-step searching of memory, thus, terminating the search when the other predictors do not meet the selection criteria.

4. *Lack of knowledge.* The recognition principle whereby choices are made randomly, that is by guessing, because no cues are recognized.

5. *Structures of information (environment)*. The recognition principle whereby choices are made based on using certain and not all of the structures of information (predictor values).

Choices based on satisficing information spur at the time of searching and embodies the criteria of the TTB (Gigerenzer, 1997). When Take The Last (TTL) is considered, "cues are generated sequentially from the most recently used to the least recently used" (Dougherty et al.,

2008, p. 200). Following the last trial target location requires memory of past cues that are not necessarily hierarchical, unlike minimalist algorism whereby the "cue generation is random," which "cannot be empirically validated" (Dougherty et al., 2008, p. 204; Yu & Huang, 2014). In regards to satisficing, "alternatives are encountered sequentially and aspiration levels stop search" (Gigerenzer, 2001, p. 4). Because effortful task-related cognitive searches underlie the "deactivation of anterior hippocampus and default network regions during elaborative verbal episodic memory retrieval," we may assume that during searches when inferences of memory overrides direct memory, inferences influence decision-making behaviors; when searches stop as a result of choosing the highest ranking memory option based on familiarity or at random when the options are all recognizable, which is discriminatory in nature (TTB), finding the discriminatory cue from random generated options (minimalist), finding the discriminatory cue based on the most to the least used in prior situations, such as with TTB and minimalist (TTL), or from meeting a certain aspiration levels whether it the highest or lowest, the searches seem to be coordinated by a distinct network rather than governed by the entire brain network (Dougherty et al., 2008; Reas et al., 2011, p. 11).

Normative-rational decision-making that involves choices based on *norms* (System II) or definite precise/presumed payoffs, goals, instructions, constraints, limited set of properties, or treatments or natural approaches are known as the expected utility (EU) theory [EUT/$U(x)$; expected value of current situations], aims to avoid risks (Berg, 2003; Bossaerts & Murawski, 2015; Gigerenzer, 2001; Jan van de Kaa, 2010; Mercier & Sperber, 2009). Consumption norms are what have been deemed more appropriate, typical, reasonable, and normal (Wansink, 2010). The prospect theory, which is also descriptive and draws from cognitive psychology instead of cognitive science, however, aims to capture human cognitive biases because kinks and

differential curvatures in the gain and loss domains are featured to capture risk attitudes to avoid risks by using methods such as the loss aversion, which presents agents with a prospect (mental shortcut) that a loss or gain will be achieved if a particular selection is chosen whereby losses are weighed higher than equivalent gains (Bossaerts & Murawski, 2015; Jan van de Kaa, 2010; Quigley, 2013). Here, descriptive related to the prospect theory indicates that decisions are actually generated by predicting present behavioral outcomes and not describing underlying processes of predicting the behaviors (Gigerenzer, 2001; Klucharev, 2014).

The most popular decision framework, the subjective expected utility (SEU), was not applied because the choice is based on the highest EU, which is never undecided; agents choose between mutually exclusive and exhaustive events, known as *states of the world*, representing uncertainties about the future mapped to predetermined value of possible outcomes, known as set of consequences (Gigerenzer, 2001; Nau, 2007). The expected utility model, thus, was not considered because this clinical trial did not aim to measure rational behaviors under uncertainty, and the random utility model (RUM) was not considered because the trial did not aim to summarize *unobserved* random (stochastic) choices, which are based on wealth maximization and the value function (Bossaerts & Murawski, 2015; Fehr & Rangel, 2011; Manski, 1988).

Various neurobiologists who study learning and memory of temporal information, how patterns of event emerge, and the mechanism of which information is retrieved believed that based on certain situations, choice under uncertainty seems to be based on mean-variance analysis (comparative values of investments) rather than the behavior portfolio theory (BPT; selection based on different risks associated with each subset of a goal) or the more traditional EUT (Bossaerts & Murawski, 2015, para. 9; Gallistel & Balsam, 2014; Statman, 2008). The functions associated with the utility mass model would have been appropriate to predict if the

benefits of natural remedies (outcome) were more useful than the benefits of conventional medicines (fixed critical variable) or the ordinal (i.e., quantile/e.g., the median) utility model would have been appropriate to predict which natural remedies is congruent to which conventional medicines; however, conventional medicines were not provided as a selection, which would have involved making complex choices (Fehr & Rangel, 2011; Manski, 1988). The BPT would have been appropriate to predict the selections based on different risks associated with each sub-goal; however, this trial does not focus on successful goal-directed actions, but more on S-R, habits, and learning (Grahn et al., 2008; Statman, 2008; Sukumar et al., 2012). In regards to neuroscience, reactions to unfair offers can be investigated so that scientists can increase acceptance by changing or manipulating activities (Klucharev, 2014).

Although no structured neuroeconomics model exists in regards to how the brain make choices, such as the revealed preference view, studying the neutron has validated the basics, when certain remedies are digested, the brain activities changes resulting in choices becoming less erratic making better optimisers (Bossaerts & Murawski, 2015; Fehr & Rangel, 2011). The neuroeconomic view of a modular, however, "raises new questions about the extent to which individual decisions can be improved by externalizing beliefs and values and forcing them into a single, coherent structure that is supposed to govern preferences across a wide range of situations" (Nau, 2007, p. 272). Although interests in how neutron activities stimulate observed choices have emerged and have been deemed irrelevant by economists, this method was not fundamental for this research because systematic biases and suboptimal choices relate to RUM (Fehr & Rangel, 2011).

Biological, technical, and instrumental limitations for this clinical trial further include the

In many cases, goals are not presumed because all information about a particular context is not and cannot be known or used because of limited knowledge about the context (Bouquet & Warglien, 1999; Gigerenzer, 2001). For this study, the context is not associated with a behavioral requirement; but the groups of foods (Smith & Mizumori, 2006). In one study where participants were given relevant information to read, the participants made a prompt decision or judgement after reading the information (De Vries et al., 2010). "Participants in the unconscious thought condition made the best decisions and outperformed participants who either thought consciously or decided immediately" (De Vries et al., 2010, p. 580).

Behavioral effects/outcomes/endpoint. After the findings revealed that the selections, which were member-reported, derived from fast and frugal heuristics, aspiration levels, and learning processes that rely on or are related to various memory systems, the effects of the selection processes and choices were evaluated for ITs or TIs (Bøyum, 2013; Deshpande et al., 2011; Dougherty et al., 2008; Gigerenzer, 1997, 2001; Mercier & Sperber, 2009; Oudman et al., 2011; Wansink, 2010). After reviewing literature on measuring the responses generated from the research, quantitative data analysts were solicited to assist with determining the most appropriate means to analyze the outcome data: optimal scaling analysis, simple correspondence analysis (SCA), multiple correspondence analysis (MCA), or orthogonal coding (Abdi & Valentin, 2007; IBM, n.d; McFadden, 1973; Starkweather, 2010). Six data analysts were asked to assist in the determination; however, only 1 responded that optimal scaling analysis may be the best option based on the reasons provided in the source that the other method "does not perform well for datasets that feature few observations, too many variables, and too many values per variable" (IBM, n.d., p. 1). The SCA and MCA represent unordered categories by row and columns whereby optimal scaling analysis is used (IBM, n.d.). Because the optimal scaling analysis is

useful in supplemental studies based on the solution or proven variables associated with a solution derived from this trial, another method was selected (IBM, n.d.).

The effects of the actual selection process and choice behaviors, which were based on the unconscious or subconscious process of information derived from sensory, social, and somatic (subliminal) cues, were measured by using the effect coding method and were supported by subjective memories and beliefs about the outcome of the selections (Kafle, 2011; Roche, 2013; Rubio et al., 2010). The effect coding scheme compared the contexts or the items listed under each subcategories associated with the independent variable to the entire sample or context selected (Starkweather, 2010). The endpoint is defined as "the measurement that will be statistically compared among treatment groups to assess the effect of treatment and that corresponds with the clinical trial's objectives, design, and data analysis" (Deshpande et al., 2011, p. 138). The discovery of the reality of the effects of natural remedies to approach symptoms associated with perimenopause, which impact the acquisition and transmission of knowledge, however, was not based on statitistics, but the beliefs and memories of the cohort members, which are supported by the works of several researchers (Kafle, 2011; **XXX, XXX**).

Although many mechanisms (explicit and implicit reasoning processes) drive inferences and decisions, ITs or TIs were drawn based on improved memories or beliefs about the outcome influences on higher education processes, learning, and practices (Bøyum, 2013; Frank et al., 2006; Maki et al., 2002). Research discovered that estrogen influences implicit memory, is responsible for the observed changes in cognition, and influences performance on tasks (Maki et al., 2002). Although Pavlov focused on the behavioral effects of stimuli (cues), and most American researchers continue to focus on the effects of the strengths of the conditional stimuli,

this projects focused on the cognitive and behavioral effects of choices selected and consumed by the female participants (Malone, 1990).

If processes or procedures become clearer, comprehension level becomes enhanced, and collaborations become understood and adaptive, then we can hypothesize that the positive effects of a targeted natural remedy consumed may become further validated as an effective remedy (PhRMA, 2007). The beliefs about the having a clearer understanding of the processes, an enhancement of compression levels, and an collaborations adaptation, however, can be perceived as an reward in conjunction with validating the effects of the natural remedies consumed. The reward-punishment based on behavioral preferences could be perceived as symptoms alleviated; however, learning decreased or remained constant or symptoms increased or remained constant; however, learning increased. Punishment based on behavioral preferences could be perceived as the symptoms and learning remained constant or symptoms increased and learning decreased based on the lack of selecting from the choice list of natural remedies or the selection of natural remedies aimed to improve the state of condition.

Validity

Internal validity was established by controlling selection, construct, attrition, confounding, and reporting biases (Lash & Fink, 2003; Oremus et al., 2012; The University of Sheffield, 2016). Although the participants experienced different perimenopause symptoms, selection bias was controlled not by grouping the women with similar symptoms in the same group (The University of Sheffield, 2016). Selection bias was controlled during the pre-screening phase by not focusing on specific symptoms that were to be approached with natural remedies and guessing about the status of the women who qualified but did not participate in the study based on the data provided during the pre-screening (Lash & Fink, 2003). To control for

attrition bias, information about the women who withdrew were recorded (The University of Sheffield, 2016).

Construct validity was established by listing compatible groups and subgroups in the CRF (Bouquet & Warglien, 1999; Deshpande et al., 2011). Although the Newcastle-Ottawa Scale (NOS) and the Jadad scale was not used in the systematic review process to establish face or content validity, the NOS scale may be the most effective to assess the overall quality of the instrument, as the modified Jadad scale was found to deem randomized controlled trials (RCTs) that measure the effects of herbal remedies on depression of low quality (Deshpande et al., 2011; Oremus et al., 2012; Yeung et al., 2014). To further establish face or content validity, future research may involve pilot testing the instrument with family members prior to the actual trial because family members influence the intervention choices (Siminoff, 2013).

Optimized non-rational behaviors, however, can be conducive of distorted beliefs whereby overconfidence and self-sufficiency stimulate "informational externality" (Berg, 2003). "Externalities occur when one person's actions affect another person's well-being and the relevant costs and benefits are not reflected in market prices [or not reflected in outcome reports]" (Library Economic Liberty, 2012, para. 4). The illusion of validity was coined to provide awareness that overjudgement or an unjustified sense of confidence can derive with clinical judgements (Kahneman & Klein, 2009). Because the selections of the choices were cohort-based based on their judgement, externalities were thus controlled to a certain degree diminishing overconfidence of the PI (Norheim et al., 2012; Siminoff, 2013; Stolper et al., 2010).

The cue assigned the highest therapeutic value to approaching a symptom(s) that stimulates the selection of particular choices is known as cue validity (Nelson-Porter, 2015a; Dougherty et al., 2008). "Cue validities in the form of conditional probabilities are assumed to

be based on the relative frequencies with which cues predict the outcome variable" (Dougherty et al., 2008, p. 200). Confounding by indication became an issue when women who did not consume the same remedies because the different symptoms aroused other differences (results) than the exposed (Lash & Fink, 2003; Psaty et al., 1999). The PI did not recommend any remedies or ceasing of intakes unless harm was detected. To control bias from uncontrolled confounders, although reported, the confounding effects were deemed unintended, unknown, or unmeasured (Lash & Fink, 2003; Psaty et al., 1999). The value in knowing the confounders that show a combination of the symptoms and exposure was not estimated or reconstructed but described by comparing the differences with others' outcome (Lash & Fink, 2003). To control selective reporting bias, although the remedies that were not selected were omitted from the results, all remedies consumed were reported (The University of Sheffield, 2016).

Internal validity was further established by allowing 2 African American women to review the framework. The conceptual framework supports the concept of behaviorism resulted from the interpretation of both forms of data obtain from the women (Cameron, 2009). The framework focuses on the difficulties of acquisition and transmission of knowledge during the perimenopausal phase when knowledge derived from external stimuli (KES) differs from knowledge stored in the subconscious (KSS). When learners become aware of an alternative approach to health problems, the information stored in their memory, which may be biased, may become replaced with an alternate solution that may rectify the problem (Hell et al., 1998).

External validity was established by generalizing the outcome to women living in Africa or supporting the results with results from prior credible studies (Leedy, 1997; Moss-Morris & Petrie, 2003). External validity may be further established by developing nations aid in conducting a clinical trial at the besides of women between the ages of 20-40 staying in hospitals

in Africa, as many do not have access to the Internet or in conducting translational research within underdeveloped African villages whereby equipped hospitals or medical research universities are at a considerable distance and are unable to house a population-based research project (PhRMA, 2007; Rubio et al., 2010). Because literacy and language barriers may exist, the PI may contract a DSMB who is fluent in English and African native languages, such as Hausa, Oromo, and Swahili (Nelson-Porter, 2015b; Thompson & Subar, 2013). This validity measure accompanied by a DSMB to monitor any high risks or vulnerable populations aims to ensure that all anomalies have been collectively exhausted or are mutually exclusive (Carlile & Christensen, 2004; Duda et al., 2014; FDA, 2015a).

Summary

Chapter 3 described the qualitative and quantitative descriptive methodologies, data collection processes, and design appropriateness for this clinical trial. This concurrent triangulation mixed methods trial did not aim to present the opinions of African American women on what they thought about natural remedies, but aimed to describe their experiences about how their perimenopause symptoms impact their academic learning processes and determine which economic beliefs guide natural remedy selections that may approach hormonal imbalances (McCormick, 2013; Prior, 1998; Sommer, 1992; Zeckhauser, 1986). The descriptive quantitative data aimed to show a quality of representation of specific nominal variables, representing natural remedies, which may be effective approaches to perimenopause symptoms (IBM, n.d.). The perceptions of the consequences of the impact of natural remedies were identified indicating a difference across cultures (Maddux & Yuki, 2006).

The clinical trial was appropriate to assess if natural remedies had anti-perimenopausal activities that impacted the ACT*ION of knowledge (Roche, 2013). The process did not

compromise the privacy, security, and health of the participants during the collections of data about perimenopause symptoms impacting academic progress, sections of natural remedies, and learning capabilities after the consumption of natural remedies (Duda et al., 2014; FDA, 2015a). For future research with a larger population, on-site visits may be necessary to validate data derive from others who do not have access to the Internet or whereby English is not their native language. Chapter 4 includes the findings from the pilot and actual clinical trials.

Chapter 4: Findings: Major Themes

The purpose of this novel concurrent triangulation mixed methods clinical trial was to identify selections of natural remedies and assess which remedies positively approach perimenopause symptoms that negatively impact the acquisition, comprehension, and transmission of knowledge in higher education settings by evaluating the effects of the selections and choices based on if improved memories or beliefs about the outcome are ITs or TIs about the influences of higher education processes, learning, and practices (Dougherty et al., 2008; Gigerenzer, 1997; Wansink, 2010). The data retrieved from the descriptive quantitative instrument that was not designed based on the results of the qualitative instrument were collected to support the data collected from the qualitative preliminary and outcome instruments (Cameron, 2009). The merged data that emerged from the case report form (CRF) aimed to answer the following questions:

RQ_1. How do hormonal imbalances impact the acquisition, comprehension, and transmission of knowledge?

ASQ_1. What higher education policies or processes consider the negative impact of perimenopause symptoms on the ACT*ION of knowledge? Explain.

ASQ_2. What higher education subjects are difficult to comprehend while experiencing perimenopause symptoms?

ASQ_3. During active learning in higher education team projects, explain how your perimenopause symptoms impact social interactions whereby behavior changes cannot be established.

RQ_2. Which economic beliefs guide food selections to approach hormonal imbalances?

ASQ_4. Are selections to approach hormonal imbalances based on rationalism?

ASQ_5. Are selections to approach hormonal imbalances based on behaviorism?

Chapter 4 presents findings from health data reported by an African American female cohort. The process of collecting and analyzing data consist of reporting the limitations and delimitations that may impede the research processes whereby inferences about the research methods and designs may influence replication. Determining if the inferences drawn from the data about the methods, designs, descriptors, or outcomes either conformed or collaborated with one another not only required a mixed methods data collection approach but a multi analysis approach (Cameron, 2009). The emergence of the major themes provided validity to the effectiveness of the methods and designs used to identify the selections of natural remedies that positively approached perimenopause symptoms that negatively impacted the acquisition, comprehension, and transmission of knowledge in higher education settings.

Limitations and Delimitations

[ADDED IN FINAL VERSION]

African American Female Cohort

[ADDED IN FINAL VERSION]

Cohort-Centered Consumption Report

[ADDED IN FINAL VERSION]

Concurrent and Intransitive Judgements

[ADDED IN FINAL VERSION]

Cohort/Observer Reported Medical Endpoint

[ADDED IN FINAL VERSION]

Chapter 5: Results and Recommendations

[ADDED IN FINAL VERSION]

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Appendix A: Qualitative Instrument (Pre-Approach Questions)

[CONTACT AUTHOR FOR INSTRUMENT]

Appendix B: Natural Healthcare Experimental Instrument (Actual Approach)

[CONTACT AUTHOR FOR INSTRUMENT]

Appendix C: Qualitative Instrument (Post-Approach Questions)

[CONTACT AUTHOR FOR INSTRUMENT]

Appendix D: Electronic Instructions

Instrument Section I - Virtual Clinical Trial by Brenda Nelson-Porter, ND

Hello [Name]

Thank you for signing the informed consent form. Attached is the first (Section I) of the 3-step virtual clinical trial processes. Please download the attached file, complete the three series of questions, save file, and return via email today by replying to ***this*** email and attaching the completed file. When saving this file upon return, add your name to the end of the file name. Step 2 (Section II) will be emailed to you upon return of this (Section I) completed file.

Thank you for your support,

Dr. Brenda Nelson-Porter, ND, DM, Primary Investigator (PI)
[phone number]

Instrument Section II - Virtual Clinical Trial by Brenda Nelson-Porter, ND

Hello [Name]

Attached is the second (Section II) of the 3-step virtual clinical trial processes. Please download the attached file, print, and read over the entire file at least 2 times prior to purchasing and consuming natural remedies (foods, vitamins, minerals, herbs, homeopathic formulas and supplements). ***DO NOT SHARE THIS INSTRUMENT WITH ANYONE***.

[**REMAINDER OF STATEMENT ADDED IN FINAL VERSION**].

If you have any questions, ensure to email or call the primary investigator. When saving this file upon return, add your name to the end of the file name. Step 3 (Section III) will be emailed to you upon return of this completed file.

Thank you for your support,

Dr. Brenda Nelson-Porter, ND, DM, Primary Investigator (PI)
[address]
[phone number]

Instrument Section III - Virtual Clinical Trial by Brenda Nelson-Porter, ND

Hello [Name]

Attached is the third (Section III) of the 3-step virtual clinical trial process. Please download the attached file, complete, and return via email today by replying to this email and attaching the completed file. If you have any questions, ensure to email or call the primary investigator. When saving this file upon return, save as previously instructed.

Thank you for participating in this virtual clinical trial.

Dr. Brenda Nelson-Porter, ND, DM, Primary Investigator (PI)
[phone number]

Appendix E: Informed Consent Form

Informed Consent Form

Date: _____

Participant Printed Full Name: _____ Age: _____

I agree to participate in a clinical trial constructed virtually by Brenda Nelson-Porter, ND, DM, primary investigator (PI). I understand the purpose and nature of the current mixed methods clinical trial, and I am participating ***voluntarily*** whereby no monetary exchange will be conducted presently or in the future for my participation. The trial is a three-part case consisting of:

[**ADDED IN FINAL VERSION**]

_____
Print Name

_____ _____
Signature Date

_____ _____
Phone Email

Appendix F: Phone Call Log

☐ Chronic Stress ☐ Cognitive Complaint, Brain Fog, Impairment ☐ Neither

Participant No.	Participant Name	Phone No.	Email

Call Date	Time of Call	Call Status	Comments