The impact of caffeine use across the lifespan on
cognitive performance in the elderly

A thesis submitted by

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Advisers: Robin Kanarek, Ph.D., Holly Talyor, Ph.D., Ayanna Thomas, Ph.D.
Abstract: Habitual caffeine consumption has often been associated with slowed age related cognitive decline in older adults. However, whether different cognitive processes are preferentially spared as a result of habitual caffeine exposure is unclear. Furthermore, it is unclear whether habitual caffeine consumption patterns based on current consumption or on a lifetime measure is a better for determining the long term effects of caffeine consumption. In the current study we gathered details about older adults’ current caffeine consumption patterns as well as details regarding their history of use, including the age in which they initially began consuming caffeine as well subjective measures of amounts of caffeine consumed earlier in life. These data were used in regression models to determine the relationship between caffeine consumption and performance on batteries of cognitive tests. While we found no direct associations between caffeine exposure and cognitive performance, we found that caffeine consumption interacted with participant SES in its association with MMSE scores, and with BMI in its association with inhibitory function and speed of processing. These findings were taken as evidence that caffeine’s long-term effect is protective in nature against the insults associated with low SES and high BMI.
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As early as the 7th century, when tea was introduced to Japan (Balentine, Harbowy, & Graham, 1998), caffeine has been an intimate partner in human history through the trade and consumption of the 60 plus plants that naturally metabolize it (Lundsberg, 1998). In fact, caffeine use has become so prolific that detectable levels of the chemical can be found in harbor seawater (Siegener & Chen, 2002). This nearly ubiquitous use of caffeine has prompted vast amounts of research directed at elucidating both the health and psychological impact of its acute and long-term consumption.

One avenue of this research has produced an inchoate body of literature regarding the relationship between caffeine consumption and the inevitable decline in health and mental ability that come with aging. Much of this research would seem to suggest that habitual caffeine use may be a means of slowing the process of cognitive decline (Hameleers et al., 2000; Jarvis, 1993; Johnson-Kozlow, Kritz-Silverstein, Barrett-Connor, & Deborah, 2002; Ritchie et al., 2007; van Boxtel, Schmitt, Bosma, & Jolles, 2003; van Gelder et al., 2007), but not all researchers are convinced that the relationship is that simple (Corley et al., 2010) and suggest instead that caffeine use may be a byproduct of other lifestyle variables such as socioeconomic status (SES) and that not all systems are equally impacted. Further, how “habitual use” is defined also appears to play a role in the magnitude of the relationship between caffeine use and its impact on cognitive performance. Specifically, if one is considering the effects of long term exposure, it is not enough to look at only consumption patterns of the last 12 months, one must also take into account the overall duration of exposure (Ritchie et al., 2007) as well as the nature of that exposure (i.e., changes in the habitual patterns: increased or decreased consumption, differences in source of consumption, etc.).

In the current study we sought to further elucidate the impact of long-term caffeine use on cognitive performance through a more detailed description of an individual’s caffeine exposure. To this end we took a latent cognitive variable approach
to determine the impact of caffeine consumption patterns on cognition with special attention on lifetime use measures. We anticipated that, like in previous studies, better overall cognitive performance would be associated with higher levels of habitual caffeine intake. Further, we anticipated that measures of lifetime use would be more strongly associated with cognitive performance as measured by our latent variables.

*Cognitive Decline*

As we age, we are subject to a variety of changes, some physiological, and some behavioral. Neurologically, we experience reduced cortical blood flow (Woodruff-Pak, 1997), cortical shrinkage of both gray and white matter (Salat, 2004; Thambisetty et al., 2010; Woodruff-Pak, 1997), decreased synaptic efficiency (de Magalhães & Sandberg, 2005) and decreased levels of neurotransmitters including dopamine and acetylcholine (Anyanwu, 2007; Peters, 2006). However, not all areas of the brain appear to be affected equally. That is, the frontal cortex and hippocampal regions are more severely impacted by the ravages of aging in that they both display greater atrophy and neurotransmitter depletion than other parts of the brain (Woodruff-Pak, 1997). With this focal deterioration, one should expect to see a predictable performance declines of processes thought to be supported by the frontal cortex and the hippocampal regions.

Indeed, the most commonly reported age-related cognitive deficits are on tasks of executive function (T. Chen & Li, 2007; Mahoney, Verghese, Goldin, Lipton, & Holtzer, 2010; Reuter-Lorenz et al., 2001), and episodic memory (Woodruff-Pak, 1997). Executive function refers to a range of processes including attention, working memory, inhibition, monitoring, and planning (Fusker, 2008), all of which are subject to reduced efficiency as a function of aging (T. Chen & Li, 2007; Mahoney et al., 2010). However, executive function also plays a part in the encoding and recall components of episodic memory (Fusker, 2008), suggesting that episodic memory deficits may be due to executive function deficits.
In addition to the domain specific deficits mentioned above, researchers have found evidence of domain general changes that impact multiple systems (Salthouse, 2009; Tucker-Drob, 2011). For example, Salthouse (1996) outlined well a prevailing theory that many age related deficits in cognitive ability may in part be due to reduced processing speed. Specifically, the theory proposes that the relation between speed and cognitive functioning is dependent upon two concepts. The concept of limited time refers to limitations on the amount of time allowed to complete a task. That is, a general slowing of processing speed leads to disproportionate use of time by earlier cognitive processes and thus leaves less time available for later processes. The related concept of *simultaneity* is based on the idea that by the time the later cognitive processes are completed information from earlier processes is no longer available, leading to a corrupted or degraded set of information available to complete the task at hand. Indeed, research has indicated a strong mediating relationship between speed of processing and other cognitive domains including memory, spatial ability (Finkel, Reynolds, McArdle, & Pedersen, 2007; Salthouse, 1993), and reasoning (Salthouse, 1993).

However, it would be folly to believe that all deficits in cognitive aging are the downstream effects of decreased processing speed as a function (Salthouse, 2009; Tucker-Drob, 2011). For example, one study exploring the relationship between processing speed and working memory on measures of fluid intelligence found that while processing speed explained some variation in working memory performance, once this effect was controlled for, variation in fluid intelligence was by in large accounted for by variation on the working memory task (Chen & Li, 2007). Furthermore, structural equation modeling implicates multiple domain general processes that appear to mediate the effects of aging on cognitive decline (Salthouse, 2005, 2009; Tucker-Drob, 2011). Thus, while the impact of processing speed may be disproportionately large, once age related variation is controlled, the impact of other general factors on cognitive
functioning is more salient (Salthouse, 2009). Taken together it is clear that any study looking at changes in cognitive function, especially in relation to aging, should take a multivariate approach to investigate the interrelationships between multiple domains.

*The Acute Effects of Caffeine Consumption*

The primary focus of research with caffeine in humans has been on the acute effects, or the observed effects of caffeine after complete absorption (around 35 – 40 minutes after consumption) and before being fully passed out of the system (around 4-12 hours after consumption; Fredholm, Bättig, Holmén, Nehlig, & Zvartau, 1999). Though caffeine is a non-selective antagonist of the adenosine receptor family, the majority of its effects seem to be mediated through the blockade of the A1R and A2AR adenosine receptor subtypes found throughout the body, but most prominently in the brain (Chen, Lee, & Chern, 2014; Fredholm et al., 1999). Specifically, the A1R receptor subtype is most densely populated in the cortex, cerebellum, hippocampus, spinal cord, and thalamic nuclei (Chen, Lee, & Chem, 2014; Fredholm et al., 1999). The adenosine A2A receptors, on the other hand, are most densely populated in the dopamine rich structures of the brain (Chen et al., 2014; Fredholm et al., 1999; Mori, 2014). The downstream effects of this antagonism include decreased cerebral blood flow through vasoconstriction, increased cerebral energy metabolism and cortical activity (Fredholm et al., 1999), as well as increased extracellular serotonin (Okada et al., 1999) and acetylcholine release as well as promotion of dopamine activity (Acquas, Tanda, & Di Chiara, 2002). Despite caffeine’s ability to induce widespread changes, the behavioral changes appear to be a result of changes in dopamine activity (Garrett & Griffiths, 1997).

Indeed, behavioral research suggests that increased dopamine activity in the frontal cortex is the primary reason for the acute effects of caffeine. That is, the most reliable acute effects of caffeine consumption, which include increased response speed (Brunyé, Mahoney, Lieberman, & Taylor, 2010; Childs & De Wit, 2006; Christopher,
Sutherland, & Smith, 2005; Harrell & Juliano, 2009; A. Smith, 2009, 2012; Sun, Zhang, He, Liu, & Miao, 2007) and increased performance on tests of sustained attention (Attwood, Higgs, & Terry, 2007; Brice & Smith, 2001; Childs & De Wit, 2006; Harrell & Juliano, 2009; Hewlett & Smith, 2006a; EEF Hogervorst et al., 2008; Oei & Hartley, 2005; A. Smith, Sutherland, & Christopher, 2005), rely on systems mediated by the dopamine rich areas of prefrontal cortex by means of modulated activity in the basal ganglia (Leisman, Melillo, & Carrick, 2013). Furthermore, beneficial effects have also been demonstrated in measures of executive control (Brunyé et al., 2010; Giles et al., 2012) and alerting function with no change in orienting function (Brunyé et al., 2010). While findings regarding caffeine’s effect on working memory have been mixed, with some finding a benefit (Giles et al., 2012) and others finding no change in response to caffeine consumption (Oei & Hartley, 2005; A. Smith, 2012), the overall pattern of results across studies is highly suggestive of an effect of caffeine in frontal cortex. However, research on caffeine’s long term effects indicate broader effects as a result of chronic exposure.

The Effects of Habitual Caffeine Use

While the effect of long-term caffeine exposure has been less well studied in humans, animal studies have provided insight into cortical and behavioral changes as a result of chronic caffeine exposure and these adaptations appear to provide some protection against both normal and pathological aging. For example, long-term exposure to caffeine results in protection against the onset of memory deficits in Alzheimer’s model mice (Arendash et al., 2009; Chu et al., 2012), protection against exposure to stress (Cunha & Agostinho, 2010) and a high fat diet (Alzoubi et al., 2013), and generally better memory performance in healthy mice (Fredholm et al., 1999). While preserved memory performance appears to be in conflict with studies suggesting no effect of acute caffeine treatment on memory function in humans (Foreman, Barraclough, Moore,
Mehta, & Madon, 1989; Hewlett & Smith, 2006b; Loke, 1988; Rogers & Dernoncourt, 1998), cortical changes in response to normal aging as well as chronic exposure to caffeine may result in a differential effect of caffeine in aged animals (Costenla et al., 2011).

As mentioned previously, caffeine has its effect primarily through its antagonism of adenosine receptors, particularly the A₁ and A₂A receptor subtypes (Fredholm et al., 1999), and the acute affects are primarily mediated through the A₂A receptor. Further, the A₂A adenosine receptor is primarily expressed in the basal ganglia with very low expression in other brain regions (Mori, 2014). However, there is a relative increase in the density of A₂A receptor expression as a function of aging providing a more prominent role in its modulation of neuronal function (Popoli et al., 1998) and a more active role in the modulation of memory performance (Costenla et al., 2011). Furthermore, while acute treatment with caffeine works primarily on A₂A receptors, likely due to less competition for binding from endogenous adenosine (Daly, Butts-Lamb, & Padgett, 1983), long-term treatment with caffeine results in an increase in the expression of A₁ adenosine receptors with no change in A₂A expression (Johansson et al., 1993), indicating an increased role of A₁ mediated modulation of hippocampal function (Cunha, 2001) and providing the possibility of a more pronounced effect of caffeine in this region. Indeed, long term exposure to high doses of caffeine has been found to increase neuronal proliferation within the hippocampus (Wentz & Magavi, 2009) as well as increased growth and spine density of dendrites in CA1 (Vila-Luna et al., 2012), together suggesting a preferential role in modulation of memory performance.

Of further interest, while the acute physiological effects of caffeine appear to focus on modulation of dopaminergic systems, the long term effects of caffeine do not. That is, while habitual use of caffeine results in increase serotonin and cholinergic receptors, there is no observed change in the dopaminergic system (Shi, Nikodijević,
Jacobson, & Daly, 1993). This would seem to suggest that the long term use of caffeine may have an impact on behavior, different than that expressed in acute treatment (Fredholm et al., 1999) and thus underline the necessity to determine the cognitive impact of long term caffeine treatment.

While research concerning the behavioral effects of long term caffeine use in humans is sparse, what exists appears to indicate a protective role. That is, increasing levels of caffeine consumption have been associated with better health in old age (Corley et al., 2010) as well as a significantly reduced chance of full dementia onset in patients with mild cognitive impairment (Cao et al., 2012). Further, research in healthy adults suggests that habitual caffeine consumption may be protective against normal cognitive declines associated with aging (Hameleers et al., 2000; Jarvis, 1993; Johnson-Kozlow et al., 2002; Ritchie et al., 2007; van Gelder et al., 2007), though the nature of the cognitive preservation is still unclear.

Of the seven studies conducted to date, six have included a measure of memory performance. Of these, four found a positive association with caffeine consumption and memory performance (Corley et al., 2010; Hameleers et al., 2000; Jarvis, 1993; Johnson-Kozlow et al., 2002), while the remaining two found no such relationship (Ritchie et al., 2007; van Boxtel et al., 2003). Four studies included a measure of response speed, all of which found a positive association with habitual caffeine use (Corley et al., 2010; Hameleers et al., 2000; Jarvis, 1993; van Boxtel et al., 2003). Four studies used a measure of verbal fluency, two of which found a positive association with habitual caffeine use, but only in women (Johnson-Kozlow et al., 2002; Ritchie et al., 2007) while the other two found no relationship (Hameleers et al., 2000; van Boxtel et al., 2003). Three used the Mini Mental State Exam and two of these studies found a positive association with habitual caffeine use (Johnson-Kozlow et al., 2002; van Gelder et al., 2007).
This pattern of results provides strong evidence of preserved speed of processing, as well as some preservation of memory function. However, the impact of caffeine on other cognitive systems affected by age, such as those sub-served by the frontal cortex (e.g. inhibition and working memory), has yet to be addressed. Further, as previously mentioned, the performance of one cognitive system can substantially impact the performance of other cognitive systems (Salthouse, 2009; Tucker-Drob, 2011) and thus it is important to determine what impact the preservation of one system (e.g., speed of processing) may have on other cognitive systems (e.g., memory).

The Current Study

The current study sought first to address individual differences between participants that may not have been fully accounted for in previous research. For example, the definition of “habitual” caffeine intake has been used loosely. With the exception of one study (Johnson-Kozlow et al., 2002), all of the previous studies have focused on current trends of caffeine use to define “habitual” caffeine use and ignored long term patterns of use as well as possible changes in those patterns (e.g. discontinuing use due to changes in health). Whereas most studies used questions such as “How many cups of coffee do you usually drink in a day?” (Jarvis, 1993), which only take into account recent trends, Johnson-Kozlow and colleagues (2002) included a measure of “lifetime use” by asking questions such as “How many years have you been drinking coffee?” and “How many cups of coffee did you drink per day?” Using these two values the researchers calculated a value of the number of cups of coffee consumed throughout the participant’s life, or “Lifetime Cups”.

Participants in the Johnson-Kozlow and colleagues (2002) study included community dwelling women and men aged 50 years or greater. Participants provided a measure of current and past caffeine consumption and then completed short and long term verbal memory tasks, a visual memory task, a trail-making task, a category fluency
task, and the MMSE. In men, current decaffeinated coffee consumption was associated with better performance on trail-making part b and current caffeinated coffee consumption with worse performance on the “WORLD backward” task from the MMSE. On the other hand, the results for women suggest a more complex relationship. Specifically, current coffee intake for women was non-significantly associated with better verbal memory performance while lifetime coffee consumption was significantly associated with performance on a visual memory task, both short and long term verbal memory tasks, as well as category fluency. In sum, these findings suggest that measures of lifetime caffeine consumption may provide a more sensitive measure of how long term caffeine consumption affects cognitive function and, further, that women may be more susceptible to the effects of extended caffeine exposure than men.

To more accurately account for lifetime caffeine use, we designed our questionnaire to not only establish recent trends in habitual caffeine use, but also to look at the individual’s caffeine history. The questionnaire was adapted from the NHANES Food Frequency Questionnaire (Thompson et al., 2002), from which included only items concerning caffeinated beverage consumption. We also added questions regarding life-long habits such as age of first use, periods of abstinence, average intake during various decades of life, and changes in the context (drink type) in which caffeine was consumed. In addition to caffeine use, we also included questions about current dietary habits as well as current and past physical activity habits. Further, as other studies have found strong associations between caffeine consumption and socioeconomic status (SES; Corley et al., 2010; Jarvis, 1993) we also included standard questions about current SES, as well as relative SES from throughout the participant’s life. Together with other general lifestyle questions, these questionnaires should provide valuable details to determine possible mediating factors of the effects of long term caffeine exposure.
Further, the current study expands upon previous studies that employed a single cognitive test to measure differences associated with habitual caffeine use. That is, while a single measure may appear sensitive to a particular variable, no task is a pure measure of an underlying cognitive construct and will include the recruitment of other cognitive processes necessary to complete the task. For example a simple choice reaction time task involves visual perception of an arrow presented in the center of a screen, comparison of that arrow to the rule maintained in working memory, motor planning based on outcome of the comparison, and the execution of the movement that is required to provide a response. By compiling a set of tasks that all purportedly rely on the same core underlying cognitive system into a single composite score we can more effectively focus on the cognitive processes involved in achieving each task individually (Tucker-Drob & Salthouse, 2009).

The authors are aware of only one study that has employed this type of analysis in exploring habitual caffeine use (Corley et al., 2010). This study focused on three main factors: a general factor, processing speed factor, and memory performance factor. However, the general factor was quite broad, including measures associated with executive function (e.g. letter-number sequencing and digit span backward) and the memory factor confounded measures of long term memory (verbal paired associates) with measures of short-term and working memory (letter-number sequencing, digit span backward, and spatial span). Furthermore, there was substantial overlap in the tasks used in the three factors, suggesting that there is room for improvement on resolution of the psychometric batteries comprising each factor. The current study seeks improve upon the batteries used in Corley and colleagues (2010) by using more focused and appropriate tests for each battery to minimize overlap between the factors and improve the resolution of each factor. As such, we employed a speed of processing battery and a medial temporal lobe battery validated in previous studies. Adapted from Gisky and Kong
(2008), the medial temporal lobe (MT) battery was designed to probe multiple domains of memory and included the Verbal Paired Associates, Logical Memory, and Face Recognition tasks. The speed of processing (SP) battery was modeled directly after the battery used by Salthouse (2005) and Tucker-Drob & Salthouse (2009) to demonstrate age-related cognitive decline in speed of processing and its relation to other cognitive processes and consisted of the Digit Symbol Substitution, Letter Comparison, and Line Comparison tasks.

However, as the MT and SP batteries ay not provide a detailed enough picture, we have included two exploratory batteries to further elucidate the impact of caffeine on cognitive function. As executive function plays a part in the encoding and retrieval processes of memory, the variability of previous findings may be explained in part by changes in executive function. To explore this possibility, our study employed two batteries designed to probe executive function. The frontal cortex (FC) battery, which consisted of consisted of the Backward Digit Span, Wisconsin Card Sorting, and Mental Control tasks, and was adapted from Glisky and Kong (2008) where it was found to be associated with better source memory performance. The second battery was exploratory in nature and consisted of tests of inhibitory function (IF), including the Stroop, Stop Signal, and Flanker tasks. While each of these tasks have been found to be uniquely sensitive to acute caffeine intake (Einöther & Giesbrecht, 2013; E. Hogervorst, Riedel, Schmitt, & Jolles, 1998; Sun et al., 2007; Tieges, Snel, Kok, & Richard Ridderinkhof, 2009), their sensitivity to the long-term effect of caffeine consumption has not yet been studied.

Importantly, while the tasks used in the FC, MT, and SP batteries have been used many times to explore age-related cognitive decline, caffeine’s influence on these tasks has not been well established, especially the effects of habitual use. As previously reviewed, habitual caffeine use has been associated with better performance on memory
and reaction time tasks, suggesting our MT and SP batteries should be sensitive to habitual caffeine use. With the exception of the Stroop task, which revealed conflicting results (no association - van Boxtel et al., 2003; positive association - Hameleers et al., 2000), the tasks in the IF battery have not been used in the context of caffeine use and aging, but have been found to be sensitive to acute intake of caffeine (Einöther & Giesbrecht, 2013; E. Hogervorst et al., 1998; Tieges et al., 2009). Further only two components of the FC have been used in studies of acute caffeine intake, finding positive effects on backward digit span (Childs & De Wit, 2006) and Wisconsin Card sorting (Snowden, 2008). However, given the sensitivity of these batteries to age related cognitive decline, as well as the positive effects of acute caffeine intake on the mentioned tasks, they represent a potential target for the effects of chronic caffeine use.

Hypothesis

The primary goal of this study was to determine what impact historical patterns of caffeine intake have on the current cognitive performance of elderly participants. The secondary goal of this study was to determine to what degree differences in cognitive performance may be affected by individual differences such as SES, as shown in previous studies (Corley et al., 2010). It was hypothesized that performance on the cognitive batteries would be associated with caffeine intake such that higher levels of habitual intake would be associated with the better composite scores on each battery. In addition, we hypothesized that these associations would be visible even after controlling for the impact of other individual variables such as SES, age, and health.

Methods

Participants

Recruited from a database of individuals who had previously indicated interest in taking part in psychological studies, participants were healthy females aged 55 – 75 years living in the greater Boston area. Potential participants were prescreened over the phone
and were invited to participate if they were community dwelling, non-smoking, had 
normal or corrected vision, suffered from no learning or cognitive disorders (e.g., 
schizophrenia, bipolar disorder, etc.), had no history of alcohol or drug abuse, and no 
history of head trauma, stroke, or seizure. Participants provided signed, informed consent 
prior to enrollment and commencement of study procedures. All recruitment and 
enrollment procedures were approved by the Social, Behavioral, and Educational 
Research Institutional Review Board at Tufts University.

*Questionnaires: Individual differences*

With the exception of the food diary, all survey data were collected via two 
online questionnaires. Participants filled out the questionnaires with the assistance of a 
trained researcher who could clarify items or transcribe the participant’s responses into 
the questionnaire to alleviate discomfort or unease at working with computers. The 
survey questions were divided into two questionnaires to provide a break and reduce 
fatigue: the Dietary Questionnaire (Appendix A) assessed general diet, caffeine 
consumption, and physical activity while the Demographics Questionnaire (Appendix B) 
collected general demographic information, SES, medical and health history, stress, and 
sleep patterns. The content of these questionnaires is described below.

*General Diet.* To determine general dietary patterns, participants indicated 
whether they were following any dietary restrictions (e.g., religious such as kosher, 
vegetarian, gluten free, lactose restriction, etc.). In addition to dietary restrictions, 
participants indicated how often they consumed breakfast, lunch, dinner, and between 
meals snacks as well as the most common composition of each meal. In addition to 
general food consumption patterns, participants indicated their alcohol consumption 
patterns in the last twelve months.

*Caffeine intake.* Caffeine consumption habits for the twelve months preceding 
the participant’s first visit to the lab were assessed using a subset of questions from the
NHANES dietary questionnaire (Thompson et al., 2002). The questions determined the use frequency for caffeinated and de-caffeinated sodas, energy drinks, coffee, and tea.

In addition to collecting details about the previous twelve months, we collected responses regarding patterns of caffeine consumption from earlier points in the participant’s life. Participants indicated the age at which they first started habitually consuming caffeine (defined as a pattern lasting greater than three months). In addition participants were asked whether they had undergone a period of abstinence from caffeine consumption. If they had, they were asked to elaborate, by indicating the age at which it occurred and the length of the abstinence period.

To further define the general patterns of caffeine consumption across the participant’s life span, we provided a series of visual analog scales (VAS) to approximate their caffeine intake. Participants were introduced to the VAS by the following prompt, “On the following scale, please indicate the average amount of caffeine you consumed per day. When rating your caffeine intake, avoid focusing on a single period in that time frame. Rather, consider your overall average intake for that time span. If an age range does not apply to you, please mark the “N/A” option to the right of the scale.” The scale was labeled with “No Intake” on the left delimiter to “Very High Intake” on the right delimiter. These values were defined, “For this scale, “Very High Intake” would be the equivalent of 12 or more cups of coffee, 34 cups of tea, 30 cans of soda, or 5 energy drinks. “No Intake” would reflect absolutely no intake of caffeine during the time frame.” The values used to define very high intake were equated based on a cup of coffee, tea, soda, and energy drink containing on average 100 mg, 30 mg, 35 mg, and 200 mg of caffeine respectively (averages compiled from Somogyi, 2010). Seven scales were provided. The first six scales corresponded to different decades of life, “20 – 30 years of age”, “30 – 40 years of age”, “40 – 50 years of age”, “50 – 60 years of age”, “60 – 70 years of age”, and “70 – 80 years of age”, the final scale corresponded to the “Last 12