Autonomic and Electrocortical Indices of Performance Monitoring and Source Memory Discrimination in Older and Younger Adults

by

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General Abstract

Reduced capacity for executive cognitive function and for the autonomic control of cardiac responsivity are both concomitants of the aging process. These may be linked through their mutual dependence on medial prefrontal function, but the specifics of that linkage have not been well explored. Executive functions associated with medial prefrontal cortex involve various aspects of performance monitoring, whereas centrally mediated autonomic functions can be observed as heart rate variability (HRV), i.e., variability in the length of intervals between heart beats. The focus for this thesis was to examine the degree to which the capacity for phasic autonomic adjustments to heart rate relates to performance monitoring in younger and older adults, using measures of electrocortical and autonomic activity.

Behavioural performance and attention allocation during two age-sensitive tasks could be predicted by various aspects of autonomic control. For young adults, greater influence of the parasympathetic system on HRV was beneficial for learning unfamiliar maze paths; for older adults, greater sympathetic influence was detrimental to these functions. Further, these relationships were primarily evoked when the task required the construction and use of internalized representations of mazes rather than passive responses to feedback. When memory for source was required, older adults made three times as many source errors as young adults. However, greater parasympathetic influence on HRV in the older group was conducive to avoiding source errors and to reduced electrocortical responses to irrelevant information. Higher sympathetic predominance, in contrast, was associated with higher rates of source error and greater electrocortical responses to non-target information in both groups. These relations were not seen for

errors associated with a speeded perceptual task, irrespective of its difficulty level. Overall, autonomic modulation of cardiac activity was associated with higher levels of performance monitoring, but differentially across tasks and age groups. With respect to age, those older adults who had maintained higher levels of autonomic cardiac regulation appeared to have also maintained higher levels of executive control over task performance.

Acknowledgements

Table of Contents

List of Tables

List of Figures

Chapter 1: General Introduction

Why is autonomic function of interest to psychology?

Cardiovascular competence and cognitive performance are inextricably entwined at the physiological level. The brain has enormous energy requirements for its small size, comprising 20-30% of the body's total usage (Benton, Parker & Donohue, 1996). In cognitively demanding conditions, absorption of glucose from the blood is measurably accelerated (Donohue & Benton, 1999; Scholey, Harper & Kennedy, 2001), and limitations in the availability of cortical glucose can have negative effects on performance (e.g., Benton et al., 1996). Having no good way to store energy, the brain is fundamentally dependent on the circulatory system to supply it with glucose and oxygen (Scholey et al., 2001). Therefore, it is highly likely that cognitive performance is related to individual differences in the responsivity of the autonomic nervous system. It is also possible that the capacity for autonomic control may influence cognition independent of the general effects of age on processing speed (e.g., Salthouse, 1996), frontal lobe decline (e.g., Raz, 2000), or inhibitory control (e.g., Chao & Knight, 1997). If so, cognitive performance for those who have maintained higher levels of autonomic responsivity into old age may be relatively preserved as compared to that of their same age peers for whom this responsivity has declined. The studies reported in this thesis were initiated to explore this issue. Ultimately, determining relationships between autonomic variables and cognitive performance outcomes in late life may be informative with respect to the development of cognitive impairment and dementia, and useful in the context of optimal or "successful" aging.

Cardiac regulation and the special role of parasympathetic control

To appreciate relationships between autonomic control and cognition, it is necessary to understand how the autonomic nervous system implements cardiac control. Heart rate is the net outcome of the competitive activity of the sympathetic and parasympathetic nervous systems on the sino-atrial node, the heart's pacemaker (Levy, 1990; Saul, 1990). Both divisions of the autonomic nervous system originate in brainstem nuclei. Sympathetic activity is associated with ergotrophic (work-related) functions such as energy mobilization, emotional arousal, and preparation for action in response to environmental challenge (Berntson et al., 1997; Porges, 1995a). Parasympathetic activity is associated with tropotrophic (growth-related) functions such as digestion and energy conservation (e.g., heart rate slowing), information intake, and focused attention (Porges, 1995a) in the absence of environmental challenge. In resting conditions, cardiac function is tonically inhibited by the parasympathetic system (Levy, 1990). The intrinsic heart rate—the rate at which the low polarization threshold of cardiac autorhythmic cells initiates heartbeats if unimpeded—is comparatively fast, about 100 bpm. However, when sitting, intrinsic heart rate is controlled so that an adult's actual heart rate is only 60-80 bpm.

However, due to differences in the latencies and courses of action of their respective neurotransmitters, norepinephrine and acetylcholine, sympathetic and parasympathetic effects are not equivalent. Adrenergic transmission is relatively slow, such that sympathetic activation requires about 4 seconds to peak, and 15-20 seconds to return to baseline (Appelhans & Luecken, 2006). In contrast, acetylcholine has a comparatively fast onset and offset. As a result, parasympathetic transmission peaks in

less than a second and requires only a second—about the length of one heartbeat—to return to baseline (Levy, 1997). Therefore, beat-to-beat control of heart rate is mediated by the fast-acting parasympathetic system (Levy, 1990, 1997; Porges, McCabe & Yongue, 1982; Spyer, 1994; van der Molen, Somsen & Orlebeke, 1985). If parasympathetic activity is reduced, so is the overall variability in heart rate. The effects of reduced HRV are consistently negative (Goldberger, 1996); low HRV has been associated with physical complaints such as hypertension (Guzzetti et al., 1988; Liao et al., 1996) and coronary heart disease (Dekker et al., 2000; Wennerblom et al., 2000), and also maladaptive emotional functioning, including anxiety (Friedman & Thayer, 1998) and depression (Rechlin, Weis & Claus, 1994; Udupa et al., 2007; van der Kooy et al., 2006). Even the reduced HRV seen in normal aging reflects a form of autonomic dysregulation (Bonnemeier et al., 2003). In a healthy human, heart rate is not steady, even during sleep (Porges, 1995a).

The physiological explanation for HRV is not simple (Porges, 1992). The electrocardiogram (ECG) is a record of cardiac electrical output that includes irregular fluctuations reflecting neural contributions from multiple physiological sources. ECG signals can be decomposed by spectral analysis into three components that reflect the influence of low-frequency circadian rhythms, medium-frequency rhythms associated with short-term blood pressure regulation, and high-frequency rhythms associated with the respiratory cycle. Combined, these multiple rhythms contribute considerable complexity to the cardiac electrical signal. Because discrete physiological sources make contributions to variation in heart rate, variability in the cardiac signal is not merely random noise. HRV represents an independent source of variance from heart rate and

conveys additional information about the nature of cardiac regulation (Seely & Macklem, 2004).

Cardiac regulation is a system characterized by non-linear dynamics

In general, health is characterized by "organized variability" (Seely & Macklem, 2004), that is, by variability that appears random in the short term, while exhibiting regularity over longer periods (Goldberger, 1996). Cardiac regulation is an example of a non-linear, biological system that has the statistical properties of fractals. A fractal is an object composed of sub-units (and sub-sub-units) that closely mimic the scale structure of the larger unit. In the physical domain, this structure is represented by coastlines, mountain ranges, and the branching of trees, including the arterial and venous "trees" of the circulatory system. In living organisms, fractal structures allow for efficient transport across a complex, widely-distributed system (Goldberger, 1996), for example, of oxygen to bodily tissues.

Fractal structure also occurs in the temporal dimension, as it does in cardiac regulation. In the heart, each heartbeat is "kick-started" by an electrical impulse from the sino-atrial node. A network of His and Purkinje cells allows rapid conduction of the pacemaker's electrical signal through the myocardium, coordinating the contractions of the ventricular muscle cells so as to produce a beat powerful enough to pump blood around the body. Breakdown of the fractal structure of cardiac control by age or disease destroys its long-range regularity, leading either to domination of the signal by a single frequency rather than multiple frequencies, as in heart failure, or to uncorrelated randomness, as in atrial fibrillation (Goldberger, 1996, 1997), a dangerous situation

where disorganized atrial electrical impulses result in uncoordinated conduction to the ventricles and an irregular heartbeat.

Greater heart rate variability indicates that the fractal structure of cardiac control is intact, and is itself a sign of health and optimal cardiac functioning (Park, Lee & Jeong, 2007). Variability in the heart rate reflects cardiovascular adaptation to the challenges of daily life. HRV also indexes the efficiency of neural feedback mechanisms to organize physiological resources (Kennedy & Scholey, 2000; Scholey et al., 2001), and by extension, behavioural adaptability (Thayer & Lane, 2000). Conversely, reduced variability in the ECG signal is a marker of autonomic dysfunction and a symptom of diminished cardiovascular health (DeMeersman & Stein, 2007).

The development of models of parasympathetic control

Until the 1970s at least, the vast majority of studies focused on sympathetic function and its arousal effects (Jennings & McKnight, 1994). This was partly because sympathetic effects were more obvious and could be readily measured as changes in heart rate, for example, in orienting paradigms (e.g., Graham & Clifton, 1966; Lacey, 1967; Obrist, Webb, Sutterer & Howard, 1970). The traditional view of cardiac regulation was that the sympathetic and parasympathetic systems acted reciprocally (in which case it was enough to measure one of them). Neglect of the parasympathetic system occurred partly because there was no good way to properly isolate and measure parasympathetically mediated HRV.

Initial time domain attempts to measure HRV, such as the standard deviation of heart rate (e.g., Porges & Raskin, 1969; Waddington, MacCulloch & Sambrooks, 1979), included all sources of variability, and did not specifically isolate parasympathetic

control. However, with the development of techniques such as spectral analysis of ECG data (Akselrod et al., 1981), polynomial filtering (Porges, 1985) or peak-valley methods (Grossman, van Beek & Wientjes, 1990) and the refinement of measures of respiratory sinus arrhythmia (RSA, Katona & Jih, 1975), it became possible to isolate parasympathetic influences. RSA, the measure used in this thesis, refers to small natural fluctuations in heart rate that are coordinated with the normal respiration cycle as a result of a common generator in the medulla (Porges, 1986). During inspiration, vagal efferent activity is briefly inhibited and heart rate increases slightly; during expiration, vagal efferent activity is reinstated, and heart rate decreases slightly. Because these fluctuations are mediated by the vagus nerve, under normal conditions they provide an index that is specific to parasympathetic activity. RSA reflects the interaction between the cardiovascular and respiratory systems in meeting the metabolic needs of the organism. The magnitude of RSA is represented by the difference between the smaller mean R-R (interbeat) interval during inspiration and the larger mean R-R interval during expiration (Yasuma & Hayano, 2004). Individual differences in this measure are significant, and stable across situations (Berntson et al., 1994; Grossman & Taylor, 2007).

In 1991, Berntson et al. introduced the notion of autonomic space, in which sympathetic and parasympathetic influences were represented as independent, rather than reciprocal, contributors to heart rate. Shortly thereafter, Porges (1992) described a model of psychophysiological functioning showing that vagally mediated cardiac modulation was critical to attentional control. The model was developed further as polyvagal theory (Porges, 1995b, 2003), postulating that mammalian modes of attention, emotion, and communication were facilitated through the evolutionary development of a dual vagal

system. According to the polyvagal perspective, the oldest vagal branch projects from the dorsal motor nucleus in the medulla to primarily sub-diaphragmatic structures, and is found in animals from lower phylogenetic orders as well as mammals. Its major function is to facilitate basic vegetative capacities such as gastric motility and digestion, and it is also connected to the heart. The more recent vagal branch, originating in the nucleus ambiguus in the medulla, projects mainly to supradiaphragmatic structures including the heart, larynx, pharynx, esophagus, and bronchi, and is thus independently positioned to facilitate uniquely mammalian competencies such as social behaviour and communication.

Porges hypothesized that the much-studied heart rate slowing seen in conjunction with the orienting reflex was mediated by the "vegetative" vagus emanating from the dorsal motor nucleus, whereas the suppression of HRV that is characteristic of sustained attention, a mammalian specialty, was mediated by the "smart vagus" that projected from the nucleus ambiguus (Porges, 1995b). The novel idea in this theory is that cognitive operations are integrated with cardiac control, and thus, limitations in autonomic functioning will influence cognitive capacities such as sustained attention. Others have vigorously challenged polyvagal theory (e.g., Grossman & Taylor, 2007), alleging that no such theorizing is necessary because the benefit of vagal control as indexed by RSA is purely physiological, that is, it simply increases cardiorespiratory efficiency (Hayano & Yasuma, 2003; Hayano, Yasuma, Okada, Mukai & Fujinami, 1996).

Discussion of relationships between RSA and cognitive or affective functioning is absent from the Hayano reports, as these authors view RSA straightforwardly as an index of cardiopulmonary reserve, with clinical significance for certain medical conditions, that

is reduced with age, stress, or disease. Grossman's approach is also primarily physiological. His principal objection to studies that are rooted in polyvagal theory involves the inferring of psychological states from physiological variables. Whereas a physiological parameter can be inferred from a behaviour or psychological state, it is a logical error to infer the reverse—unless the physiological parameter is a marker for the behaviour/psychological state, that is, there is a one-to-one relationship between the marker and the state. Otherwise, relations between autonomic indices and psychological outcomes may be the result of unmeasured third variables rather than the autonomic index (for an example, see Masi, Hawkley, Rickett & Cacioppo, 2007). Certainly, RSA measured during task performance is determined by multiple processes, including baseline levels, the amount of change for task performance, etc., and one cannot assume a one-to-one relationship between on-task RSA and task variables. One way to get around this problem is by using a multivariate approach in which some determinants of RSA are controlled, thus reducing the number of determinants to a few, or possibly even one predictor (Berntson, Cacioppo & Grossman, 2007). Another way to get around it is to use resting RSA as a general index of physiological reserve, that is, the baseline capacity of the parasympathetic system to respond to the metabolic demands of behavioural and cognitive processes, as has been done here.

The neurovisceral integration model

Irrespective of the aforementioned critiques (e.g., Grossman & Taylor, 2007; Hayano & Yasuma, 2003), subsequent researchers built on Porges' foundation, developing a model of neurovisceral integration in which peripheral regulation of autonomic function is modulated by higher regions of the brain, in accord with changing

environmental contingencies. Earlier work had already shown that the limbic system can directly influence the brainstem nuclei that control the vagus nerve (e.g., Schwaber, Kapp & Higgins, 1980), and that blocking acetylcholine transmission (Dellinger, Taylor & Porges, 1987), or depressing vagal tone by anesthesia (Donchin, Feld & Porges, 1985), has a detrimental effect on attention. More recent research focused on a number of brain regions that form a central autonomic network in medial frontal cortex that influences autonomic regulation (CAN, Benarroch, 1993; Benarroch, 1997; Fisk & Wyss, 1997; Terreberry & Neafsey, 1987). The CAN incorporates structures from the neocortex to mid-brain to brainstem, including anterior cingulate cortex (ACC), insular and ventromedial cortices, the central nucleus of the amygdala, the paraventricular and other hypothalamic nuclei, periaquaductal gray matter, the parabrachial nucleus, the nucleus of the solitary tract, the nucleus ambiguus, ventrolateral and ventromedial medulla, and the medullary tegmental field (Friedman, 2007; Thayer & Lane, 2000).

Through multiple distributed paths and reciprocal connections among its structural components, the CAN receives sensory inputs and external information from the environment and integrates this information with physiological responses in the service of goal-directed behaviour, including the direction of blood flow to particular regions, changes in respiration, and the release of hormones such as cortisol (Thayer & Lane, 2000). Via direct connections between ACC and autonomic brainstem nuclei (Ter Horst & Postema, 1997), the CAN's output modulates the activity of preganglionic sympathetic and parasympathetic neurons in the stellate ganglia and vagus nerve, respectively, and through them, influences the activity of the sino-atrial node. Variability in the cardiac signal reflects output of the CAN (Saul, 1990). By indexing the interplay of

higher central and lower peripheral mechanisms, and thus, the efficiency of central-peripheral neural feedback mechanisms, baseline measures of HRV allow us to quantify the capacity for self-regulation (Thayer & Lane, 2000). Greater capacity for self-regulation permits greater behavioural flexibility, increasing the potential for adaptive responding in the face of an ever-changing environment.

ACC, performance-monitoring, and autonomic control

One of the most important structural components of the CAN is anterior cingulate cortex. ACC is a large expanse of medial frontal cortex wrapped around the rostral end of the corpus callosum. It is activated in a wide range of contexts. The most rostral portion of ACC modulates autonomic activity and emotional responses (e.g., Whalen et al., 1998), whereas the more dorsal section is associated with response selection, motor activity, cognitively demanding information processing, and responses to noxious stimuli (Bush, Luu & Posner, 2000; Devinsky, Morrell & Vogt, 1995; but see Vogt, Berger & Derbyshire, 2003). ACC activation also appears to be critically involved with the initiation of goal-directed behaviours and the motivational significance of actions (Kennerly, Walton, Behrens, Buckley & Rushworth, 2006). Thus, there is no brain region more appropriate for the purpose of examining relationships between autonomic function, cognitive outcomes and behaviour, than ACC.

ACC has been identified as a neural interface between cognitive and biobehavioural systems, that is, between high-level appraisal systems and low-level visceral systems (Critchley, Tang, Glaser, Butterworth & Dolan, 2005). Importantly, during effortful cognitive or motor operations, ACC supports the generation of appropriate states of cardiovascular arousal (Critchley et al., 2003; Critchley et al., 2005;

Gianaros, Van der Veen & Jennings, 2004; Hoshikawa & Yamamoto, 1997) via projections to the brainstem nuclei of the sympathetic and parasympathetic nervous systems (Devinsky et al., 1995). In addition to its role in autonomic regulation, ACC is part of a reward-based learning system (e.g., Amiez, Joseph & Procyk, 2006; Shidara & Richmond, 2002) that is activated in response to behavioural errors (e.g., Falkenstein, Hohnsbein, Hoormann & Blanke, 1991), the prospect of poor outcomes (Bartholow et al., 2005), and situations where the outcome of an action suddenly disconfirms expectations (Oliveira, McDonald & Goodman, 2007).

In a reinforcement learning account of ACC activation, Holroyd and Coles (2002) postulated that a phasic drop in the activity of mesencephalic dopaminergic neurons in the basal ganglia disinhibits neurons in ACC, which initiates an event-related potential (ERP) in the EEG waveform at medial fronto-central sites, i.e., the error-related negativity (ERN; Gehring, Goss, Coles, Meyer & Donchin, 1993), or error negativity (Ne; Falkenstein, Hohnsbein, Hoormann & Blanke, 1990). When errors cannot be perceived internally, external error information can elicit a similar, feedback-related negativity (FRN) in the same region (e.g., Miltner, Braun & Coles, 1997; Müller, Möller, Rodriguez-Fornells & Münte, 2005; Nieuwenhuis, Slagter, von Geusau, Heslenfeld & Holroyd, 2005). The dependence of error negativities on mid-brain dopamine is supported by the fact that ERN amplitudes are increased after the administration of D-amphetamine, an indirect dopamine agonist (de Bruijn, Hulstijn, Verkes, Ruigt & Sabbe, 2004).

ACC activity does not itself represent executive processing (Critchley et al., 2005) and ERNs/FRNs do not represent a direct attempt of ACC to cope with aversive or

difficult situations, but rather are thought to alert other frontal brain regions (such as dorsolateral prefrontal cortex) to the need for increased cognitive control (Botvinick, Braver, Barch, Carter & Cohen, 2001) and an immediate change in response strategy (Bartholow et al., 2005; Ridderinkhof, Ullsperger, Crone & Nieuwenhuis, 2004). ACC signals also constitute a local record of the consequences of recent actions, indicating which ones were successful (and worth performing again in the future) and which were not (Amiez et al., 2006; Kennerly et al., 2006). This record would be most important in cumulative learning tasks, where participants are expected to learn from error information and use this knowledge on future trials.

The neurovisceral model and cognition

The bulk of research on autonomic and psychological functioning has been in the context of emotional regulation (e.g., Agelink et al., 2004; Cacioppo, Berntson, Larsen, Poehlmann & Ito, 2000; Frazier, Strauss & Steinhauer, 2004; Movius & Allen, 2005; Rottenberg, 2007; Sack, Hopper & Lamprecht, 2004). The neurovisceral integration model itself was developed with respect to dysfunctional emotional responding as seen in anxiety disorders (e.g., Friedman, 2007; Friedman & Thayer, 1998; Hagemann, Waldstein & Thayer, 2003). However, this model has also been discussed in the context of selective attention and self-regulation (Thayer & Lane, 2000). An important part of self-regulation is the ability to select important information and to ignore irrelevant information, making rapid attentional shifts or sustaining focus as needed. This suggests, along with recent findings in HRV research, that the framework could be extended to include cognitive processes, and may have particular relevance for executive functions, including attentional control.

Higher tonic levels of vagally mediated HRV have been associated with reduced attentional capture during Stroop performance (Johnsen et al., 2003), greater working memory ability (Hansen, Johnsen & Thayer, 2003), and better scores on tests of intelligence (Melis & van Boxtel, 2007) in younger adults. There is little work in this area with respect to older adults, though presumably autonomic relationships in older groups would be of interest, since autonomic functioning undergoes systemic age-related change (for reviews see DeMeersman & Stein, 2007; Low, 1997; e.g., Umetani, Singer, McCraty & Atkinson, 1998). Sporadic exceptions exist. In an unpublished paper, Porges et al. (1973) showed that older adults with higher HRV have faster reaction times than a comparable group with lower HRV. A recent population study has linked lower HRV to increased risk of cognitive impairment in older disabled women (Kim et al., 2006). In addition, hypertensive status—characterized by unchecked sympathetic predominance of heart rate—is associated with performance decrements in cognitive tasks (Kuo, Sorond, Iloputaife, et al., 2004; Robbins, Elias, Elias & Budge, 2005), and cognitive impairment later in life (e.g., Farmer et al., 1990; Launer et al., 2000). Thus, it was of interest to examine ACC activation and HRV in conjunction with performance of cognitive tasks, particularly those that evoked executive functions in older and younger adults.

The nature of the tasks

ACC function has typically been measured using the standard Eriksen flanker task. However, researchers have recently begun to adjust the task, varying it to examine ACC function with respect to diverse psychological variables such as the timing of action monitoring (e.g., van Veen & Carter, 2002), effects of motivation and personality correlates (e.g., Pailing & Segalowitz, 2004), response monitoring in autism (e.g.,

Henderson et al., 2006), and effects of emotional faces on psychopaths (e.g., Munro et al., 2007), to name a few. Researchers have also turned to different paradigms, such as feedback tasks, to explore performance monitoring and ACC function. These paradigms are designed so that participants are unable to discern internally when they have made an error and must rely on external feedback for that information. Feedback related negativities (FRNs) to error information have typically been elicited in guessing or gambling tasks (e.g., Donkers, Nieuwenhuis & van Boxtel, 2005; Hajcak, Moser, Holroyd & Simons, 2006; Yeung & Sanfey, 2004), difficult time-estimation tasks (e.g., Mars, de Bruijn, Hulstijn, Miltner & Coles, 2004; Miltner et al., 1997) and tasks where reward contingencies are impossible to learn (e.g., Nieuwenhuis et al., 2002; Nieuwenhuis, Slagter et al., 2005). In these paradigms, the outcome of each trial has no relation to any other trial.

However, with more investigation of response-monitoring and autonomic regulation in the ACC, it has become clear that ACC activity reflects the history of recent actions and their outcomes (Amiez et al., 2006; Kennerly et al., 2006) and that this has implications for future performance (e.g., Rushworth, Walton, Kennerly & Bannerman, 2004; Walton, Croxson, Behrens, Kennerly & Rushworth, 2007). When an error occurs following a run of successful choices (and is thus surprising), the ACC error signal is larger. Serendipitously, this result distinguishes the unsuccessful choice so that it is not repeated in upcoming trials.

Error information may become very salient another way. A cumulative learning task that requires participants to acquire item and configural information and retain it for subsequent use would make error information very important, and thus it would be more

likely to elicit maximal responses from ACC. Because spatial learning requires the cumulative acquisition of item and configural information via attentional control and working memory (i.e., executive functions), errors in this task would be very likely to evoke responses in ACC. Because spatial learning would engage executive functions, it is also likely to require considerable physiological support (Aasman, Mulder & Mulder, 1987; Critchley et al., 2003) and thus would be likely to engage autonomic modulation by ACC. Therefore, a novel maze-learning task with three levels of difficulty (Snyder et al., 2005) was selected for the present studies. We expected that better cardiac autonomic control, that is, greater parasympathetic influence on heart rate (higher RSA) would be correlated with better maze-learning performance, particularly at the more difficult levels.

In an earlier study, we reported relationships between autonomic indices and task outcomes using a source memory task that was highly dependent on both attentional control and working memory (Dywan, Mathewson & Segalowitz, submitted). In older adults, higher levels of RSA were correlated with lower source error rates, but no relationships were found between RSA and performance of a contrasting Eriksen letter flanker task for older or younger adults, even though this task was originally conceived of as a test of executive functioning (Eriksen & Eriksen, 1974). However, it was not clear from our study whether the discrepancy was due to the differential cognitive processing elicited by each task, or whether the source task was simply a more difficult assignment. In the present series of studies, we sought to explore the model suggested by the results of Dywan et al. (submitted). Replication of the pattern of parasympathetic relationships with performance of the source memory but not the flanker task would support the conclusion that parasympathetic function as measured by RSA was particularly beneficial

for cognitive tasks requiring attentional control and working memory. In addition, we included a more difficult letter flanker task (van Veen & Carter, 2002). If attention and working memory processes were critical to eliciting relationships between autonomic function and task outcomes, then we would expect to find them only in relation to source memory performance, and not in relation to flanker trials—even difficult ones—that could be completed using available visual information. Conversely, if relationships with autonomic variables were a function of task difficulty, they should vary across the two levels of the flanker paradigm, and would be seen in the difficult flanker task as well as the source memory task, but not in the standard flanker task. This discrepancy was also tested in a novel maze-learning task with two contrasting conditions: initial learn trials, in which participants were totally dependent on feedback to discover a given maze path, and repeated test trials, in which spatial memory could be consulted to assist with decision-making during maze performance.

In sum, three kinds of executive function tasks were administered in the present set of studies. Because subjective perceptions of task difficulty and time pressure influence HRV independent of objective task performance (Derrick, 1988), at the end of the testing session we asked participants to rate how difficult each task was for them.

Autonomic assessment

In these studies, four autonomic indices were calculated from resting ECG and resting blood pressure readings to represent the autonomic capacities of each individual, unconfounded by the influence of task demands. These measures may be thought of as personal characteristics or capacities.

Resting heart rate, the net outcome of the interplay between parasympathetic and sympathetic activity, is included in our analyses because it provides the simplest picture of cardiac behaviour. Its standard deviation can serve as an index of overall HRV, and thus, a rough measure of parasympathetic control. However, indices that isolate parasympathetic capacity specifically are more sensitive to cognitive demands than global estimates of HRV, in both younger and older adults (Lyness & Porges, 1985). Therefore, RSA was calculated from heart rate derived from ECG recordings. Having indices of the functioning of both divisions of the autonomic nervous system would provide a more comprehensive picture of age-related change in autonomic control vis-à-vis cognitive processing. Therefore, systolic blood pressure (SBP) was assessed before and after the testing session to provide a mean resting sympathetic measure. SBP and heart rate were used to calculate rate pressure product (RPP; heart rate x SBP, divided by 100), a reliable indirect measure of cardiac oxygen consumption and thus, cardiac workload (Fredericks, Choi, Hart, Butt & Mital, 2005). Since myocardial contractility increases cardiac oxygen use and is increased primarily via sympathetic activation, RPP was used as a proxy for sympathetic drive. Thus, we used two general indices of autonomic functioning (heart rate and systolic blood pressure) and two measures more closely associated with the separate influence of each division of the autonomic nervous system (RSA and RPP) on the heart.

Synopsis

The research presented in the following three chapters represents separate studies of electrophysiological and/or autonomic responses and behaviour in the context of two well-known tasks—source memory and flanker paradigms—and a novel maze-learning

task. Each of the three studies is based on data from a single sample of 20 older adults and 20 younger adults. Participants were tested in two three-hour sessions about a week apart, alternating between the source memory and flanker tasks on the first day, and completing the maze task in one sitting on the second day, with breaks as needed. However, due to some recording and data-processing difficulties and issues with adequate performance of the tasks, the sample sizes differ between studies.

The focus for the first study is the effect of age-related decline in ACC functioning on the acquisition of spatial knowledge by older and younger adults in the maze-learning task. The second study involves age-related change in the relations between autonomic control variables and behavioural and electrophysiological responses in the maze-learning task. In the third study, relationships between autonomic control variables and cognitive outcomes from the source monitoring task versus the flanker task are explored in each age group. Analyses of behavioural performance (errors, response times), electrophysiological measures of on-line cortical activity (event-related potentials; ERPs) and resting autonomic control variables (heart rate, blood pressure, RSA, rate pressure product) are presented for each study. Finally, a general discussion presents four possible mechanisms by which parasympathetic cardiac control may contribute to the performance of complex executive functions, and suggests some directions for future research in the area of autonomic and cognitive function with respect to preserving cognitive capacity in late life.

Chapter 2: Aging and electrocortical response to error feedback during a spatial learning task

Abstract

Event-related potentials were collected as older and younger adults responded to error feedback in an adaptation of the Groton Maze Learning Test, an age-sensitive measure of spatial learning and executive skills expected to maximally involve anterior cingulate cortex (ACC). Older adults made more errors and produced smaller feedback-related negativities (FRNs) than young controls. LORETA source localization revealed that for young adults, neural activation associated with the FRN was focused in ACC and was stronger to negative feedback. Older adults responded with less intense and less differentiated ACC activation, but FRN amplitudes did relate to error rate in the most difficult mazes. The feedback P3 was sensitive to negative feedback but played no role in the prediction of error for either group. These data reflect the selective age-related decline of ACC response but also its continued contribution to performance monitoring in aging.

Introduction

There are at least two ways in which humans gain information about their own performance of a given activity (Müller et al., 2005). One is through an internal monitoring system that responds when it is apparent that the consequences of a choice or action are other than intended. The other involves the attention paid to external feedback about performance in circumstances where it is impossible to know the accuracy of one's actions. The neural response to internally- and externally-based error feedback can be investigated through two closely related electrophysiological responses. The error-related negativity (ERN) is a response-locked waveform that is associated with the internal monitoring of errors. There is also a feedback-related negativity (FRN), a stimulus-locked waveform that is generated in response to error information acquired from the environment. The FRN is topographically and morphologically similar to the ERN (e.g., Holroyd et al., 2004; Nieuwenhuis et al., 2002) and generators of both components have been localized to anterior cingulate cortex (ACC; e.g., Dehaene, Posner & Tucker, 1994; Miltner et al., 1997).

The ACC is part of a reward-based learning system (e.g., Amiez et al., 2006; Shidara & Richmond, 2002) that is activated when the outcome of an action is contrary to expectations (e.g., Oliveira et al., 2007) and response strategy must be adjusted (Bartholow et al., 2005; Ridderinkhof et al., 2004). In a reinforcement learning account of error-related negativities, Holroyd and Coles (2002) have suggested that medial frontal negativities (ERNs, FRNs) occur when the basal ganglia signal frontal brain regions, including the ACC, through phasic drops in the activity of mesencephalic dopaminergic neurons that occur when outcomes are worse than expected. The suggested link between

dopamine levels and ERN response has received support by examining the effects of psychopharmacological manipulation of dopamine (de Bruijn, Hulstijn, Verkes, Ruigt & Sabbe, 2005).

It is not surprising then, that the ERN is reduced with age (Falkenstein, Hoormann & Hohnsbein, 2001; Gehring & Knight, 2000; Kok, 2000; Mathewson, Dywan & Segalowitz, 2005; Nieuwenhuis et al., 2002), given the evidence of an age-related decline in available dopamine within both nigrostriatal (Reeves, Bench & Howard, 2002) and mesolimbic (Cruz-Muros et al., 2007) dopamine systems. A decline in dopamine receptors (D2/D3) has been observed across the lifespan in the striatum as well as extrastriatal regions such as the ACC (Kaasinen et al., 2000), along with a decline in dopamine synthesis in these same regions (Ota et al., 2006). However, mapping the association between age-reduced ERNs and age-related change in behavior has not been straightforward. For example, ERNs are reduced in older adults even when their accuracy levels are the same or better than young adults on speeded perceptual tasks (Falkenstein et al., 2001; Nieuwenhuis et al., 2002). In young adults, within-group correlational analyses have provided some evidence of relations between size of ERN and error rate (e.g., Hajcak, McDonald & Simons, 2003; Herrmann, Römmler, Ehlis, Heidrich & Fallgatter, 2004), but these relations were not found within older groups with respect to ERP and accuracy data collected during a standard letter flanker task (Mathewson et al., 2005). This suggests that, in older adults, successful performance may be independent of the robustness of the error signal but, to our knowledge, these within-group relations have not been specifically examined in other studies of performance monitoring in older adults.

Much less is known about age effects with respect to the FRN. In perhaps the only study to date, Nieuwenhuis et al. (2002), experiment 2, found that FRNs, like ERNs, were smaller in older than in younger adults when elicited during a probabilistic learning task. However, for older adults, the FRN response pattern was not wholly consistent with a major prediction of reinforcement learning theory (Holroyd & Coles, 2002). According to this model, one would expect that, as the correct representation of stimulus-response mappings become internalized over a number of trials, the FRN should reduce in size because external feedback becomes redundant. Awareness of making an error would occur in conjunction with the incorrect response, thus producing a larger ERN and a much diminished FRN. This is exactly what happened for the younger adults in the Nieuwenhuis et al. study. However, for older adults there was no evidence that FRN amplitudes were sensitive to the validity of feedback or to the amount of learning that had occurred.

One could conclude that error-related ERP components simply reflect the reduction of dopamine in the system and tell us nothing more about the nature of age-related change in performance monitoring or general cognitive decline. Alternatively, it may be that the tasks used to assess performance monitoring have not engaged the anterior cingulate to the degree necessary to observe the link between neural response and behavior in older adults. FRNs have typically been elicited in gambling or guessing tasks (e.g., Donkers et al., 2005; Hajcak et al., 2006; Yeung & Sanfey, 2004), time-estimation tasks (Mars et al., 2004; Miltner et al., 1997), and tasks where it is impossible to learn about reward contingencies (Nieuwenhuis et al., 2002; Nieuwenhuis, Slagter et al., 2005).

Nonetheless, as researchers continue to parse the functions of the ACC and related brain regions in animal and human studies, it has been shown that the ACC is most involved when error feedback is based on a history of actions and outcomes (Amiez et al., 2006; Kennerly et al., 2006). In such contexts, variation in ACC activity in response to trial outcome can predict learning rate (Behrens, Woolrich, Walton & Rushworth, 2007). However, as Nieuwenhuis et al. (2002) observed, the tasks used with older adults have not required an extended learning trajectory in that they reach asymptote quite quickly. Spatial learning tasks, on the other hand, require cumulative acquisition of item and configural information, invoking executive functions such as attention and working memory. Thus, it was our goal to examine electrophysiological indices of ACC activity in older and younger adults using a modified version of the Groton Maze Learning Test (Snyder et al., 2005). This computer-based task involves finding a hidden pathway through a grid of tiles by trial and error while receiving informative visual feedback after each move. Its outcome measures (e.g., errors and completion times) are sensitive to age differences in spatial learning efficiency and correlate with scores on neuropsychological tests of executive function, such as planning and sustained attention (Pietrzak, Cohen & Snyder, 2007).

Age-related decline in spatial learning ability has been well documented (Driscoll et al., 2003; Lövdén, Schellenbach, Grossman-Hutter, Krüger & Lindenberger, 2005; Moffat, Elkins & Resnick, 2006; Moffat, Kennedy, Rodrigue & Raz, 2007; Newman & Kazniak, 2000). These deficits have been associated with structural and chemical changes in the hippocampus (Driscoll et al., 2003). Others (e.g., Moffat et al., 2006) have linked this reduced activation in hippocampal and extra hippocampal regions to higher levels of

activation in the ACC and medial frontal cortex. Thus, the hippocampal decline could be expected to place more load on midbrain error monitoring capacity and maximally engage the ACC (see also Yoshida & Ishii, 2006). It is also of interest that ACC neurons, with their links to premotor and motor cortices (Hatanaka et al., 2003), select for spatial aspects of a rewarded motor response (e.g., Shima & Tanji, 1998), suggesting that maze learning should be particularly effective in eliciting ACC activation.

For our adaptation of the maze learning task, the initial presentation of each maze required the use of a trial-and-error strategy to find the maze within a grid, with feedback occurring after each move. Negative feedback was expected to elicit FRN responses in both groups, albeit smaller ones in the older group. On the initial "learning trial" for each maze, discovering the maze within the grid would depend totally on feedback, thus eliciting a learn-trial FRN that could be contrasted with the FRN from repeated trials. Even though feedback continued to be provided during the repeated trials, in these "test trials", maze location would become increasingly internalized, so that the memory representation of a given maze configuration could be consulted during the re-tracing of its path. The development of internal memory representations was expected to increasingly allow for internal realization of errors, leading to a gradual reduction in the reliance on feedback and hence a reduction in the amplitude of the FRN response (Holroyd & Coles, 2002).

In order to ensure activation of the ACC, we also varied maze difficulty in a stepwise fashion while maintaining consistency with regard to user interface, instructions, task requirements, and feedback at each level. We anticipated that larger mazes would force participants to rely more heavily on the strategic control of attention and hence

require greater involvement of the ACC (e.g., Paus, Koski, Caramanos & Westbury, 1998). Because ERP responses to negative feedback are hypothesized to signal the need for increased top-down control and altered behaviour, we expected that smaller FRN responses would relate to reduced learning efficiency. Finally, because FRN activation has not been imaged in older adults, we used low resolution tomography (LORETA) to find plausible solutions for the neural generators of the electrical activity seen at the scalp and to test for significant differences between positive and negative feedback conditions.

Method

Participants

Twenty undergraduates from Brock University (15 female; 18-26 years, $M =$ 20.4), and 20 older adult volunteers (15 female; 65-87 years, $M = 74.6$) from the surrounding community of St. Catharines, Ontario, Canada, participated in this study. Exclusion criteria included neurological or psychiatric conditions or use of psychoactive medications.[1] Participants had normal or corrected-to-normal vision, and were fluent English speakers. Older adults scored within the normal range (27-30, $M = 28.6$, $SD =$ 1.08) on the Mini-Mental Status Examination (Folstein, Folstein & McHugh, 1975). There was no difference in education levels between the two groups ($M_{Young} = 13.7$, SD = 2.14 years; $M_{Older} = 14.5$, SD = 2.17 years, $p > .2$) but, as expected, older adults' vocabulary level, as measured by the SCOLP "Spot the Word" task ($M = 87\%$ correct) exceeded that of the younger group ($M = 79\%$ correct), $t_{(37)} = 4.04$, $p < .001$, (Baddeley, Emslie & Nimmo-Smith, 1992). The study received clearance from the Brock University Research Ethics Board and all participants provided written informed consent. Most

students received partial course credit. All others, including older adults, received a small monetary stipend for their time.

Stimuli and Experimental Design

The Groton Maze Learning Test (Pietrzak et al., 2007; Snyder et al., 2005), developed by Peter J. Snyder and loosely based on an earlier design by Milner (1965), was modified so that responses could be time-locked to ERPs recorded from individual subjects. To increase spatial memory load and demands on attentional capacity, we included three difficulty levels: easy (4 × 4 grid), moderate (6 × 6 grid), and difficult (8 × 8 grid). At each difficulty level, participants were asked to find a maze path that was hidden within a grid of square grey tiles (Figure 2.1). Beginning in the upper left corner and travelling toward the lower right corner, participants used a stylus to indicate which tile they thought might be next in the hidden path on the touch-screen of a tablet laptop computer.[2] Allowable choices were up, down, left, or right of the current tile. Diagonal and backward moves were not allowed. Progress through each maze was self-paced but the timing of feedback was controlled to ensure sufficient time for the recording of feedback-related ERPs. After every step, the selected tile either turned green for a correct choice or turned red for an incorrect choice. If participants chose an incorrect tile, they were obliged to return to the previous correct tile and make a new selection.

Figure 2.1

In the initial "learn" trial of each maze, participants were completely dependent on external feedback to learn the maze path. However, on subsequent repeated "test" trials, they would also be able to access a developing internal map of the stimulus field in

memory, even though trial-by-trial provision of feedback continued. Thus, the initial learn trial constituted a pure learning condition, whereas the repeated test trials would be expected to reflect an increase in the degree to which performance could be guided by a growing internal representation of the maze. Behavioural outcomes included total time to completion and the total number of steps required to complete a trial, with raw error scores being calculated off-line. Eight unique mazes were presented at the 4×4 grid size. Each involved the initial learn trial plus two test trials. A perfect score for a 4×4 maze comprised 10 correct moves. Four unique mazes were presented at the 6×6 grid size, with one learn and three test trials per maze and a perfect score comprising 20 moves. For 8×8 grids, two unique mazes were presented, with one learn trial and five test trials per maze. A perfect score for an 8×8 maze comprised 30 moves. Thus, larger grid sizes involved fewer mazes but included more test trials per maze.

Procedures

A paper-and-pencil health questionnaire, the SCOLP vocabulary test, and a blood pressure reading were administered prior to the computerized maze tasks. A health index was informally coded on the basis of each participant's health history (0 = *no health issues reported*, 1 = *at least one minor health issue*, 2 = *at least one significant health condition, such as high blood pressure*, 3 = *overall health is of concern*).

Participants responded to all three levels of the maze task in a single session while seated in a dimly lit, electrically and acoustically shielded room. Maze stimuli were presented using E-Prime research software (Psychological Software Tools, Inc.) on a tablet computer (an Acer Travelmate C300 laptop with touch-screen). EEG was recorded throughout. Following completion of the maze task, participants rated the subjective

difficulty of the mazes at each grid size using a paper and pencil rating sheet with a 5-point scale.

Electrophysiological recording and measures

EEG scalp data were recorded from 250 scalp sites using a Geodesic Sensor Net (Electrical Geodesics Inc., Eugene, Oregon). The acquisition program was NetStation (version 4.0.1, EGI). Electrode impedances were generally kept below 50 kΩ. The signals were sampled at 500 samples/s and digitized with a 16-bit analog-to-digital converter. All recordings were referenced to Cz in NetStation. Data were processed off-line with a 1 – 30 Hz band-pass filter and segmented into 1000-ms epochs with a 200-ms baseline time-locked to the onset of the feedback. For correct trials, all epochs in which amplitudes at midline sites exceeded 75 µV were automatically excluded. Because there were fewer error trials, each error epoch was visually inspected and eye artifacts corrected as necessary using regression programs. Feedback-locked, artifact-free epochs were converted to an individual average, re-referenced to the common averaged reference, baseline-corrected, and then combined to create group averages using the ERPScore analysis program (Segalowitz, 1999).

Because the FRN appeared to be superimposed on a larger positive wave (Miltner et al., 1997), we used Brain Electromagnetic Source Analysis (BESA, version 5.1, MEGIS) to conduct separate principal components analyses (PCA) of the group-averaged waveforms from error trials across the time window of the FRN/P3 complex (lasting from the FRN peak to the P3 peak) for each condition, age group, and level (see also Yeung, Holroyd & Cohen, 2005). These analyses indicated that two components accounted for the majority of variance, 97.5%- 99.3% (M_{comp1} = 91.9%; M_{comp2} = 6.6%)

across this time window for younger adults in all conditions, and between 94.7% and 98.9% of the variance ($M_{comp1} = 90.7\%$; $M_{comp2} = 6.6\%$) for older adults across all conditions. Consistent indications of two distinct components in the FRN/P3 complex in every condition and in both age groups confirmed the independence of the FRN and feedback P3 and indicated that it was appropriate to analyze them separately.

As is evident in Figures 2.4 and 2.5, both error-related components peaked slightly later for older than younger adults. Therefore, to more accurately reflect responses for each age group, FRN amplitude was defined as the most negative peak between 250 and 400 ms following negative feedback for younger adults and, for older adults, as the most negative peak between 300 and 400 ms. For younger adults, P3 amplitude was scored as the mean amplitude within a 360-460-ms latency window, and for older adults, between 400 and 520 ms.

LORETA analyses

We submitted averaged ERP data to (LORETA) software (LORETA-Key-01 Free Brain Ware) to illustrate likely brain electrical sources for the ERPs, and to compare the activation at the time of the ERP peaks across positive and negative feedback conditions (Pascual-Marqui, Esslen, Kochi & Lehmann, 2002). LORETA software allows quantitative localization of neuronal electrical activity from EEG recordings. In LORETA, brain volume is modelled as a dense three-dimensional grid composed of 2,394 volume elements (voxels) at 7mm spatial resolution, which together represent the hippocampus and grey matter volume of a reference brain that has been digitized according to the Talairach atlas (available from the Brain Imaging Centre, Montreal Neurologic Institute).

A long-standing problem in electrophysiology is that any pattern of electrical activity at the scalp can be accounted for by an infinite variety of neural generators or sources. To deal with this, LORETA makes use of a physiological constraint, namely, that adjacent neurons fire more synchronously and simultaneously than neurons that are farther apart. This allows a single, three-dimensional solution to be calculated from a particular electrical distribution. Based on the linear, weighted sum of electrical potentials from across the scalp, LORETA calculates the current source density for each voxel. For every moment (2 ms = 1 time point) in a designated time window, the program produces "blurred-localized" images of neural point sources, retaining the areas of maximum activity but with a certain amount of dispersion. The program also produces a non-parametric, voxel-by-voxel statistical comparison of activation across the whole brain, yielding a two-tailed t test corrected for multiple comparisons.

Data from all 250 electrode sites were reduced to 81 standard sites in BESA (5.1) and then converted to voxels in the LORETA program. Voxel-by-voxel comparisons of individuals' whole-brain activation were made at the peak timing of the FRN and P3 elicited from error trials versus those elicited from correct trials for each maze condition, level, and age group. The data were not normalized or log-transformed.

Statistical analysis

Behavioural and electrophysiological data (stimulus-locked ERPs) were analyzed using $3 \times 2 \times 2$ mixed model ANOVAs, with grid size (4×4, 6×6, 8×8) and trial type (learn trials vs. test trials) as within-group factors and age group (older vs. younger adults) as the between-group factor, followed by Bonferroni-corrected pairwise-comparisons or individual comparisons where required. When the number of degrees of

freedom in the numerator was greater than one, the Huynh-Feldt correction was applied. Results are reported using the original degrees of freedom and corrected p-values. Both error-related components were then analyzed for associations with behavioural performance using hierarchical regression.

Results

Behavioural data

Data from participants with scores from all three grid sizes (19 younger, 14 older adults) were entered in this and all subsequent analyses. Some older participants were unable to complete the highest levels of the maze task because of the difficulty these levels posed. Data from one young adult were lost due to technical error. As expected, older adults ($M = 3.35 \pm .24$) rated the task as more difficult than younger adults ($M = 2.52 \pm .20$), $F(1, 27) = 7.00, p < .02, \eta^2 = .21$, and difficulty ratings increased with grid size ($M_{4x4} = 2.20 \pm .13; M_{6x6} = 2.91 \pm .14; M_{8x8} = 3.69 \pm .24$), $F(2,54) = 46.08, p < .001, \eta^2 = .63$. Grid size also interacted with group, $F(2, 54) = 3.59, p < .05, \eta^2 = .12$, such that both groups rated the largest mazes as equally difficult ($p > .30$) but the medium and small mazes were rated as more difficult by older than younger adults ($ps < .02$). Within each age group, difficulty ratings were independent of age, education, vocabulary score, and estimated health status ($ps > .09$). For younger adults only, difficulty levels related to error scores during test trials at each grid size ($ps < .001$).

Raw error scores were calculated by subtracting perfect scores (10, 20, or 30 steps, for each grid size, respectively) from the mean number of steps made across all trials at that maze level. Because each incorrect move required backing up one step to the last correct tile, the net scores were divided by two. As evident in Figure 2.2, the main

effects of age, trial type, and grid size were significant (*ps* < .01) but were superseded by a three-way interaction, $F(2, 62) = 10.94$, $p < .001$, $\eta^2 = .26$. Follow-up analyses indicated that for learn trials, errors increased with grid size to the same degree in both groups. However, on test trials, when differential learning rates became relevant, older adults made proportionally more errors than younger adults, and these increased with grid size.[3] (See Table 2.1).

Figure 2.2 and Table 2.1

Maze completion times were estimated on the basis of total time taken to complete each maze and analyzed in the same way as for errors. Again, all main effects were significant (*ps* < .001) but were superseded by interactions between grid size and trial type, $F(2, 42) = 31.02$, $p < .001$, $\eta^2 = .60$, and grid size and group, $F(2, 42) = 11.20$, $p < .001$, $\eta^2 = .35$. Follow-up analyses indicated that, as would be expected, overall completion times increased with grid size for both groups irrespective of trial type (*ps* < .001). However, for test trials on their own, the increase in completion times as a function of grid size was greater for older than younger adults (see Figure 2.3 and Table 2.2). Thus, it would appear that the groups did not differ markedly on learn trials (the first presentation of each maze) when everyone had to depend on feedback for each trial. However, on test trials, when differential learning rates became relevant, the difference between age groups was clearly evident (see also, Footnote 3).

Figure 2.3 and Table 2.2

ERP response

Displayed in Figures 2.4 and 2.5 are the overlaid averaged ERP waveforms for correct and error trials at representative midline sites (Fz, FCz, and Cz) for learn and test conditions for younger adults (Figure 2.4) and for older adults (Figure 2.5). Figures 2.6 and 2.7 depict topographical maps for younger and older adults with respect to the FRN and P3 to error feedback for learn trials (Figure 2.6) and test trials (Figure 2.7). Both represent data collapsed across all eight unique mazes presented at the 4 × 4 grid size. The patterns of activity for the larger grids were similar and so have not been displayed here. However, the actual amplitude and latency data for all grid sizes across conditions for both groups are presented in Table 2.3 (FRNs) and Table 2.4 (P3s). Trial rejections due to excessive artifact or recording difficulties resulted in some ERP analyses being conducted with fewer participants than others.

Tables 2.3 and 2.4

Visual inspection of Figures 2.4 and 2.5 indicates the lack of early sensory components, N1 and P1. These were absent because the visual system was loaded with visual input from the entire maze grid throughout task performance. Response accuracy was indicated by the selected tile transforming to red or green, which presented a very subtle change in visual sensation. Thus, the P2, a more endogenous component, represents the first clear ERP response to feedback, occurring at approximately 200-250 ms post-feedback for both groups. It is also evident (Figures 2.4 and 2.5) that positive feedback failed to elicit the FRN or feedback P3. Only error-related data were examined with respect to these components.

FRN. Peak FRN amplitudes were analyzed in the same way as the behavioural data except that site (Fz, FCz, Cz) also served as a within-group factor. There was a marginal effect for site, $F(2, 38) = 3.44$, $p < .07$, $\eta^2 = .15$, which was due to the FRN being slightly larger at Fz than at either of the other midline sites. There were also main effects for age and grid size, but these were superseded by an interaction among group, grid size, and trial type, $F(2, 38) = 3.82$, $p < .04$, $\eta^2 = .17$. Follow-up analyses indicated that FRN amplitudes were shallower for larger grid sizes ($p < .02$), but this grid size effect was seen primarily in the older adults and occurred primarily for test trials ($p < .05$). The size of the FRN was not reduced during test trials relative to learn trials ($p > .69$), as might be expected according to Holroyd and Coles (2002) reinforcement learning theory. However, further analysis revealed a marginal effect of trial type (learn versus test) for maximum FRN amplitudes (at Fz) for young adults ($p < .09$), but no effect of trial type for FRNs at Fz for older adults ($p > .60$). This suggests that FRN amplitudes tended to become smaller with learning, consistent with reinforcement learning theory (Holroyd & Coles, 2002), but only in younger adults (cf. similar findings in Nieuwenhuis et al., 2002).

A parallel ANOVA of FRN peak latencies confirmed that the FRN occurred later for older than younger adults but also produced a group × site interaction, $F(2, 38) = 21.19$, $p < .001$, $\eta^2 = .53$. Simple comparisons revealed that the FRN was manifest earlier at the more central (Cz) than frontal (Fz) site for younger adults ($ps < .02$) but that latency did not differ across sites for the older group ($ps > .10$).

P3. A feedback P3 component occurred at approximately 450 ms for older adults and 400 ms for the younger group. Mean P3 amplitudes were analyzed in the same way

as the FRN. There was a main effect of site, $F(2, 38) = 7.88$, $p < .01$, $\eta^2 = .29$, indicating that P3 amplitudes were largest at Cz. There were no other main effects, but there was a group $\times$ trial type interaction, $F(2, 38) = 5.67$, $p < .03$, $\eta^2 = .23$. Follow-up analyses of P3 amplitudes at Cz (maximal site) indicated that for younger adults, the P3 was generally larger during test trials than learn trials ($p < .01$), whereas for older adults, this distinction did not occur ($p > .30$).

Figures 2.4 to 2.7

LORETA comparisons. In a series of statistical analyses, we compared neural activity associated with negative relative to positive feedback at the moment of the maximal FRN peak (based at Fz) or P3 peak (based at Cz). The calculation is a *t* test of voxel-by-voxel comparisons of activation across the whole brain for the two conditions compared against a critical value and corrected for multiple comparisons. Analyses were done separately for each age group, for each trial type, and at each maze level.

Presented in Table 2.5 are the *t* statistics for each comparison and its respective critical value for *t*. These *t*-values are those associated with maximal brain activation in whole-brain comparisons of the negative versus positive feedback conditions. For young adults, the neural activation associated with the FRN peak was always greater in response to negative relative to positive feedback ($ps < .01$). For older adults, differences in activation between negative feedback and positive feedback were not as consistent, occurring only in one of six conditions, that is, on learn trials for the 6×6 grids ($p < .05$). In contrast, the neural activation associated with the peak amplitude of the feedback P3 was always greater for negative relative to positive feedback for both age groups, for both

trial types (learn and test), and for all grid sizes. Overall, activation associated with the feedback-related P3 appeared to be stronger and more consistently sensitive to the nature of the feedback than that associated with the FRN.

Table 2.5

It should be noted that when the *t* test for whole-brain comparisons of responses to negative verses positive feedback was calculated, the regions of maximal differentiation identified by LORETA were sometimes distributed outside of the medial prefrontal cortex. Because we were interested primarily in ACC activation, we next tested the degree to which greater activation to negative versus positive feedback could be observed specifically within medial prefrontal cortex. The LORETA brain maps (Figures 2.8 and 2.9) provide a graphical representation of the LORETA *t* statistics comparing response-related activation associated with the FRN (Figure 2.8) and feedback P3 (Figure 2.9) only as evident in mid-sagittal regions.[4] The red color indicates areas of increased activity associated with negative versus positive feedback. The presence of a red asterisk indicates that the *t* statistic for the comparison in this local medial region exceeded the critical t-value for significance across the whole head.

Figures 2.8 and 2.9

First, with respect to the FRN in young adults, it is evident from visual inspection of Figure 2.8 that medial brain regions were involved in the maximal differentiation between negative and positive feedback on both learn and test trials and across all levels of task difficulty. Also, although not specifically tested, the focus of the differentiation in

learn trials appeared to be more anterior for the most difficult maze, that is, for 8 × 8 grid size. For older adults, it is of particular interest that, despite some evidence for significant levels of FRN differentiation between negative versus positive feedback at the whole brain level (Table 2.3, column 2), the differential levels of activation did not generally occur in medial regions during either trial type for mazes of any grid size. The only exception was in learn trials at the 6 × 6 grid size. In this condition, older adults appeared to generate an ACC-focused error-related response in conjunction with negative relative to positive feedback. In all other conditions, the differential neural response to feedback for older adults in medial regions seemed much weaker and more diffuse than for the younger adults.

Figure 2.9 depicts differences in activation between negative and positive feedback in medial prefrontal regions at the peak latency of the feedback P3. In young adults, differential levels of activation in response to negative relative to positive feedback tended to be quite widespread across medial cortex for both learn and test trials. Moreover, older adults also produced some strongly focused activation in response to negative relative to positive feedback, but mostly during test trials. The neural activity associated with this differentiation was less evident during learn trials for older adults except for a modest effect in the initial learn trials on the 4 × 4 grids.

Correlates of behavioural response

We examined the degree to which error rates could be predicted by the amplitude of the FRN and feedback P3. Using error rate as our dependent measure we ran regression analyses separately for each trial type and grid size. In each case, we first entered group, then FRN amplitude, followed by their interaction. A similar set of

analyses was done to examine the feedback P3. In no case did the amplitude of the P3 account for additional variance to the prediction of maze error (ps typically $> .67$) over that accounted for by group. However, as can be seen in Table 2.6, there was some evidence of a relation between FRN amplitude and error.

Table 2.6

First, for learn trials, we see that group, when entered on the first step, is a good predictor of error rate only for the 4 × 4 mazes ($p < .01$). However, FRN amplitude added to that prediction when entered on the second step, and when considered together, FRN amplitude explained 13% unique variance relative to group (5%), suggesting that it is the better predictor. There was no group effect for the initial learn trials for 6 × 6 or 8 × 8 mazes ($ps > .09$), but for the smaller mazes, FRN amplitude added uniquely to the prediction of learn trial error rate over and above any effects of group ($ps < .03$).

For test trials, we see that the effect of group on step 1 was large for all three grid sizes ($ps < .01$). Group accounted for 18 to 34% unique variance when considered together with FRN amplitude in the 4 × 4 and 6 × 6 mazes. It was only for the 8 × 8 mazes that FRN amplitude added to that prediction ($p < .04$; step 2) and also interacted significantly with group in predicting test trial errors ($p < .001$; step 3). This robust interaction (see Figure 2.10) was based on the fact that, for young adults, the amplitude of FRNs (Fz) associated with negative feedback during the 8 × 8 mazes did not predict test trial error rate, $r = .15$, ns. The relationship for older adults, however, was strong, $r = .86$, $p < .001$.

Figure 2.10

What these analyses indicate is that both age group and FRN amplitude can predict error variance on the maze learning task. The size of these relations seems to depend on the context in which they occur. In the learn trials, because error rates are quite similar between groups, the group variable would be unlikely to serve as a predictor of error rate unless it captures the same variance as FRN amplitude, which it does on the 4 × 4 maze (i.e., this maze captures the relationship between group membership and the size of the FRN). FRN amplitude, however, may be a more relevant predictor because error feedback is so important in initially learning the route. Those who produce larger FRNs may have better error monitoring capacity and would be less likely to make perseverative errors during learn trials. That is, they would be less likely to make a choice that had already been designated as an error.

Test trials present a different situation. Here, group differences in spatial memory become relevant, and we see that age group now accounts for most of the variance in predicting error rate, as would be expected. Error feedback may be less relevant because many of the participants may depend more on the internal representation of the maze that they built up during the learn trials, especially for the small and medium size mazes. Thus, the size of the FRN may capture less of the variance in predicting test trial performance. That is, error rates might best be predicted by memory ability, which is best captured by age group, rather than error-monitoring capacity per se. However, in the case of the largest maze, it is less likely that a stable internal representation will have emerged

after a single learn trial, so that error-monitoring capacity (as evidenced by larger FRNs) would remain highly relevant across trials, especially for the older adults.

What is apparent, however, is that whenever a relation between FRN and error rate occurs it is positive, i.e., a shallower FRN is associated with a higher error rate. This is consistent with the general model that a more efficient error monitoring system would produce a larger electrocortical response to error feedback, and the responsivity of this system would be associated with the reduced likelihood of making an error. Behavioural results are presented together with autonomic and electrocortical results in Table 2.7.

Table 2.7

Discussion

We examined the effects of aging on ERP indices of performance monitoring using a hidden-maze learning task designed to capture age differences in spatial learning ability. This cumulative learning task, presented at three levels of difficulty, was expected to maximally engage the performance-monitoring capacity of the medial prefrontal cortex, particularly the ACC. We expected reduced ACC activation in older adults and tested whether such a reduction might be specifically related to spatial learning within this group.

Behavioural data were entirely consistent with expectations (e.g., Moffat et al., 2006; Newman & Kazniak, 2000), in that older adults found the maze-learning task to be more difficult than did the younger group. Older adults responded to error feedback as well as the younger adults on initial learn trials, that is, when the location of the maze was unknown and all participants were forced to rely solely on the feedback received

after each trial. It was on subsequent test trials, when spatial learning began to play a greater role in finding the hidden maze, that older adults made significantly more errors than their younger counterparts. Such performance differences would be in keeping with well-documented age-related changes in hippocampal structure and function (e.g., Driscoll et al., 2003); however, differences in electrophysiological indices of error processing suggest that reduced performance monitoring may also play a role.

Older adults' neural response to the feedback provided during this task differed substantially from that of the younger adults, suggesting diminished ACC activation during maze learning, with possible consequences for the recruitment of executive resources (e.g., Moffat et al., 2007). FRNs produced by older adults were generally reduced in size relative to those produced by the younger participants, a difference that was evident during the initial learning trials for each maze and during subsequent test trials for all three levels of task difficulty. These data replicate the age-related reduction in FRN amplitude reported by Nieuwenhuis et al. (2002). They are also consistent with the broader literature on the response-locked ERN, which is diminished with age (Falkenstein et al., 2001; Gehring & Knight, 2000; Kok, 2000; Mathewson et al., 2005).

It is true that reduced certainty of having made an error has been associated with shallower error-related ERPs (Coles, Scheffers & Holroyd, 2001; Pailing & Segalowitz, 2004; Scheffers & Coles, 2000) and that older adults may be more likely to be uncertain about the accuracy of their responses as suggested by Band and Kok (2000). However, in this study, because all participants were given unambiguous feedback on every trial, error uncertainty cannot be considered a contributor to the diminished FRNs observed here (see also Nieuwenhuis et al., 2002). We note also that the FRNs of older adults were

diminished on initial learn trials when they did as well as younger adults, and on test trials when their error rate was markedly greater. Together, these results are consistent with the view (e.g., Falkenstein et al., 2001; Mathewson et al., 2005; Nieuwenhuis et al., 2002) that the age reduction in the amplitude of error-related ERPs is due to a general phenomenon, such as a decline in dopamine levels that seems intrinsic to the aging process (e.g., Cruz-Muros et al., 2007; Kaasinen et al., 2000; Ota et al., 2006; Reeves et al., 2002).

The hidden-maze task was well suited to engage the ACC because finding one's way through the mazes across a number of trials requires the accumulation of spatial information, and this incorporation of the recent history of actions and outcomes is a process particularly associated with ACC activation (Kennerly et al., 2006). Maze learning was also likely to engage ACC neurons because of their links with premotor and motor cortices (Hatanaka et al., 2003) and their responsivity to spatial aspects of a rewarded response (Shima & Tanji, 1998). As well, greater engagement of the ACC would be expected as difficulty levels increased (Paus et al., 1998). Thus, we anticipated that the maze learning task would provide an optimal vehicle with which to study the ACC activation as it related to error-related ERP components, task parameters, and age.

LORETA analyses provided two sorts of data. First, we found that for young adults, overall neural activation at the time of the FRN was consistently and robustly greater in response to negative as opposed to positive feedback. This is what one would expect with a well-functioning error monitoring system (e.g., Ridderinkhof et al., 2004). However, this activation was decidedly less robust and less consistent for our older adults, with differential levels of activation reaching statistical significance very

sporadically, that is, only during the learn trial of the 6×6 grid size mazes. This age difference was also apparent in a more focused analysis of the differential activation specifically within medial prefrontal cortex. For young adults, the activation of medial brain regions was clearly evident in the differentiated FRN response to error feedback, whereas for older adults, differential activation in the ACC was very modest and again remained significant in only one condition: for learn trials of the 6×6 grid size mazes.

These data are consistent with other evidence that the ACC is particularly vulnerable to age-related decline (Schultz et al., 1999; Vaidya, Paradiso, Boles Ponto, McCormick & Robinson, 2007) and also with data reported by Ferrandez and Pouthas (2001). Using BESA source localization, the latter found that ACC activation was markedly reduced in older relative to younger participants during two attention-demanding tasks. This reduced ACC activation was apparent even though their older adults (46-62 years) were much younger than those in our study.

The next question was whether the strength of the FRN response would be related to performance accuracy. Group differences do not really speak to these issues because one can find diminished error-related components in older adults in situations in which the older adults' actual performance is as good as or better than that of the younger group (Falkenstein et al., 2001; Nieuwenhuis et al., 2002). Smaller ERNs may be due to a general age-related limit or reduction in the availability of mid-brain dopamine (e.g., Volkow et al., 1998). As well, there are many differences between young university students (mean age of 20 years) and older community volunteers (mean age of 75 years) that could account for differential accuracy rates. To get around this problem, we examined individual differences in error counts as predicted by FRN amplitudes, after

regressing out any general effects due to age. The results of these analyses did not provide overwhelming support for the relation between FRN amplitude and accuracy although there were some intriguing exceptions.

Whenever relations were found, they were in the expected direction, that is, the smaller the FRN, the higher the error count (Table 2.6), with the most robust example of this being observed for older adults in the test trial performance of the largest maze. When the FRN did add variance to the prediction of error (as in learn trials of the 4×4 and 6×6 mazes and test trials of the 8×8 maze), it accounted for more unique variance than age group. As discussed above, the relation between error rate and FRN amplitude may depend on the degree to which error feedback, relative to memory ability, is central to the task. Thus, we have demonstrated that FRN amplitude does relate to error rate in some conditions, as has been shown with respect to the ERN in young adults (e.g., Hajcak et al., 2003; Herrmann et al., 2004). As well, the relations between these measures may often be difficult to see because they depend on sufficient variance in both ERP and behavioural measures, which may not always occur when using the same tasks with younger and older individuals. Error scores tend to congregate more on the left side of the distribution for young adults and the right side for the elder participants. The same may happen, of course, if the variance in the physiological measure is truncated for either group (see also Mathewson et al., 2005).

In this study, the range in error rate for older adults was greater in the 8×8 grid (Figure 2.10) than in other smaller grids and in comparison to the younger group, resulting in a very large relation with FRN amplitude. Thus, although it was true that FRNs and hence ACC activation were reduced in the older relative to the younger group,

ACC activation seems, nonetheless, to make a difference with respect to error response. That is, *within* the older group, performance was not independent of the robustness of error signals.

We also examined the feedback P3. Principal component analysis had indicated that the feedback P3 formed a separate ERP response, which was also obvious from the scalp maxima and LORETA activation maps. The feedback P3 proved to be particularly sensitive to overall activation patterns associated with negative relative to positive feedback at the whole-brain level for both younger and older adults. Examining medial regions specifically, activation associated with the feedback P3 was still significantly differentiated for all grid sizes and conditions for young adults. We also noted that P3 activation was more clearly responsive to negative relative to positive feedback in older adults during test trials, albeit rather minimally in the learn trial situation. However, despite this differential activation by condition, there was absolutely no evidence that individual differences in feedback P3 activation related to error counts. This may, of course, be due to a lack of variance in the degree of P3 response or, more interestingly, to the fact that the P3 plays a different role in the monitoring of task performance.

It is significant that the distinction between FRN and P3 responses observed in these data involve neural systems that are differentially susceptible to the effects of age. The responsivity of the FRN is based on the viability of dopaminergic enervation of medial prefrontal cortex, a system that has been shown to decline with age (e.g., Cruz-Muros et al., 2007; Kaasinen et al., 2000; Ota et al., 2006; Reeves et al., 2002; Volkow et al., 2000). Conversely, the feedback P3 appears to behave as one would expect of the standard P3 in that it is highly reactive to motivationally significant events, in this case,

to feedback about having made an error. This responsivity is thought to depend on the viability of the locus coeruleus-norepinephrine system (Nieuwenhuis, Aston-Jones & Cohen, 2005; Polich, 2007)—a system that appears to be much more robust in the face of age-related change (Matsunaga, Isobe & Shirokawa, 2006; Nakai, Matsunaga, Isobe & Shirokawa, 2006). In fact, when a decline does occur in noradrenergic cortical axon terminals it is more likely to be associated with atypical changes that have serious implications for cognition (Herrmann et al., 2004; Rommelfanger & Weinshenker, 2007) and therefore, we might expect that an aberration in the feedback P3 would be indicative of non-normative decline, whereas a reduction in the FRN would be associated with normal aging.[5]

Our data also speak to some issues with respect to the general understanding of the error-related ERP response. First, a central prediction of the reinforcement learning account of the FRN is that FRN amplitudes should decline as an internal representation of stimulus-response mapping is established (Holroyd & Coles, 2002). In the present case, this would mean that, as participants developed an internal representation of the maze, they would be more likely to recognize an error on their own, which would generate a response-locked ERN and external feedback would be less informative and hence elicit a smaller FRN. However, a learning-based reduction in FRN amplitude was not evident in this study, even in the neural responses of our younger adults where reduced error rates indicated that an internal representation had been formed. Thus, these data do not provide support for this aspect of the reinforcement learning perspective and suggest that the degree to which the diminishment of the FRN occurs depends on the type of paradigm used, as well as the nature of the feedback and the age of the participant (Nieuwenhuis et

al., 2002). It is intriguing, however, that the relations between FRN amplitude and error rate were more evident in those trials in which the reliance on feedback was central, which is likely to have occurred on 4×4 and 6×6 learning trials and on test trials for the largest mazes.

A second issue involves the differential role played by the FRN and P3 in reinforcement learning situations. Yeung and Sanfey (2004) have reported that the FRN tends to be larger in response to losses than gains, but insensitive to the absolute magnitude of the loss/gain. However, in their study the P3 was sensitive to the size of the loss/gain but did not change as a function of the negative/positive valence of the outcome (correct vs. error). The authors interpreted these results as indicating that the FRN does not represent the absolute value of the outcome, only that the outcome is negative, which is consistent with our data and with the dopamine hypothesis (Holroyd & Coles, 2002). However, our results involving the P3 are inconsistent with their observations in that the feedback P3 for both young and older adults in the present study appear to be acutely sensitive to feedback valence, a discrepancy that may be due to differences in task parameters. Yeung and Sanfey's participants were engaged in a gambling study where P3 amplitudes reflected degrees of real losses and gains over which participants had no control. By contrast, in the hidden-maze learning task, making an error served a utilitarian function with respect to the actual improvement of performance on the subsequent trial. Thus, the P3 in the maze task could be considered in the same light as the Pe in standard response-locked paradigms, that is, as an index of the salience of the error within the context of a task in which one has some power to control outcomes (Mathewson et al., 2005).

In summary, the results of this study have shown that older adults are less able than younger adults to learn a series of hidden mazes and that they do not respond to negative feedback during their attempts in the same way as younger adults. Most discrepant was the neural response associated with the FRN. For younger adults this component was clearly associated with feedback-specific activation in the anterior cingulate and adjacent regions in the medial cortex, a situation that did not hold for our older adults whose neural response, whether measured at the scalp or through LORETA source localization, revealed a weak and diffuse level of activation suggesting a less focused or strategic response (Rajah & D'Esposito, 2005). However, despite the weak and diffuse nature of the ACC response, it was not irrelevant to error monitoring performance. Amplitude of the FRN related strongly to error rate for older adults when they were solving the largest mazes. In addition, given that there was little significant activation elsewhere in the brain at the moment of the FRN peak, the link between FRN amplitude and accuracy is not likely due to compensatory activation outside of the ACC.

It was interesting as well that the feedback P3 was robustly sensitive to error feedback for both groups. Given the growing consensus that the P3 and FRN reflect different neural processing systems associated with different neurotransmitter support (Nieuwenhuis, Aston-Jones et al., 2005), their dissociation in this data set lends support for the separable decline of these systems in the course of normal aging. Further in regard to the dissociation between these components, it is of interest to note that any relations found between the ERP feedback components and performance occurred only with respect to the FRN and by extension, the differential feedback-related activation in ACC. Finally, although generally supportive of the reinforcement learning hypothesis regarding

feedback negativities (Holroyd & Coles, 2002), these data also present some challenges to our understanding of the association between response-based and feedback-based components that eventually will have to be reconciled.[6]

Chapter 3. Autonomic control and maze-learning performance

in older and younger adults

Abstract

The capacity to make phasic adjustments in heart rate was examined as it related to cognitive performance in older and younger adults. Resting cardiac measures and on-line electrocortical brain activity were recorded as participants received error feedback while working through a hidden-maze task. Cognitive demands were increased by expanding maze size. Results indicated that cardiac indices of autonomic regulation were predictive of performance. Increased errors were associated with lower levels of respiratory sinus arrhythmia (RSA), an index of phasic parasympathetic cardiac control, mainly for young adults; in older adults, increased errors were associated with higher rate pressure product (RPP), an index of cardiac workload. These relations were most apparent when the demand for controlled processing was substantially increased.

Introduction

Autonomic processes associated with cognition

Heart rate variability (HRV)—variation in the length of the interval between heart beats—is a hallmark of adaptive physiological self-regulation (Porges, 1992; Thayer & Lane, 2000). Individuals with higher HRV demonstrate greater physiological flexibility, whereas lower HRV represents reduced ability to organize physiological resources in the service of goal-directed behaviour (Thayer & Lane, 2000). Although HRV has often been examined in the context of emotional regulation (e.g., Appelhans & Luecken, 2006; Friedman & Thayer, 1998), stress responses (e.g., Gianaros et al., 2005; Hall et al., 2004), and social development (e.g., Fabes, Eisenberg, Karbon, Troyer & Switzer, 1994; Porges, 2001), few researchers have used HRV to predict cognitive performance (for exceptions, see Hansen et al., 2003; Johnsen et al., 2003; Melis & van Boxtel, 2007), and even fewer have examined these relations in older populations. However, since aging has important effects on autonomic functioning (Low, 1997), it was our goal to examine these relations as they occur in both older and younger adults.

Heart rate is the net outcome of competitive innervation of the heart by the sympathetic and parasympathetic divisions of the autonomic nervous system (ANS). However, the peripheral output of these divisions is modulated directly by a number of higher brain regions in medial frontal cortex that form a central autonomic network (CAN; Benarroch, 1993; see also Ahern, Sollers, Lane et al., 2001). To generate adaptive responses, the CAN integrates sensory inputs and external information from the environment (Thayer & Lane, 2000). Neural output from the CAN influences sympathetic and parasympathetic neurons in the stellate ganglia and vagus nerve,

respectively, and through these systems, affects the function of the heart's pacemaker, the sino-atrial node. Thus, variability in the cardiac signal is closely associated with CAN output (Thayer & Lane, 2000). An important part of this network, the anterior cingulate cortex (ACC) mediates central autonomic regulation during the performance of cognitive tasks (Critchley et al., 2003; Critchley et al., 2005; Matthews, Paulus, Simmons, Nelesen & Dimsdale, 2004).

The effects of the two autonomic divisions on HRV are competitive but not equivalent, due to differences in the latencies and courses of action of their respective neurotransmitters. Sympathetic activation occurs when post-ganglionic sympathetic fibres release norepinephrine, a neurotransmitter with a relatively slow onset. It requires about 4 seconds to peak, returning to baseline after about 15-20 seconds (Appelhans & Luecken, 2006). In contrast, parasympathetic transmission peaks in less than one second on the release of acetylcholine by post-ganglionic parasympathetic nerves—a neurotransmitter with comparatively fast onset and offset. Thus, high frequency modulation of heart rate is mediated by the parasympathetic system, and low-frequency modulation is mediated sympathetically (Levy, 1990, 1997). Resting HRV is dominated by parasympathetic influences throughout life. If parasympathetic activity is reduced, so is overall HRV, and with it, the flexibility of behavioural responses.

Parasympathetic control declines significantly in healthy aging (e.g., DeMeersman, 1993), shifting the relative balance between the two branches of the autonomic nervous system toward greater sympathetic predominance (Bonnemeier et al., 2003; Waddington et al., 1979) and lower overall HRV (e.g., Singh, Vinod, Saxena & Deepak, 2006). Thus, physiological aging results in a form of autonomic dysregulation

(Bonnemeier et al., 2003). Because lower HRV is also seen in depression (Rechlin et al., 1994; Udupa et al., 2007), anxiety (Friedman & Thayer, 1998), hypertension (Guzzetti et al., 1988; Liao et al., 1996), and coronary heart disease (Dekker et al., 2000; Wennerblom et al., 2000), the reduction of HRV is not fundamentally a benign developmental change. Our focus is on the degree to which dysregulation in this system affects cognitive processing. We expect cognitive outcomes to be adversely affected when HRV is reduced.

The role of the ACC in autonomic and cognitive function

In addition to its role in autonomic regulation, ACC activity has been closely associated with performance monitoring. The ACC is part of a reward-based learning system (e.g., Amiez et al., 2006; Shidara & Richmond, 2002) that is activated when the outcome of an action violates expectations (e.g., Holroyd & Coles, 2002; Oliveira et al., 2007). Event-related potentials in the EEG waveform, that is, the error-related negativity (ERN, Gehring et al., 1993), or error negativity, Ne, (Falkenstein et al., 1990) are reported to be generated in or very near the ACC. When errors cannot be discerned internally, a feedback-related negativity (FRN, Miltner et al., 1997) is generated in the same region (e.g., Holroyd et al., 2004; Nieuwenhuis, Slagter et al., 2005). ERP responses to negative information are hypothesized to signal the need for increased top-down control and a change of strategy (Bartholow et al., 2005; Ridderinkhof et al., 2004), and they are generally attenuated with age (Falkenstein et al., 2001; Nieuwenhuis et al., 2002).

Whenever an error is made, cognitive and physiological resources must be coordinated within milliseconds to assess the unexpected result and reorganize behaviour

so as to offset the consequences or avoid further errors (Thayer & Lane, 2000). Thus, errors will evoke central modulation of cardiac autonomic control by dorsal ACC (Critchley et al., 2005; Thayer & Lane, 2000) and elicit transient cardiac slowing (Crone et al., 2003; Somsen, van der Molen, Jennings & van Beek, 2000), as do situations requiring cognitive manipulation (e.g., Jennings, van der Molen & Debski, 2003) or the inhibition of responses (Jennings, van der Molen, Brock & Somsen, 1992). Because controlled processing has higher physiological costs than automatic processes (Aasman et al., 1987) or tasks that draw on prior knowledge (e.g., Melis & van Boxtel, 2007) or visual information (e.g. Middleton, Sharma, Agouzoul, Sahakian & Robbins, 1999), it is more likely to be affected by the ability to organize physiological resources in the service of goal-directed behaviour (Critchley et al., 2003; Schneider, Dumais & Schiffrin, 1984).

In previous work with older adults, we reported a strong relation between higher HRV and better performance in a source monitoring task, a relation not seen in a standard letter flanker task requiring speeded responses (Dywan et al., submitted). However, source monitoring is also more difficult for older adults than is performing a flanker task (e.g., Nieuwenhuis et al., 2002), so it was possible that this dissociation was not due to differences in task requirements, but rather, in task difficulty. Another focus of this study was to disentangle these two factors.

The present study

We examined behaviour, cardiac autonomic control, and electrophysiological indices of ACC activity in younger and older adults using a spatial learning task—a modified version of the Groton Maze Learning Test (Snyder et al., 2005). This computer-based task involves finding a hidden pathway through a grid of tiles by trial and error,

receiving informative visual feedback after each move. Outcome measures (e.g., errors and completion times) have proven sensitive to age differences in spatial learning efficiency, and correlate with scores on neuropsychological tests of executive function, such as planning and sustained attention (Pietrzak et al., 2007). Negative feedback was expected to elicit FRN responses in both age groups.

Each maze was repeated several times, with feedback provided after every response throughout each trial. In the initial trial for a maze, participants learned the hidden maze path by trial and error and were entirely dependent on external feedback. However, on subsequent repeated trials, they were able to access a developing internal map of the stimulus field in addition to receiving feedback. The cognitive requirements of the two conditions differed, in that initial learning trials were similar to many of the guessing tasks currently used to collect FRNs (e.g., Hajcak et al., 2006; Yeung & Sanfey, 2004), whereas the repeated trials were expected to reflect the extent to which participants had learned the maze. We expected to find better performance in these additional trials than in the learn trials, and increasingly improved performance across repetitions. Autonomic relationships from these two contrasting conditions could be compared. If relationships between autonomic variables and task outcomes differed by trial type, this would support the hypothesis that task requirements were an important factor in eliciting them.

An advantage of the adapted maze-learning test is that it can be administered at more than one level of difficulty, with consistent instructions, user interface, task requirements, and feedback at each level. This allowed us to test whether relationships between autonomic control and cognitive processing would be stronger when difficulty

increased within the task. If larger mazes showed stronger associations with autonomic measures than smaller ones, this would suggest that relationships between autonomic control and task outcomes are a function of difficulty level.

Age-related decline in spatial learning ability has been well documented (Driscoll et al., 2003; Moffat et al., 2006; Newman & Kazniak, 2000). This decline has been associated with structural and chemical changes in the hippocampus (Driscoll et al., 2003), changes that are reported to place more load on midbrain error monitoring capacity, making it likely that a spatial learning task would maximally engage the ACC (e.g., Moffat et al., 2006; Yoshida & Ishii, 2006). As well, ACC activation is greatest when expectations are violated, so that activation could be said to reflect the local history of recent actions and outcomes (Amiez et al., 2006; Kennerly et al., 2006). Thus, tasks that are in some sense cumulative are likely to maximally activate this brain region. To date, however, FRNs have typically been elicited in guessing or gambling tasks (e.g., Donkers et al., 2005; Hajcak et al., 2006; Yeung & Sanfey, 2004), time-estimation tasks (e.g., Miltner et al., 1997), and tasks where reward contingencies are impossible to learn (e.g., Nieuwenhuis et al., 2002; Nieuwenhuis, Slagter et al., 2005). In these paradigms, no trial has any direct consequence for any other trial. In contrast, spatial learning requires cumulative acquisition of item and configural information that must be retained for use in subsequent trials. Thus, in a spatial learning task, ACC signalling would be largest after an error that followed a run of successful choices, potentially reducing the likelihood of the error being repeated in the next trials (Kennerly et al., 2006).

Despite our primary interest in parasympathetically mediated HRV, because the two divisions of the autonomic nervous system function independently of each other

(Berntson et al., 1994), the viability of both divisions was assessed. For a parasympathetic index, we calculated respiratory sinus arrhythmia (RSA) from the cardiac signal. This is a commonly used, vagally mediated measure of the natural variation in interbeat interval that is linked to the respiratory cycle. Rate pressure product (RPP), a proxy for myocardial oxygen demand, was calculated as an index of cardiac workload (Monroe & French, 1961; Nelson et al., 1974). As would be expected from a sympathetic measure, RPP is reported to increase in stressful conditions, such as exercise (Robinson, 1967), public speaking, anger recall (e.g., Merritt, Bennett, Williams, Sollers & Thayer, 2004), and the performance of arithmetic problems (Robinson, 1967). Resting heart rate and blood pressure were also recorded. These four autonomic indices were analyzed with behavioural performance and the error-related ERPs elicited by negative feedback in the spatial learning task.

We anticipated that spatial learning would be less efficient in older than younger adults. We also expected that within each age group, higher resting levels of RSA would correlate with better behavioural performance (fewer errors) and more robust cognitive responses to errors (larger error-related ERPs). Because RPP was computed mainly as a control measure, we made no prediction about resting measures of cardiac workload with respect to behavioural performance or electrocortical responses.

An in-depth examination of the ERP correlates of error feedback during the maze learning task has been undertaken and reported in chapter 2 (see also Mathewson, Dywan, Snyder, Tays & Segalowitz, in press). However, in order to examine RSA in the context of behavioural and electrocortical indices of error feedback during the maze

learning task, it is necessary to provide some information regarding task outcomes to allow evaluation of their relationship to RSA.

Method

Participants

Participants were drawn from the same subject group (20 older and 20 younger) as the first study (chapter 2). Because not all participants were able to complete all of the mazes, particularly the largest ones, behavioural data from one younger adult and six older adults were incomplete. Data from these seven participants were excluded from analysis, leaving data from the same 33 participants (19 young; 14 older), as in chapter 2. Cardiac data from one older adult were unusable due to the frequent presence of a cardiac anomaly (possible premature atrial contractions) unrelated to autonomically mediated heart rate variability. However, this person's behavioural and electrocortical data were retained due to our small sample size.

Stimuli and experimental design

These were the same as those outlined in chapter 2.

Procedures

In addition to the testing procedures described in chapter 2, trained laboratory personnel recorded blood pressure readings before and after the testing session using a manual sphygmomanometer while participants were comfortably seated.

Cardiac measures

Electrocardiogram (ECG) recordings were collected during a 5-minute pre-session rest period, throughout maze performance at each difficulty level, and during a 5-minute post-session rest period after all computer tasks were completed. ECG signals

were recorded from two electrodes placed on the participants' chest, about 2.5 cm below the left clavicle and about 5 cm below the top of the sternum, at the midline, with a hardware gain of 1000.[7] ECG signals were sampled at 500 Hz and digitized with a 16-bit ADC, then edited by hand and analyzed using a commercial software package (MindWare HRV 2.51, Lafayette Instruments). R-R (interbeat) intervals were visually checked in the MindWare program by a trained laboratory technician and edited where necessary according to principles advocated by Berntson and Stowell (1998). Minute-by-minute estimates of RSA (heart rate variability at the respiratory frequency, 0.12–0.4 Hz) were calculated via spectral analysis of the heart beat series (Fast Fourier Transform) using a Hamming window. These estimates, along with average interbeat interval (IBI), were calculated for each rest period.[8] RPP during rest periods was derived by multiplying mean blood pressure readings together with mean minute-by-minute estimates of resting heart rate, then dividing by 100.

Electrophysiological (EEG) recording and measures

EEG scalp data were recorded as described in chapter 2, from 250 scalp sites using a Geodesic Sensor Net with signals sampled at 500 samples/s.

Scoring and analyses

Autonomic indices were analyzed in 2 × 2 mixed model ANOVAs with period (pre-session vs. post-session) as the within-subjects factor and group (older vs. younger adults) as a between-subjects factor. As outlined in chapter 2, behavioural and electrophysiological data (FRNs) were analyzed using 3 × 2 × 2 mixed model ANOVAs, with grid size and trial type as within-group factors and age group as the between-group

factor. Autonomic indices were then examined for associations with behavioural performance and electrocortical measures (FRNs) using hierarchical regression.

Results

Autonomic indices

IBI (heart period; the inverse of heart rate) was assessed in a mixed model ANOVA with phase (pre-test, post-test) as the within-subjects factor and age group as the between-subjects factor. Overall, heart period did not differ between older ($M = 889 \pm 35$ ms) and younger adults ($M = 823 \pm 28$ ms; $p > .15$) but there was a main effect of phase, $F(1, 26) = 26.86, p < .001, \eta^2 = .51$, such that IBIs were shorter ($M = 830 \pm 22$ ms) prior to testing than in the post-test period ($M = 882 \pm 23$ ms). There was no significant interaction ($p > .09$), but participants' heart rates were generally slower after testing than prior to the testing session.

Subjecting RSA to a similar analysis revealed that, as expected, RSA was higher in younger ($M = 6.17 \pm .30$ ln ms^2) than older adults ($M = 4.59 \pm .38$ ln ms^2; $p < .01$) and lower during the pre-testing rest period ($M = 5.11 \pm .29$ ln ms^2) than during the post-testing rest period ($M = 5.65 \pm .21$ ln ms^2; $p < .01$). However, age group interacted with phase, $F(1, 26) = 5.04, p < .04, \eta^2 = .16$, such that the shift was significant from pre- to post-test for older ($p < .02$) but not for younger adults ($p > .10$). Because RSA appeared to be particularly suppressed during the pre-test period for the older adults relative to their post-test levels, we surmise that the pre-test period may have been more stressful for them.

Systolic blood pressure (SBP) measures from the pre- and post-test rest periods were also compared in an age group by phase (pre- or post-task) mixed model ANOVA.

SBP was significantly higher in older ($M = 140 \pm 2.3$ mm Hg) than younger adults ($M = 105 \pm 2.8$ mm Hg), $p < .001$, with a marginal age by phase interaction, $F(1, 18) = 4.01$, $p < .07$, $\eta^2 = .18$. Follow-up analyses showed that SBP did not change significantly for either group ($ps > .15$), but the directions of change differed, with younger adults declining slightly and older adults increasing slightly to account for the interaction.

RPP measures were calculated for the resting periods before and after testing, and similarly compared in a mixed model ANOVA. RPP was higher in older ($M = 95 \pm 3.6$) than younger adults ($M = 76 \pm 4.4$), $F(1, 13) = 11.19$, $p < .01$, $\eta^2 = .46$, and higher before testing began ($M = 90 \pm 3.7$) than at the end of the session when testing was complete ($M = 82 \pm 2.8$), $F(1, 13) = 5.53$, $p < .04$, $\eta^2 = .30$. There was no interaction with age ($p > .80$).

Thus, resting autonomic measures showed group differences that were consistent with age-related decline in cardiac autonomic control, i.e., lower indices of parasympathetically mediated HRV, and higher indices of blood pressure and cardiac workload in the older sample, even though resting heart rate did not differ between groups.

Separate correlational analyses among autonomic measures indicated that in young adults, IBI was positively correlated with RSA ($r = .57$, $p < .02$) and negatively correlated with RPP ($r = -.69$, $p < .01$), demonstrating that in this age group, resting heart rate was predominantly under parasympathetic control (Levy, 1990). In addition, RPP was correlated with SBP ($r = .72$, $p < .01$). Thus, in the younger group, RPP appeared to be equally driven by blood pressure and heart rate, as one would expect, given how RPP is calculated. Among the older adults, RPP was inversely correlated with both RSA ($r = -.64$, $p < .04$), and IBI ($r = -.79$, $p < .01$) as expected, but was unrelated to SBP ($p > .15$),

suggesting that RPP variance in this group was more reflective of variance in resting heart rate than blood pressure. The inverse correlation between RSA and RPP in the older group also suggests that resting parasympathetic and sympathetic influences were reciprocal in this group. This relation failed to reach significance for younger adults ($p > .06$).

Behavioural responses

Older adults ($M = 3.35 \pm .24$) rated the task as more difficult than did younger adults ($M = 2.52 \pm .20$, $p < .02$), and difficulty ratings were higher for larger mazes ($M_{4x4} = 2.20 \pm .13$; $M_{6x6} = 2.91 \pm .14$; $M_{8x8} = 3.69 \pm .24$, $p < .001$). Grid size interacted with age group, $F(2,54) = 3.59$, $p < .05$, $\eta^2 = .12$. Older adults rated the small and medium mazes as more difficult than younger adults ($ps < .02$); however, both groups rated the largest mazes as equally difficult ($p > .30$). Within each age group, difficulty ratings were unaffected by age, education, vocabulary score, and estimated health status ($ps > .09$). At each grid size, difficulty levels were specifically associated with test error scores for younger ($ps < .001$) but not older adults ($ps > .12$), with no relationships between difficulty ratings and learn errors for either group (all $ps > .06$).

As outlined in chapter 2, main effects of age, trial type, and grid size on error rates were all significant ($ps < .01$), but were qualified by a three-way interaction, $F(2, 62) = 10.94$, $p < .001$, $\eta^2 = .26$ (Table 2.1). Follow-up analyses indicated that errors increased with grid size to the same degree for both groups in learn trials (interaction: $p > .80$), as would be expected when participants were completely dependent on feedback. However, on test trials, when differential learning rates became relevant, errors increased with grid size ($p < .01$), especially for older adults ($p < .001$; see Footnote 3). In addition,

the difference between performance of the initial learn trial and the very first test trial for each grid size, that is, the mean drop in errors from the learn trial to the first test trial, was assessed by a mixed model ANOVA with age group and grid size as relevant factors. As would be expected, the drop in errors differed as a function of grid size, (M_{4x4} = -5.67 ± .4; M_{6x6} = -10.25 ± 1.1; M_{8x8} = -14.81± 2.0), $F(2, 46)$ = 17.15, $p < .001$, η^2 = .43, simply because larger grids provided more opportunities for mistakes. More importantly, younger adults (M = -13.23 ± 1.1) learned more from the initial learn trial for each maze than did older adults (M = -7.27 ± 1.6), $F(1, 23)$ = 9.87, $p < .01$, η^2 = .30. There was no interaction ($p > .08$).

Relations between behavioural performance and autonomic measures

We examined the degree to which autonomic variables (resting measures of IBI, RSA, SBP and RPP) related to behavioural performance in a series of regression analyses, separately for each autonomic measure, trial type, and size. As measures from the pre-testing period were unaffected by the testing session and deemed most representative of individual differences in autonomic control variables, these resting measures were used as independent predictors. Error rates constituted the dependent measure. Group was always entered on the first step, followed by the autonomic measure on the second step, and the interaction term last.

IBI did not predict errors at any grid level for either trial type ($ps > .15$). The interaction term predicted test errors, but only in the largest maze ($p < .05$). Follow-up analyses to explain the interaction indicated that longer IBI was a marginal predictor of reduced test errors in the 8 × 8 maze for older adults ($p < .09$) but not younger ones ($p > .80$).

Predicting learn errors. Group was a significant predictor of variance in learn errors in the 4 × 4 maze ($p < .01$). RSA did not add to this prediction when entered on the second step of the regression analysis. However, when they were both in the equation, RSA and group accounted for similar amounts of variance in the prediction of learn errors in both the smaller mazes and neither variable accounted uniquely for it (see Table 3.1). The pattern was the same for RPP. The exception was for the 8 × 8 maze where, in separate analyses, RSA ($p < .01$), RPP ($p < .01$), and the interaction of RPP with group ($p < .02$; Table 3.1) accounted for significant variance in learn trial errors (see Figures 3.1 and 3.2). Thus, higher RSA and lower RPP were associated with better learning of the most difficult maze and there was no evidence that any variance could be accounted for by group. This was expected since the groups did not differ in terms of the number of errors made on learn trials. It could be argued that the cognitive processes elicited during initial learn trials of the largest maze were very similar to those of test trials, since learning 30 correct moves while responding to error feedback in the largest mazes required considerable attentional control and working memory capacity. Overall, parasympathetic control and sympathetic predominance appeared to explain significant amounts of variance in learning at the level of the largest maze. Neither IBI nor SBP nor their interaction terms predicted learn errors at any grid level ($ps > .18$).

Figures 3.1 and 3.2 and Table 3.1

Predicting test errors. As expected, group was a significant predictor of error variance in test errors at all grid levels ($ps < .01$) since these depend on spatial memory, a challenge for the older group. However, RSA also accounted for significant additional

variance in test errors, beyond group, at all maze levels ($ps < .05$; see Table 3.2). In each case, the amount of variance accounted for by group was reduced once RSA was included in the same model, indicating some overlap in the variance accounted for by these variables. However, both group and RSA continued to account for at least 10% of the variance when considered together, indicating that, despite the overlap, each contributed uniquely to test trial error. Interactions between group and RSA did not predict test errors at any level ($ps > .60$), indicating that higher RSA was associated to some extent with better performance in both groups. Thus, these findings with respect to test trials were in the expected direction. Consistent with our earlier report, higher RSA was associated with better performance on a complex, attention-demanding task (Dywan et al., submitted).

Although it is unusual to explore data further when interactions are not significant, because of the *a priori* hypothesis central to this thesis, namely, that higher RSA would be associated with better performance of tasks requiring high levels of attentional control and working memory, separate correlational analyses were carried out to isolate the role of RSA with respect to errors within each group. No relationships between RSA measures and errors reached significance for older adults (all $ps > .15$), but for younger adults, RSA was marginally related to test errors in the 4×4 maze ($p < .08$), and significantly correlated with test errors in the 6×6 and 8×8 mazes ($ps < .04$; see Figure 3.3). The significant relationships for young adults (but not older adults, $prs > .25$) were retained when adjusted for resting heart rate ($prs < .05$). In general, younger adults with higher resting RSA performed test trials better than their compatriots with lower RSA.[9]

Neither IBI nor SBP, nor their interaction terms, reliably predicted test errors (typically, $ps > .16$). However, analyses indicated that although RPP itself did not predict test errors across groups ($ps > .20$), at all three grid sizes, the interaction of RPP with group ($ps < .03$) contributed significantly to test error prediction by group ($ps < .01$). The robustness of the interaction terms was based on the fact that for young adults, there were no relationships between RPP and learn errors or test errors ($ps > .15$), but for older adults, higher RPP was associated with higher test error rates (4×4: $p < .07$; 6×6, 8×8: $ps < .05$; see Figure 3.4). In general, higher RPP in older adults appeared to be detrimental to maze test performance whereas there was no such association for young adults.

Figures 3.3 and 3.4 and Table 3.2

Since subjective difficulty ratings were correlated with test errors at each grid level, these ratings were also entered in regression analyses with autonomic variables, separately for each grid level, with group entered first as usual. The RSA $\times$ group interaction ($p < .02$) for the 8×8 mazes and marginal relation for the 6×6 mazes, ($p < .07$), indicated an association between higher difficulty ratings and lower RSA in the younger group. This was supported by the pattern of bivariate correlational analyses (younger: 4×4: $p < .06$; 6×6, 8×8: $ps < .02$; older: all $ps > .80$). Thus, younger individuals with higher resting RSA rated the larger mazes as less difficult than did those with lower RSA, in addition to performing them better. There were no significant relations between difficulty ratings and IBI, SBP, RPP, or their interactions for any grid size (all $ps > .15$).

FRN response to feedback

Based on visual inspection, FRN amplitude, which was unique to error trials, was defined as the most negative peak between 250 and 400 ms following negative feedback for younger adults and, for older adults, between 300 and 400 ms, as explained in chapter 2. The age difference ($p < .001$) was confirmed in an ANOVA of FRN latencies. (See the overlaid averaged ERP waveforms for correct and error trials at representative midline sites (Fz, FCz, and Cz) for each group in Figures 2.4 and Figure 2.5).

As described in chapter 2, overall, peak FRN amplitudes were deepest in the 4 × 4 maze ($p < .01$), and larger for younger than older adults ($p < .03$). They also tended to be largest at Fz, relative to other midline sites ($p < .06$), although these main effects were qualified by an interaction among group, grid size, and trial type, $F(2, 38) = 3.82, p < .04,$ $\eta^2 = .17$. Follow-up analyses indicated that FRN amplitudes were shallower for larger grid sizes ($p < .02$), especially with respect to test trials ($p < .05$) for older adults.

Autonomic correlates of electrophysiological response

To determine whether cardiac variables related directly to electrocortical function, ERP amplitudes from each trial type and grid size were analyzed in the same way as behaviour. Another series of hierarchical regression analyses was carried out using FRN amplitudes at Fz as the dependent variable for each trial type and grid size, with autonomic variables (IBI, RSA, SBP and RPP) as predictors, followed by separate correlational analyses for each group. The results of these analyses indicated that when group was entered first in the regression analysis, autonomic variables were not generally associated with FRN amplitudes. The only exception was that higher RPP was linked to shallower FRNs to test errors in the 4 × 4 maze ($p < .02$; see Table 3.4), accounting for

25% of the variance, but with no interaction ($p > .13$). This sporadic result suggests that, across groups, signalling for increased cognitive control was stronger (deeper FRNs) when resting cardiac workload (sympathetic predominance) was lower.

Figure 3.5 and Tables 3.3 and 3.4

Autonomic relationships a function of increased difficulty or task demands?

We had planned to formally test our hypothesis that the relationship between cardiac autonomic control and behavioural outcomes would be stronger as difficulty increased. However, the ranges of the significant correlations across grid sizes were obviously quite small, being -.51 with respect to test errors and RSA in the larger mazes (6×6, 8×8) for young adults, and ranging from .58 to .59 with respect to test errors in the larger mazes and RPP for older adults (Table 3.5). Thus, it would appear that the strength of the relationships between cardiac autonomic variables and test performance varied little across difficulty levels. Any apparent increase in the steepness of the slope of the regression lines in the more difficult mazes could be attributed to the confounding of difficulty level and grid size, i.e., greater numbers of errors were possible in larger mazes. Furthermore, because the pattern of relationships between performance and cardiac autonomic variables was observed more consistently for test trials (Table 3.2), than for learn trials (where it was seen only in the largest, most complex mazes; Table 3.1), we concluded that task requirements were most influential in determining these relationships, rather than increased challenge within a task, at least across the difficulty levels tested here. No relations were seen with respect to autonomic indices for learn trials until task demands evoked working memory, at a high threshold of difficulty, in the 8×8 maze.

Table 3.5

Discussion

Cardiac autonomic regulation in older and younger adults was examined in relation to performance of a spatial learning task. Negative feedback following errors in the maze task was expected to engage the performance monitoring capacity of medial prefrontal cortex, and to elicit feedback-related negativities (FRNs). Age differences were expected in resting indices of cardiac autonomic control, task performance, and response to feedback. We tested whether, within their respective groups, younger and older participants with higher HRV would show better performance of the maze-learning task.

Behavioural results were in line with expectations: older adults rated the mazes higher in difficulty than did younger adults, suggesting that they had to exert greater effort to cope with the basic demands of the task. Older adults also made more errors overall, mainly because of their vulnerability in repeated test trials. Thus, despite evidence of learning in both groups, older adults experienced the maze-learning task as subjectively more difficult in terms of the effort required, and objectively, in terms of their actual performance. In addition, the processes by which mazes were learned appeared to differ by age group. Whereas younger participants acquired most of the necessary information about maze paths during the initial learning trial of a maze, older participants learned the maze paths incrementally, i.e., making frequent errors up to and including the later test trials. These findings are consistent with age-related deficits in executive skills required for spatial learning (cf. Moffat et al., 2006), as well as deficits in

learning reward contingencies (e.g., Mell et al., 2005) and limited ability to increase attentional effort (e.g., Chao & Knight, 1997).

The relationships between cardiac autonomic control variables and task outcomes differed by group. Overall, higher resting RSA was associated with lower difficulty ratings and better learn- and test-trial performance in larger mazes. As indexed by RSA, the capacity to flexibly regulate heart rate appeared to be important for the efficient organization of physiological resources and correct responses in our cumulative spatial learning task, particularly within the younger group. For younger adults, these relationships remained significant even when resting heart period was controlled, suggesting that RSA accounted for unique variance in performance in the larger mazes that was not explained by heart period. In addition, difficulty ratings for this group were highly correlated with test trial performance at each grid level (all $rs > .76$, $ps < .001$). Thus, young adults with higher resting RSA completed test trials with greater ease than did those with lower RSA. Although correlations between RSA and test trial performance within the older group did not reach significance, the direction of association was the same for both young and older adults, indicating that the relation of RSA to performance was similar in both groups, albeit weaker for older adults.

In general, analysis of individual levels of resting RPP revealed associations between resting cardiac workload and learn and test trial performance in older adults of the larger mazes. That is, higher RPP in the older group, reflecting increased sympathetic predominance (Monroe & French, 1961; Nelson et al., 1974), was associated with relatively poor test trial performance. No relationships with RPP were found in the younger group. In addition, common measures of autonomic regulation such as resting

heart rate and systolic blood pressure did not generally relate to performance outcomes or FRN magnitude.

Our finding associations between performance and autonomic variables is in line with reports of enhanced attentional control and working memory performance with higher RSA in young adults (e.g., Hansen et al., 2003; Johnsen et al., 2003). They also corroborate results from a study in our lab where higher RSA in older adults was associated with better performance of an attention-demanding source monitoring task (Dywan et al., submitted). Our RPP results in the older group are consistent with studies showing links between pathological sympathetic predominance (e.g., hypertension) and poor performance of a variety of cognitive tasks, including tests of continuous task-switching (e.g., Trail-making B; Kuo et al., 2004), verbal and visual memory (e.g., logical memory and visual reproduction; Elias, Elias, Sullivan, Wolf & D'Agostino, 2003), and spatial problem-solving and abstract reasoning (block design and similarities; e.g., Robbins et al., 2005). More effective blood pressure recovery after cognitive testing has also been linked to superior performance of memory tests in older adults (e.g., visual paired associates; Wright, Kunz-Ebrecht, Iliffe, Foese & Steptoe, 2005). Together these studies suggest that when sympathetic activity is unchecked by adequate parasympathetic function (as seen in older adults), cognitive outcomes are adversely affected.

The hypothesis that relationships between autonomic indices and performance would be stronger with increased task difficulty was not fully supported. Although it was clear that relationships between cardiac autonomic control variables (RSA or RPP) and performance were generally significant for test trials, they did not strengthen appreciably as grid size increased, for either group. In contrast, for learn trials, no relationships were

seen with autonomic variables until a level of difficulty was reached that imposed demands on attention and working memory comparable to those required in test trials. Although this suggests some sensitivity to task difficulty, in general, our results support the hypothesis that these relationships do not vary as a function of simple changes in task parameters, unless the difficulty becomes sufficient to elicit higher level executive functioning. Thus, the requirement for executive skills appears to be more important to evoking relations with cardiac control variables than within-task difficulty per se (cf. Mulder, 1986).

We have also shown that deeper FRN amplitudes were associated with lower learn error rates in the 4×4 and 6×6 mazes across groups (Mathewson, Dywan, Snyder, Tays & Segalowitz, 2008), consistent with reports showing inverse relationships between error negativities and accuracy in young adults (e.g., Hajcak et al., 2003; Herrmann et al., 2004). In the present study, deeper FRN amplitudes to negative feedback in initial maze-learning (4×4 test trials) in younger adults were associated with greater parasympathetic influence on heart rate and reduced sympathetic predominance. Thus, for young adults, deeper FRNs were linked to better performance and to greater cardiac control in the easiest maze conditions. In contrast, the FRN responses of older adults peaked later, irrespective of trial type or task difficulty, suggesting that older adults were slower than younger adults to process negative feedback (cf. Hillman, Belopolsky, Snook, Kramer & McAuley, 2004). The FRNs of older adults were also comparatively shallow and undifferentiated across midline sites, and did not discriminate well between negative and positive feedback in either trial type (see Figure 2.5 and Eppinger, Kray, Mock &

Mecklinger, 2008; Mathewson et al., 2008)[10], nor were they related to RSA or RPP at any grid level ($ps > .13$).

Attenuated FRNs are consistent with age-related reductions in available dopamine (e.g., Kaasinen et al., 2000; Volkow et al., 1998), and there is evidence to suggest that they may be linked to reductions in stimulus-reward association learning (e.g., Mell et al., 2005). When errors are detected, ACC signals initiate the activation of top-down mechanisms (e.g., Bartholow et al., 2005; Holroyd & Coles, 2002; Walton, Devlin & Rushworth, 2004), to deal with the situation and stabilize deteriorating performance. According to Sarter et al. (2006), this stabilization is hypothesized to occur via greatly increased cholinergic activity in prefrontal cortex. To increase top-down control, prefrontal cortex engages the cholinergic system through neurons that project to the basal forebrain, which innervates all cortical areas and layers (Gaykema, van Weeghel, Hersh & Luiten, 1991). However, the resulting efflux of acetylcholine that leads to the implementation of top-down control is subject to mesolimbic regulation, because mid-brain dopaminergic neuronal firing controls the excitability of the cortical cholinergic input system (Gaykema & Zabosky, 1996; Smiley, Subramanian & Mesulam, 1999). The reduced availability of mid-brain dopamine with age may interfere with the capacity of prefrontal cortex to implement top-down control through the cholinergic system. This hypothesis may explain why shallower FRN amplitudes in young adults are associated with poor performance in the smaller mazes, and why older adults have greater difficulty learning the mazes in general. It is also consistent with the suggestion of Neiuwenhuis et al. (2002), namely, that performance deficits are due to both inefficiency in the

monitoring processes that call for increased top-down control, that is, shallower error negativities, and inefficiency in actually implementing executive control thereafter.

Summary and conclusions

Sympathetic and parasympathetic influences interacted with performance in a challenging spatial learning task differentially for older and younger adults. In younger adults, higher trait-like measures of HRV as measured by pre-test resting RSA were associated with better performance of test trials, and learn trials of the largest maze, suggesting that greater capacity to modulate heart rate via the parasympathetic system was related to more efficient learning of spatial information. In the older group, RSA did not relate directly to performance; however, poorer cardiac regulation (as indexed by higher pre-test resting cardiac workload, or RPP) was associated with poorer test performance in general and with poorer performance in learn trials of the largest maze, suggesting that the relative increase in sympathetic predominance with age was related to poor learning and/or maintenance of spatial information. We also found some support for the idea that efficient feedback monitoring (larger FRN amplitude) was linked to lower error scores and better autonomic control in the younger group.

Overall, our data suggest that greater sympathetic predominance in the regulation of cardiac autonomic control was detrimental to performance of test trials, where differential learning rates were relevant, but not to learn trials, where only guessing was required, unless the demand for executive processing was substantially increased. Thus, it seems that the requirement for executive skills is necessary to reveal relationships between cardiac autonomic control and cognitive function. This leads us to suggest that some of the cognitive processes involved in constructing internalized representations,

interpreting feedback, and withholding the tendency to repeat errors made previously were linked to adequate autonomic modulation, that is, to greater parasympathetic influence and less sympathetic predominance. Because this balance is important for maximal performance levels in both age groups, as age reduces the capacity for parasympathetic regulation, older adults will be increasingly disadvantaged with respect to performance of executive function tasks.

Chapter 4: Autonomic influence on recollective response:

Source memory, aging, and ERPs

Abstract

The anterior cingulate is considered an interface between cognitive and autonomic control systems. To test effects of age on these systems, resting cardiac measures from older and younger adults were compared with ERPs and performance on an age-sensitive source memory task and a standard letter flanker task given at two levels of difficulty. Aging was associated with a threefold increase in source memory error and a less differentiated ERP response to targeted study words relative to familiar but non-target lures. Also, poorer cardiac vagal control predicted a larger ERP response to lures and increased lure error. These relations were less reliable in the younger group and for flanker task errors irrespective of difficulty level. Results suggest that cardiac vagal control is relevant for the monitoring of internally maintained information in the service of response selection and inhibitory control as these functions decline with age.

Introduction

Memories involve not only the reconstruction of previous experience, but attributions about where and when a particular event was originally encountered (Jacoby, Kelley & Dywan, 1989; Johnson, 2005). Whenever it is difficult to recall the actual details of the context in which an event took place, reasonable but not necessarily correct attributions about the initial context may be made. Source monitoring paradigms provide a way to understand how plausible but incorrect attributions can occur in a variety of situations, including eye-witness testimony (Loftus, 1975), and stereotyping (Mather, Johnson & De Leonardis, 1999), but this tendency is typically exaggerated by aging (e.g., Dywan & Jacoby, 1990; Dywan, Segalowitz & Arsenault, 2002; Jacoby, Bishara, Hessels & Toth, 2005; Jennings & Jacoby, 1997). When easy access to the context of an event is unreliable, resolving the ambiguity of its source in order to make a correct attribution evokes effortful, controlled processing (Jacoby et al., 2005). Because this kind of processing has higher physiological costs than automatic processes (Aasman et al., 1987; Melis & van Boxtel, 2007; Middleton et al., 1999), it is likely to be affected by the ability to organize physiological resources in the service of goal-directed behaviour (Critchley et al., 2003; Schneider et al., 1984). We hypothesized, therefore, that the executive functioning required for source monitoring by older adults would be more directly related to cardiac autonomic control than less effortful processing.

The role of autonomic function with respect to age and cognitive control

Heart rate variability (HRV) is a hallmark of adaptive physiological self-regulation and behavioural flexibility (Porges, 1992; Thayer & Lane, 2000). Overall variability in heart rate reflects central modulation of the sympathetic and

parasympathetic divisions of the ANS (Benarroch, 1997; Thayer & Lane, 2000). Greater variability in the cardiac signal is associated with youth (Park et al., 2007), health (Masi et al., 2007; Singh et al., 2006), and physical fitness (DeMeersman & Stein, 2007; Sandercock, Bromley & Brodie, 2005). With increased age, HRV declines, beginning from the late twenties (DeMeersman, 1993; Waddington et al., 1979). This effectively shifts the balance between the two branches of the autonomic nervous system toward relatively greater sympathetic predominance (e.g., Bonnemeier et al., 2003). Thus, aging involves a form of autonomic dysregulation. This dysregulation has been explicitly associated with various conditions that accompany aging, including the development of hypertension (Liao et al., 1996), cardiovascular disease (Wennerblom et al., 2000), and diabetes (Lindmark et al., 2005; Takayama, Sakura, Katsumori, Wasada & Iwamoto, 2001). However, our focus was on determining the relationship between autonomic regulation, as indexed by HRV, and higher order cognitive control.

Because of differences in the latencies and courses of action of their respective neurotransmitters, the sympathetic and parasympathetic systems have different roles in cardiac control. Local, beat-to-beat modulation of heart rate is dominated by the parasympathetic system (Levy, 1990, 1997). Peak parasympathetic transmission (primarily affecting heart beat timing) is reached in less than one second and reverts quickly to baseline because acetylcholine, the neurotransmitter released by parasympathetic nerves, is easily synthesized and metabolized. Thus, the parasympathetic division of the autonomic system is most likely to be sensitive to changing cognitive demands. In contrast, during sympathetic transmission, post-ganglionic sympathetic fibres release norepinephrine, a relatively slow-acting neurotransmitter that increases the

strength and speed of ventricular contractions, but requires about four seconds to peak and returns to baseline after about 15-20 seconds.

Respiratory sinus arrhythmia (RSA) is a common index of parasympathetically mediated HRV that can be estimated via spectral analysis of ECG. This natural form of variation in the cardiac signal is yoked to the respiratory cycle and mediated almost entirely by the vagus nerve. Thus, RSA provides a relatively pure and non-invasive estimate of parasympathetic influence on HRV (Brownley, Hurwitz & Schneiderman, 2000; Porges, Doussard-Roosevelt, Portales & Seuss, 1994). In examining potential sources of HRV, estimates of the viability of both branches of the autonomic nervous system must be considered because the two divisions of the ANS function independently of each other (Berntson et al., 1994). However, it is impossible to get an estimate of purely sympathetic influence on HRV via spectral analysis. Rate pressure product (RPP), an indirect measure of myocardial oxygen demand and thus, cardiac workload (Merritt et al., 2004; Monroe & French, 1961; Nelson et al., 1974; Robinson, 1967) provides a measure that reflects sympathetic influence on cardiac control. Like a sympathetic measure, RPP increases during exercise (Robinson, 1967), and in stressful conditions such as public speaking, anger recall (e.g., Merritt et al., 2004), and performing arithmetic problems (Robinson, 1967). It may be considered an index of sympathetic predominance in cardiac control.

Autonomic responses to physical demands, such as the orthostatic stress of changing from a supine to standing position, are generally quite uniform across younger adults. However, autonomic responses to psychological stressors tend to be more idiosyncratic (Berntson et al., 1994). These idiosyncratic differences are stable across a

variety of psychological tasks and reproducible across time (Pitzalis et al., 1996). They have been well studied in the context of affective functioning (e.g., Beauchaine, 2001), including emotional regulation (e.g., Appelhans & Luecken, 2006; Friedman & Thayer, 1998), stress (e.g., Gianaros et al., 2005; Hall et al., 2004), and social development in infants and children (e.g., Fabes et al., 1994; Porges, 2001). Although there have been relatively few studies using HRV to predict cognitive performance, those extant have yielded intriguing results. For example, higher HRV has been reported in association with enhanced attentional control and working memory performance in young adults (e.g., Hansen et al., 2003; Johnsen et al., 2003). In addition, Kim et al. (2006) recently showed that lower overall HRV was associated with greater risk of cognitive decline in an older, community-dwelling population. However, mechanisms for these associations have been largely unexplored.

The source memory exclusion paradigm (Dywan & Jacoby, 1990; Jennings & Jacoby, 1997) is known to be particularly sensitive to age. In this paradigm, older and younger participants are asked to review a list of words, and then to distinguish the previously seen words from new words in a running recognition test. (See Figure 4.1). The test list also contains lures—new items that have been repeated in the test list. By their repetition, the lures become familiar and thus, confusable with the studied items. Resolving the ambiguous status of lures while resisting the tendency to call them study items because of their familiarity requires effortful, controlled processing.

Figure 4.1

Typically, older adults have much greater difficulty with this task. Although they are as able as younger adults to correctly identify the previously studied words and reject any new items, they are much more likely to designate lures as having come from the study list (e.g., Dywan et al., 2002; Dywan, Segalowitz & Webster, 1998; Dywan, Segalowitz, Webster, Hendry & Harding, 2001). The assumption is that younger adults are more able to rely on early, more automatic processes to make this distinction, whereas older adults are more dependent on controlled processes to reject the repeated lures. That is, because older adults are less able to rely on early detection, they are thought to rely more on later correction to avoid making source memory errors (Dywan et al., 2002; Jacoby et al., 2005; Jacoby, Kelley & McElree, 1999).

When attempts at late correction fail, the result is a greater inability to withhold a prepotent response to lures, a function for which the recruitment of frontal lobe processes is thought to be most essential (e.g., Janowsky, Shimamura & Squire, 1989; Miller & Cohen, 2001; Spencer & Raz, 1994). Frontal lobe functions are considered especially vulnerable to decline with age (e.g., Murphy, West, Armilio, Craik & Stuss, 2007; Raz, 2000). Candidate regions for decline include structures in the medial frontal lobe (e.g., the ACC). ACC areas modulate parasympathetic and sympathetic activity via projections to their brainstem nuclei and to diencephalic brain regions (Devinsky et al., 1995) and are reported to modulate autonomic function in conjunction with cognitive demands (e.g., Critchley et al., 2003; Gianaros et al., 2004). The ability to make appropriate autonomic adjustments has also been shown to account for significant variance in the performance of difficult cognitive tasks in healthy young adults (e.g., Melis & van Boxtel, 2007). Taken further, this suggests that for older adults with relatively preserved autonomic

control, executive processing (including source monitoring) may be better maintained, relative to their same age peers. Indeed, differential performance in a source monitoring task has been reported in older adults with higher HRV (Dywan et al., submitted). In the present study, we sought to replicate and extend these results.

ACC and performance monitoring

ACC is involved in autonomic regulation during task performance, but it also has a role in performance monitoring, as it is activated after an unintended behavioural error or when the outcome of an action otherwise violates expectations (e.g., Holroyd & Coles, 2002; Oliveira et al., 2007). Event-related potentials (ERPs) resulting from this activation, that is, the error-related negativity (ERN; Gehring et al., 1993), or error negativity, (Ne; Falkenstein et al., 1990) signal the immediate need for increased top-down control to deal with the negative situation (Bartholow et al., 2005; Ridderinkhof et al., 2004). Via the local record created by these signals, the ACC is thought to assess the consequences of individual actions (Walton et al., 2004), providing feedback as to which actions are worth performing in future and which are not.

Error negativities have been extensively researched in speeded response tasks such as the flanker task (Eriksen & Eriksen, 1974). Although this task has been described as a test of executive function due to the interference from flanking letters on target identification, it appears to be easier for older adults to avoid flanker errors than source memory errors (Mathewson et al., 2005). Flanker error rates of older and younger adults are often comparable (e.g., Falkenstein et al., 2001) and sometimes even lower in older adults (e.g., Nieuwenhuis et al., 2002). However, older adults typically make 2-3 times as many source errors as their younger counterparts in source monitoring exclusion

paradigms (e.g., Dywan et al., 2002; Mathewson et al., 2005). Whereas speeded response tasks require attentional control, they do not require the manipulation of stored information and thus do not draw on working memory resources to the same degree as source monitoring does.

Electrocortical responses are generally sensitive to the repeated occurrence or target status of stimuli, being larger for previously encountered information (e.g., Bentin & McCarthy, 1994), and larger for targets than non-targets (e.g., P300, Polich & Criado, 2006). In the source memory test used here, we measured the late positive component (LPC) from correct trials to three stimulus types: targeted study words, non-target lures, and non-target foils. The LPC has sometimes been described as reflecting incidental recollection or recognition of a previously encountered stimulus (e.g., Wilding & Rugg, 1997). However, in the source memory exclusion task, previously seen items can seem familiar either because they were recently studied, or because they were just encountered a few items back in a test list. Distinguishing between these two sources of familiarity represents more than simple recognition and is likely to elicit active information processing (Dywan et al., 1998). Thus, the stimulus-locked LPC in this task may be seen as a response to the salience of an important event (e.g., Dywan et al., 1998).

Whereas younger adults typically produce large LPCs to correctly selected study words and appropriately little activation to non-target foils and lures, the electrophysiological responses of older adults are consistently less differentiated by targetness, and are sometimes even larger for correctly rejected non-target lures than for study items (e.g., Dywan et al., 1998). This greater electrophysiological reactivity to lures may reflect failed early discrimination that has to be overcome, increasing the likelihood

that they will be responded to as though they were targets (Dywan et al., 1998). Although we have shown autonomic associations with response-locked error signals in the source memory task in another sample (Dywan et al., submitted), the electrocortical indices of attention allocation, i.e., LPCs, may also be associated with differences in autonomic modulation. To our knowledge this has not been reported to date.

The present study

Our main goal was to ascertain whether executive processing was more efficient in older adults whose HRV was preserved relative to their same age peers. To do this, associations between individual differences in cardiac autonomic control variables and the behavioural and electrophysiological responses of younger and older adults were tested in a source monitoring task and a contrasting letter flanker task.

For autonomic measures, resting blood pressure and resting ECG were collected at the start and end of the testing session. Three indices of autonomic control were derived from the ECG recordings, each of which represented important aspects of participants' baseline capacity for autonomic regulation. Mean interbeat interval (IBI), the net outcome of various competing sources of innervation of the heart, served as a global index of cardiac behaviour (i.e., heart rate). To estimate the influence of the two major branches of cardiac control, RSA was derived from spectral analysis as an estimate of parasympathetic function, and RPP was calculated (heart rate × systolic blood pressure; SBP) as a proxy for sympathetic influence on HRV.

Age effects were expected in RSA, RPP, and SBP, but our model presupposes that individual differences in autonomic control explain variance in test outcomes over and above that explained by the general consequences of aging. Our main hypothesis was

that the relations among RSA, ERNs, and source memory error (Dywan et al., submitted) would be replicated and extended to another ERP component, the stimulus-locked LPC. We expected that those older adults with poorer autonomic regulation, i.e., poorer parasympathetic regulation and greater sympathetic predominance, would make more source memory errors and would be less able to suppress the LPC associated with lures during the test situation.

In contrast to the source memory task, associations between autonomic control indices and outcomes in previous work (i.e., behavioural performance and ERN responses) were conspicuously absent when it came to the standard flanker task (Dywan et al., submitted). Accordingly, they were not expected in the current study. However, it was not clear from our initial experiment whether the failure to find associations between autonomic variables and error responses on the flanker task was due to a markedly different type of cognitive demand (i.e., the reliance on internally-maintained working memory information in the source memory task) or simply to differences in task difficulty. To explore this issue, a more challenging flanker task (van Veen & Carter, 2002) was administered (to younger adults) and the results correlated with autonomic variables. If autonomic relationships were found for both source monitoring and the difficult version of the flanker task but not the standard version, this would suggest that task difficulty was the dimension most relevant for autonomic control. If they were found for source monitoring alone, this would suggest that specific cognitive operations—in this case, the dependence on monitoring internally held information—were most relevant for autonomic control.

Method

Participants

The participant groups were the same as in the first study (chapter 2). However, due to the challenge presented by the longer words used in this particular source memory task, a number of participants demonstrated a tendency toward either a strong positive response bias or a very conservative response bias. Therefore, using behavioural discrimination between study words and foils as a criterion, we eliminated data from any participants who scored lower than 40% correct on the study words or higher than 25% on foil errors[11], leaving data from 30 participants (16 young; 14 older) available for analysis. Cardiac data from one older adult were unusable due to the frequent presence of a cardiac anomaly in the signal that did not reflect autonomically mediated heart rate variability, but his behavioural and electrocortical data were retained due to our small sample size.

Procedures

A paper-and-pencil health questionnaire, the SCOLP vocabulary test, and a mood screening measure (Zigmond & Snaith, 1983) were administered prior to the computerized tasks. In addition, trained laboratory personnel recorded blood pressure using a manual sphygmomanometer, before and after completion of the computer tasks.[12] Heart rate was recorded during a 5-minute rest period pre- and post-task. Cardiac and electrophysiological measures were also recorded throughout task performance. Participants responded to both the source memory and flanker tasks in a single session while seated comfortably in a dimly lit, electrically and acoustically shielded room. On

completion of testing, participants rated the subjective difficulty of each task using a paper and pencil 5-point Likert scale.

Behavioural measures

Source memory task. Participants read aloud a study list of 25 common words that were between 5 and 8 letters long and equated for frequency and imageability (MRC Psycholinguistic Database, U.K.). Single words were presented in white lower case letters on a black background for 1989 ms by computer, with a stimulus onset difference of 3978 ms. Each word was 1-3 cm in height and 8-11 cm in length, subtending approximately 7.5-10.5° of visual angle when viewed from about 60 cm (unfixed). The display refresh rate was 75 Hz. At test, 139 words were presented in capital letters for 496 ms with an onset difference of 2992 ms. These included 6 practice words, and 125 test words, with 8 fillers, that is, 8 foils that were inserted to maintain adequate spacing between lures but for which response data were not analyzed. Targets were 25 study words, interspersed with 75 new foils, 25 of which were presented twice, always separated by 6 intervening words. Repetition of new foils resulted in a set of words that were familiar (lures), although they were not from the study list. Participants' task was to identify whether a word was from the study list (studied words) or not (new words and lures) by key press, on each trial. The assignment of keys to letters was counterbalanced across participants, and response times were measured from stimulus onset to the beginning of the key press.

Accurate performance required participants to override the tendency to respond "yes" to the familiar lures. Speed and accuracy were equally emphasized. To ensure sufficient trials for stable ERPs, a second block of trials, with new stimuli, was presented

after a 25-minute break during which participants completed the standard flanker task and had a short rest. Data from both blocks were scored and combined for subsequent analyses.

Standard flanker task. Older and younger adults also engaged in a standard letter flanker task (Eriksen & Eriksen, 1974). Congruent (HHHHH or SSSSS) and incongruent (HHSHH or SSHSS) letter strings were randomized and presented by computer on a black background in white upper case letters, 1.5 cm high, spanning 6-8 cm, subtending a visual angle of approximately 5.5 - 7.5° when viewed from an unfixed distance of about 60 cm. Stimulus duration was 189 ms with an interstimulus interval of 1243 ms. Participants were asked to identify the central letter in the string ("H" or "S") by key press as quickly and accurately as possible. The assignment of keys to letters was counterbalanced across participants. Response times were measured from stimulus onset to the beginning of the key press. Congruent trials were presented with a probability of .33 (80 trials each) and incongruent trials with a probability of .67 (160 trials each), comprising 480 trials in all. Two short breaks of 5988 ms each occurred immediately after 160 trials and after 320 trials, during which the screen remained black.

Difficult flanker task. Younger adults also participated in a more difficult letter flanker task modelled after one developed by van Veen and Carter (2002). The second task was not administered to older adults due to its rapid presentation rate and complexity.

The more difficult flanker task presented randomized 5-letter strings having the same visual stimulus properties as the standard flanker task, with the object again being to identify the centre letter as quickly as possible by button press. The letter strings

represented three contrasting conditions: congruent (SSSSS, HHHHH, XXXXX, PPPPP), stimulus incongruent (SSXSS, XXSXX, HHPHH, PPHPP), and response incongruent (SSPSS, PPSPP, XXHXX, HHXHH). Participants were instructed to always respond to S or X with one hand, and to H or P with the other hand. The assignment of keys to letters was counterbalanced. In the congruent condition, centre letters and flankers were identical. In the stimulus incongruent condition, flankers differed from the central letter, but the response required by either type of letter was mapped to the same hand. In the response incongruent condition, the response required for the central letter was mapped to one hand but the response associated with the flanking letters was mapped to the other hand (van Veen & Carter, 2002).

Each trial began with a central fixation cross. To increase the difficulty of task performance, flanking letters appeared slightly before the central letter. Flanking letters were presented for 243 ms, whereas the central letter appeared 147 ms later and remained on the screen for 96 ms, so the array for each trial spanned a total of 243 ms. To prevent phase-locked anticipation of stimuli, the interstimulus interval varied by 200 ms increments between 496 ms and 1296 ms. Response times were measured from the onset of the central letter to the beginning of the key press. To minimize fatigue, randomized trials were presented in two blocks of 360 trials each, with a short break of 5988 ms after 180 trials in each block during which the screen remained black. In each block, congruent trials were presented with a .50 probability (180 trials) and stimulus incongruent and response incongruent trials were each presented with a probability of .25 (90 trials each). Results indicate that each succeeding level is more difficult than the one before it (van Veen & Carter, 2002).

Autonomic measures

Electrocardiogram (ECG) recordings were collected during a 5-minute pre-session baseline rest period and a 5-minute post-session rest period. R-R (interbeat) intervals were checked and edited by a trained laboratory technician using commercial software (Mindware HRV 2.51). Estimates of RSA (HRV at the respiratory frequency, 0.12–0.4 Hz) were calculated via fast Fourier transformation in five 1-minute periods and averaged for each rest period (pre- vs. post-session). Mean IBI was calculated for each resting period, and RPP for each rest period was derived by multiplying resting blood pressure readings together with mean estimates of resting heart rate, then dividing by 100.

Electrophysiological (EEG) recording

As in the previous two studies, EEG scalp data were recorded from 250 scalp sites using a Geodesic Sensor Net. All recordings were referenced to Cz (site 257 in NetStation). Data were processed offline with a 1-30 Hz bandpass filter and segmented in 1000 ms (flanker tasks) or 2000 ms (source memory task) epochs with a baseline of 200 ms time-locked to the onset of the response (flanker tasks, - 600 to - 400 ms relative to the onset of the response) or word stimulus (source memory task, -200 to 0 ms relative to stimulus onset).

Analyses and scoring

Behavioural and electrophysiological data (ERPs) were analyzed using mixed model ANOVAs and Bonferroni-corrected pairwise-comparisons. Trial rejections due to excessive artefact or recording difficulties resulted in some analyses being conducted with fewer participants than others. The Huynh-Feldt correction was applied when the

degrees of freedom in the numerator were greater than one; results are reported using the original degrees of freedom and corrected *p*-values.

Results

Indices of autonomic function

IBI, RSA, SBP and RPP from each resting period were assessed in separate mixed model ANOVAs with condition (pre-test, post-test) as the within-subjects factor and group as the between-subjects factor.

A group by period (pre- vs. post-session) ANOVA of IBI showed that resting heart rate was faster in the younger ($M = 814 \pm 30$ ms) rather than older adults ($M = 918 \pm 37$ ms), $F(1, 21) = 4.75$, $p < .05$, $\eta^2 = .18$, but there was no difference between rest periods and no interaction with group ($ps > .40$). Thus, IBI was averaged across the two rest periods to provide a trait-like measure of resting heart period. However, RSA was higher in younger adults ($M = 6.32 \pm .34$ ln ms^2) than older adults ($M = 4.41 \pm .43$ ln ms^2), $F(1, 21) = 12.08$, $p < .01$, $\eta^2 = .37$, with no effect of period and no interaction ($ps > .30$). Therefore, RSA measures from the two rest periods were averaged for a trait-like index of resting parasympathetic control. In contrast, SBP was higher for the older group ($M = 140.6 \pm 5.1$ mm Hg) than for the younger group ($M = 107.4 \pm 4.9$ mm Hg), $F(1, 23) = 21.73$, $p < .001$, $\eta^2 = .49$, but there were no other effects ($ps > .13$). Thus, the mean was used as an index of resting systolic blood pressure. We noted that SBP in this unselected older group was in the borderline hypertensive range (e.g., about 140 mm Hg; Erdine et al., 2006). RPP, calculated for the resting baseline periods before and after testing, was also higher in older ($M = 93.6 \pm 5.2$) than younger adults ($M = 77.7 \pm 4.1$), $F(1, 16) = 5.75$, $p < .03$, $\eta^2 = .26$, but there was no effect of baseline period or interaction ($ps > .80$).

Therefore, RPP from the two rest periods was averaged for an index of resting sympathetic predominance.

Age-related differences in autonomic control included lower parasympathetic control (resting RSA) in older adults than younger ones, despite a slower baseline resting heart rate for older adults, and higher indices of sympathetic influence (resting SBP and RPP).

Separate correlational analyses among autonomic measures for each group indicated that higher RSA was significantly associated with longer IBI (slower heart rate) in the older group ($r = .81, p < .01$), but only marginally in the younger group ($r = .49, p < .07$). Thus, parasympathetic influence was reflected more strongly in the resting heart rate of older adults than younger adults, although the direction of the relations was the same for both groups. In older adults, higher RPP correlated with a significantly faster resting heart rate (shorter IBI; $r = -.76, p < .01$), but was only marginally related to blood pressure ($r = .58, p < .07$). In contrast, for younger adults, higher RPP was significantly correlated with higher blood pressure ($r = .76, p < .01$), but was unrelated to IBI ($p > .25$). This suggests that resting RPP in older adults more closely reflected resting heart rate, whereas in younger adults it primarily reflected resting blood pressure. Finally, RSA was negatively correlated with RPP in older ($r = -.68, p < .03$) but not younger adults ($r = .002, p > .99$), suggesting that for older adults, the relationship between parasympathetic and sympathetic influences on heart rate was reciprocal, but in young adults these measures were independent. This pattern of results suggests that quantitative changes in individual aspects of cardiac autonomic control may also result in qualitative changes in the nature of this control with age.

Source memory task: Behavioural data

The mean percentage of "yes" responses to study words, lures, and foils were submitted to a group by stimulus-type mixed model ANOVA. Main effects of age ($p <$ .001) and word type ($p < .001$) were qualified by an age-by-word-type interaction, $F(2,56) = 18.60, p < .001, \eta^2 = .40$, indicating that although the groups did not differ on study word accuracy ($M_{Older} = 64 \pm 3 \%$; $M_{Younger} = 65 \pm 3 \%$; $p > .90$), older adults ($M = 48 \pm 4 \%$) were three times as likely to endorse lures as having been in the study list as younger adults ($M = 16 \pm 4\%$; $p < .001$) and made more foil errors ($M_{Older} = 10 \pm 1 \%$) than younger adults ($M_{Younger} = 4 \pm 1\%$; $p < .01$. See Figure 4.2 and Table 4.1). A similar analysis of response times to correct trials showed that foils were responded to marginally more slowly ($M = 1094$ ms ± 129) than study words ($M = 917 \pm 81$ ms) and lures ($M = 901 \pm 74$ ms) in both groups, $F(2, 22) = 4.00, p < .06, \eta^2 = .27$, but there was no overall age difference in response times and no interaction with condition ($ps > .30$; see Table 4.2).

Figure 4.2 and Tables 4.1 and 4.2

Autonomic variables and behavioural results from the source memory task

Accuracy data for each word type were regressed on mean resting IBI, RSA, SBP and RPP measures in four series of hierarchical analyses in which group was always entered on the first step to account for variance attributable to age, followed by the autonomic variable on the second, and the interaction, third.

In the series with IBI as the autonomic variable, group, as expected ($p < .001$), and IBI ($p < .01$), selectively predicted lure errors (interaction: $p > .20$). Longer IBI

(slower heart rate) was associated with fewer lure errors (see Table 4.3). Neither IBI nor the interaction was related to study responses ($ps > .08$) or foils ($ps > .26$).

Table 4.3

In the second series, where RSA was the autonomic predictor, group ($p < .001$), RSA ($p < .01$), and the interaction ($p < .04$), all predicted lure errors (see Table 4.4). The interaction indicated that the relationship was seen in the older group ($p < .01$) rather than the younger group ($p > .50$). In general, higher RSA was associated with fewer lure errors. Neither RSA nor the interaction was associated with study responses ($ps > .14$) or foil errors ($ps > .14$).

Table 4.4

In the third series, SBP and its interaction with group were unrelated to behavioural responses to any word type ($ps > .20$). In the fourth series, using RPP as the autonomic variable, both group ($p < .001$), and RPP ($p < .01$), selectively predicted lure errors (interaction: $p > .07$; see Table 4.5). Higher RPP was correlated with more lure errors. Neither RPP nor the interaction was associated with study responses ($ps > .70$) or foil errors ($p > .30$). Similar patterns were obtained for IBI, RSA, and RPP using responses to study words or lures adjusted for positive response bias, that is, with foil responses covaried from the dependent variables. Thus, both simple and adjusted responses yielded the same relations between performance and autonomic variables.

Follow-up analyses for each group separately revealed that better performance in the older group (i.e., fewer lure errors) was associated with slower heart rate (longer IBI: $r = -.68$, $p < .03$), higher RSA, ($r = -.79$, $p < .01$), and lower RPP ($r = .67$, $p < .03$; see Figures 4.3 to 4.5 and Table 4.6). Lure errors were inversely associated with IBI in younger adults ($r = -.64$, $p < .01$; see Figure 4.3), but with no other autonomic measures (all $ps > .17$). There were no relationships for study words or foils for older (all $ps > .10$) or younger adults (all $ps > .09$). These results indicate that autonomic influences on HRV were strongly and specifically related to the degree to which older adults could refrain from endorsing a familiar but non-target lure.

Figures 4.3 to 4.5 and Tables 4.5 and 4.6

Because RSA and RPP predicted lure errors in opposite directions in the older group, the question arose as to whether they accounted for the same variance. This was addressed by an additional hierarchical regression analysis in which RSA and RPP were entered together on the second step, after group. The model on the second step of the analysis was significant ($p < .01$). Within this model, group ($p < .01$), RPP ($p < .04$) and RSA ($p < .07$) uniquely explained 11%, 6%, and 5% of the error variance, respectively. This suggests that, despite some overlap, the two autonomic variables and group did not account for exactly the same variance in lure errors. Thus, autonomic measures are not merely substitutes for age group. One of the interaction terms (group × RSA; $p < .04$) on the third step accounted for a further 6% of lure error variance, consistent with the fact that significant prediction of lure errors by RSA was limited to the older group.

Source memory task: ERPs

To compare ERP responses across the different experimental conditions, stimulus-locked LPCs were averaged for each word type (study words, repeated lures, foils). LPCs occurred between 500 ms to 725 ms post stimulus onset. To ensure sufficient trials to form a reliable LPC, correct trials from the two blocks of the source memory task were combined. LPC amplitude data from 10 young and 8 older participants were available for inclusion in the waveforms. Figure 4.6 depicts the LPC response at midline sites to study words, lures and foils for each group.

Figure 4.6

Examination of topographical maps in BESA (5.0.1) revealed that the LPC to study words (on correct trials) was centred approximately at midline parietal sites including Pz (88, 89, 100, 131 in the EGI 256-channel net). Accordingly, LPC amplitudes at these 4 sites were averaged and this composite LPC measure was submitted to a mixed model ANOVA with word-type (study, lure, or foil) as the within-group factor, and group as a between-group factor. There was no overall difference in EEG amplitude between groups ($p > .20$). However, the ANOVA revealed a marginal word-type by group interaction, $F(2, 36) = 3.30, p < .07, \eta^2 = .16$. Follow-up analyses revealed that the younger group produced a larger LPC to study words ($M = 1.09 \pm .23$ μV) than to new foils ($M = .32 \pm .19$ μV, $p < .01$), with responses to lures ($M = .60 \pm .22$ μV) in-between, whereas little differentiation was seen in the older group ($p > .60$; see Table 4.7). However, the average waveform may hide individual differences in the older group (note the wide standard deviations in Table 4.7 for older adults). The overall pattern of results

is similar to earlier findings (e.g., Dywan et al., 1998; 2001; 2002) where LPC activation was largest in the younger group for targeted study words, as expected, and LPC amplitudes were undifferentiated between target and non-target information in the older group.

Table 4.7

To determine the relationship between brain responses to each stimulus type and behavioural performance, lure errors were regressed on LPC amplitudes to lures, controlling for age group. Age group ($p < .001$) predicted lure errors, and LPC amplitudes ($p < .05$) added to this prediction, but the interaction term did not ($p > .75$). There were no such relationships for study words ($ps > .20$) or foils ($ps > .45$) and their respective LPCs and interactions. When this analysis was repeated using LPCs to lures corrected for reactivity (i.e., corrected for LPCs to foils) as an independent predictor, and lure errors corrected for positive response bias (i.e., corrected for foil errors) as the dependent variable, a significant interaction was found ($p < .01$). Separate correlational analyses by group indicated that the larger the difference between the LPCs to lures and LPCs to foils (indicative of a large electrocortical reaction to lures and a small reaction to foils), the poorer the adjusted performance in older ($r = .77, p < .03$) but not younger adults ($p > .60$).

Autonomic variables and LPCs from the source memory task

Mean LPC responses for each word type were regressed on resting IBI, RSA, SBP, and RPP measures in four series of hierarchical analyses, respectively. Like the regression analyses of behaviour, group was always entered on the first step, the

autonomic variable on the second, and the interaction, third. In the series with RSA as the autonomic predictor, being in the older group predicted attenuated LCP responses to study words ($p < .01$), whereas RSA and the interaction did not ($ps > .20$; see Table 4.8). However, higher resting RSA predicted smaller LPC responses to familiar lures ($p < .02$), whereas neither group nor the interaction did ($ps > .20$). Higher RSA also predicted smaller LPC responses to foils ($p < .04$), whereas the other variables did not ($ps > .20$). Thus, higher RSA was associated with a diminished electrocortical response to non-target information, for both younger and older adults.

Table 4.8

The older group generated smaller LPC responses to study words ($p < .03$), but neither RPP (our estimate of sympathetic predominance) nor the interaction term predicted LPCs to study words ($ps > .80$). However, higher resting RPP predicted larger LPC responses to non-target lures ($p < .01$), whereas group and the interaction did not ($ps > .30$; Table 4.9). Higher RPP was also associated with larger LPC responses to foils ($p < .04$), whereas group and the interaction ($ps > .15$) failed to reach significance. A similar pattern was obtained for RPP using adjusted LPC activation to lures, that is, with LPC activation to foils covaried from the dependent variable ($p < .04$). Thus, simple and adjusted LPC measures were both associated with RPP. With respect to the remaining autonomic measures, IBI, SBP, and their interactions added nothing to the prediction of our electrocortical measures (all $ps > .08$).

Table 4.9

Separate correlational analyses by group indicated that for older adults the ability

to limit attentional allocation to non-target lures as reflected in a reduced LPC was

associated with higher RSA ($r = -.69, p < .06$) and lower RPP ($r = .75, p < .04$; see Table

4.10, Figures 4.7 and 4.8). For younger adults, those with lower RPP were also better

able to abort the processing of lures ($r = .71, p < .03$, Figure 4.8). Thus, larger LPC

responses to lures appeared to be associated with higher sympathetic drive in both

groups, and marginally associated with reduced parasympathetic influence in the older

group. These relationships must be viewed with caution, however, because in both groups

they depended on single participants with unusually high levels of RPP.

Figures 4.7 and 4.8 and Table 4.10

The issue of whether RSA and RPP accounted for the same variance in LPC

amplitudes to lures was addressed by an additional hierarchical regression analysis in

which RSA and RPP were entered simultaneously, after group. Models on the second (p

$< .01$) and third ($p < .03$) steps were both significant. In the second model, age group

uniquely explained 28% of LPC variance ($p < .01$) and RPP explained 26% ($p < .01$),

whereas RSA did not add significant unique variance to this prediction ($p > .20$). Thus,

the variance in LPC amplitudes to lures accounted for by RSA overlapped with variance

explained by other predictors (RPP, group), but clearly RPP and group did not substitute

for each other. The RSA $\times$ RPP interaction on the third step accounted for an additional

19% ($p < .01$), suggesting that RSA was associated with the prediction of LPC amplitudes only at particular levels of RPP.

To summarize: whereas membership in the older group was associated with smaller LPC responses to targeted study words, in this group lower parasympathetic control (RSA) and higher sympathetic drive (RPP) were both associated with larger parietal LPC responses to non-target information (lures and foils). These findings are consistent with the behavioural analyses showing links between better performance (i.e., fewer lure errors) and lower RSA in the older group, and better performance and more relaxed heart rate (longer IBI) in the younger group. Thus, both the ERP and behavioural results are consistent with a model in which parasympathetic capacity was conducive to supporting the performance demands of a cognitively complex source memory task, whereas sympathetic predominance, typically seen in older adults, was detrimental to it.

Flanker tasks

Standard flanker task. A mixed model ANOVA of difficulty ratings indicated that participants from both groups rated the source memory task ($M = 3.12 \pm .18$) as more difficult than the standard flanker task ($M = 1.93 \pm .17$, $p < .001$), and older adults ($M = 2.84 \pm .17$) rated the tasks as more difficult than younger adults overall ($M = 2.22 \pm .16$, $p < .02$), with no interaction ($p > .07$).

Data from one younger adult who made too few errors for a reliable ERN were omitted from analyses, leaving data from 20 older and 19 younger adults. Behavioural results from this task were typical for both groups. A mixed model ANOVA with condition (congruent or incongruent) as a within-subjects variable and group as a between-subjects variable indicated that participants were less accurate on incongruent

trials ($M = 91 \pm 1$ %) than congruent trials, ($M = 94 \pm 1$ %), $F(1, 37) = 24.84$, $p < .001$, η^2 = .40, but there was no effect of age on accuracy and no interaction ($ps > .80$; see Table 4.11). A parallel ANOVA of response times indicated that participants responded more slowly to incongruent trials ($M = 511 \pm 11$ ms) than congruent trials, ($M = 470 \pm 11$ ms), $F(1, 37) = 291.64$, $p < .001$, $\eta^2 = .89$, and that older adults ($M = 539 \pm 16$ ms) were slower to respond than younger ones ($M = 441 \pm 16$ ms), $F(1, 37) = 19.08$, $p < .001$, $\eta^2 =$ .34, with no interaction ($p > .14$; see Table 4.12). In sum, older adults were slower to respond, but they were not less accurate than younger adults.

Tables 4.11 and 4.12

Figure 4.9 depicts the ERP response at midline sites following flanker errors for each group, respectively. Amplitudes were submitted to a mixed model ANOVA with site (Fz, FCz, Cz, or Pz) as the within-subjects variable and group (younger versus older) as the between-subjects variable. The ERN produced by younger adults ($M = -5.31 \pm 1.3$ µV) was larger than that of older adults ($M = .33$ µV ± 1.3, $p < .01$), and overall, the ERN was deepest at Cz ($M = -3.60 \pm 1.0$ µV, $p < .001$). Site also interacted with group, $F(3, 102) = 5.53$, $p < .01$, $\eta^2 = .14$, such that the ERN of older adults was less differentiated across midline sites ($p > .40$) compared to that of younger adults, ($p < .001$; see Table 4.13).

Figure 4.9 and Table 4.13

To estimate the effect of interference from the flanking letters on identification of the centre letter, that is, the "flanker effect," accuracy data from congruent trials (mainly reflecting a motor response to the stimulus array), were covaried from accuracy data in incongruent trials, and similarly, response times from the congruent condition were covaried from response times from the incongruent condition. The resulting residuals were regressed on resting IBI, RSA, SBP, and RPP measures in separate hierarchical regression analyses with group on the first step, the autonomic variable next, and the interaction third. None of these variables predicted residual accuracy or residual response times (all $ps > .13$). ERN amplitudes at Cz (maximal site) were analyzed similarly. Although group predicted shallower ERN amplitudes ($ps < .01$), none of the autonomic variables or their interactions was significantly related to the ERN ($ps > .30$).

Difficult flanker task. A more challenging flanker task was administered only to the younger adults. Subjective difficulty ratings for the two flanker tasks were compared in a repeated measures ANOVA. As expected, young adults rated the second flanker task ($M = 3.40 \pm .29$) as more difficult than the first one, ($M = 2.00 \pm .25$), $F(1, 18) = 32.79$, $p < .001$, $\eta^2 = .65$. Data from one young adult were eliminated prior to analyses due to random responding.

Correct hits were submitted to a block (one or two) by condition (congruent, stimulus incongruent, or response incongruent) repeated-measures ANOVA. Results were typical for this task: accuracy did not differ between the congruent ($M = 91 \pm 1\%$) and stimulus incongruent ($M = 92 \pm 2\%$) conditions, but was significantly lower in the response incongruent condition ($M = 81 \pm 2\%$), $F(2, 36) = 49.33$, $p < .001$, $\eta^2 = .73$. There was no effect of block, or interaction ($ps > .15$; see Table 4.14).

Table 4.14

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Response times, analysed similarly, increased monotonically between congruent

trials ($M = 434 \pm 12$ ms), stimulus incongruent trials ($M = 455 \pm 11$ ms), and response

incongruent trials ($M = 503 \pm 15$ ms), $F(2, 36) = 57.98$, $p < .001$, $\eta^2 = .76$. They were

faster in the first block ($M = 479 \pm 12$ ms) than the second block ($M = 449 \pm 13$ ms), $F(1,$

$18) = 24.24$, $p < .001$, $\eta^2 = .57$, although this did not interact with condition ($p > .80$; see

Table 4.15). Taken together, the behavioural results confirm that difficulty was greatest

in the response incongruent condition, and greater in the stimulus incongruent than

congruent condition, replicating the behavioural results originally reported by Van Veen

and Carter (2002).

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Table 4.15

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EEG data were collapsed across blocks 1 and 2 of the difficult flanker task to

obtain stable ERP waveforms and are depicted in Figure 4.10. A repeated-measures

ANOVA of peak ERN amplitudes confirmed a typical ERN in the difficult flanker task,

which was deepest at FCz ($M = -5.36 \pm .88$ μV), $F(3, 42) = 20.27$, $p < .001$, $\eta^2 = .59$.

There was no effect of block, and no interaction ($ps > .13$; see Table 4.16). Thus, the

ERN from the difficult flanker task was not in any way unusual.

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Figure 4.10 and Table 4.16

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To estimate the effect of interference in the stimulus incongruent and response incongruent conditions, that is, the "flanker effect" in the difficult flanker task, accuracy data from congruent trials were covaried from accuracy in response incongruent trials, and similarly, response times from the congruent condition were covaried from response times from the more difficult stimulus incongruent and response incongruent conditions. The resulting residuals were regressed on resting IBI, RSA, SBP, and RPP measures in separate hierarchical regression analyses. None of these variables predicted residual accuracy (all $ps > .70$) in this task, nor residual response times for either stimulus incongruent (all $ps > .20$) or response incongruent trials (all $ps > .30$). Autonomic variables were also entered as predictors in hierarchical regression analyses with ERN amplitude as the dependent variable. IBI, RSA and SBP were unrelated to ERN amplitudes at FCz ($ps > .12$), but higher RPP was associated with shallower ERNs at FCz, ($p < .05$). This isolated finding is consistent with our model, in which higher sympathetic drive would be expected to be associated with less efficient error-monitoring.

Discussion

Good performance on a source monitoring exclusion task requires high-level executive skills to resolve the ambiguous status of lures and to control the prepotent tendency to respond to them simply on the basis of familiarity. Consistent with previous research (Dywan et al., 2002; Jennings & Jacoby, 1997), older adults were less able to withhold responding to lures even though they were as good as younger adults at identifying the targeted study words. In contrast, their performance accuracy in the standard flanker task was equal to that of younger adults. This differential performance

by older adults may reside in the contrast between source monitoring, where older adults are more dependent on executive processes to make complex discriminations that younger adults make quickly and automatically (Dywan et al., 2002), and perceptual discrimination in the flanker task, which does not present the same kinds of demands.

Autonomic regulation also differed between older and younger adults. Resting RSA, a measure of parasympathetic control, was significantly lower in the older group, but resting systolic blood pressure and RPP (measures of sympathetic influence) were significantly higher, at the level of borderline hypertension (e.g., Erdine et al., 2006). In addition, resting RSA and resting RPP were reciprocally related in older adults, suggesting less independence between parasympathetic and sympathetic function in this group than typically seen in younger adults (Berntson et al., 1994). For younger adults, RSA and RPP clearly represented independent sources of cardiac regulation.

Consistent with our model, higher resting levels of RSA in the older group were associated with more successful rejection of non-target lures but were unrelated to the endorsement of study words or foils. We note that Dywan et al. (submitted) reported a very similar relationship between higher levels of RSA and lower levels of adjusted source error for older adults. No RSA relationship was found for younger adults in either of these studies, but in the current study, slower resting heart rate (suggesting more relaxed cardiac control) was associated with better source monitoring performance in both groups. Also consistent with our model, higher resting levels of RPP were associated with worse performance, being specifically correlated with lure errors across groups, but not with study words or foils. This indicates that relatively greater

sympathetic influence on resting heart rate (especially in older adults) was specifically associated with the commission of source memory errors.

Electrophysiological measures such as the LPC reflect cognitive responses in real time. Here, being in the younger group was associated with generating larger LPC responses to targeted study words. However, after any effects of group were accounted for, higher RSA added to the prediction of efficient attentional control, that is, higher RSA predicted a smaller electrocortical response to non-target lures and foils across groups. Note that ERPs were averaged only for correct trials, which means that even when accurate decisions were made, those with higher sympathetic drive were more reactive to the non-target stimuli. Similarly, higher RPP was associated with larger LPCs to non-target lures and foils (but not study words) across groups, although given the small numbers in the analyses, these relations relied on single cases. The LPC results were consistent, however, with the behavioural results, suggesting that greater sympathetic predominance in cardiac control resulted in a greater reactivity to salient but non-target stimuli, which was likely to make the inhibition of prepotent responses more difficult, especially for older adults. Thus, higher parasympathetic and lower sympathetic influence on HRV at rest were selectively associated with smaller electrocortical responses to salient but non-target lures (and to a lesser extent, non-target foils) in both groups.

In contrast, no relationships were found between resting autonomic indices and performance or ERPs for either group in the standard flanker task, similar to results reported by Dywan et al. (submitted). To test the hypothesis that the differential associations between autonomic activity and task outcomes were due to the qualitatively different type of task requirements rather than simply to difficulty level, we added a more

complex version of the flanker task (van Veen & Carter, 2002). Even here, almost no relations between autonomic indices and flanker effects or electrophysiological indices were found. Thus, the overall pattern of results supported the hypothesis that greater parasympathetic capacity and lower sympathetic predominance in older adults are beneficial in tasks that require internal monitoring of response contingencies and the need for inhibitory control, i.e., functions specifically linked to the frontal lobes (Bunge, Ochsner, Desmond, Glover & Gabrieli, 2001; Miller & Cohen, 2001; Spencer & Raz, 1994).

In general, our results with older adults using an age-sensitive source memory task are in line with other studies showing that greater HRV is conducive to good cognitive performance. For example, Johnsen et al. (2003) demonstrated in an emotional Stroop task that greater attentional control (i.e., reduced capture by words associated with dentistry) was associated with higher HRV in young dental phobics. Hansen and colleagues have shown that higher HRV in young navy men was associated with greater working memory capacity (2003) and better learning over time (2004). With respect to older adults, Kim et al. (2006) have recently shown that the odds of cognitive impairment in older, disabled, community-dwelling women were several times higher for those whose HRV was in the lowest quartile. These studies highlight the importance of cardiac vagal control in relation to good cognitive outcomes, and the present results demonstrate that these relations are evident in both younger and older adults.

The RPP results with respect to source monitoring performance are consistent with studies showing links between autonomic measures, specifically pathological sympathetic predominance—hypertension—and poor performance of other complex

cognitive tasks, including memory tests (e.g., Elias et al., 2003), task-switching (e.g., Kuo et al., 2004), spatial problem-solving and abstract reasoning (e.g., Robbins et al., 2005), and the Wisconsin Card Sort Test (e.g., Raz, Rodrigue & Acker, 2003). Other studies have demonstrated associations between hypertension and increased risk of long-term cognitive impairment (Kilander, Nyman, Boberg, Hansson & Lithell, 1998; Launer et al., 2000), whereas treatment of hypertension has been reported to decrease that risk (Forette, Seux, Staessen, Lutgarde & al., 2002; Peila, White, Masaki, Petrovich & Launer, 2006). Together these studies make a strong case for reduced cognitive capacity when sympathetic activity is largely unchecked by adequate parasympathetic regulation.

Being in a state of emotional arousal is reported to disrupt attentional control in younger adults (e.g., Derryberry & Reed, 2002; Eysenck, Derakshan, Santos & Calvo, 2007), effectively decreasing goal-directed attentional functioning and increasing the extent to which attention is influenced by "bottom-up" stimulus factors. Undue arousal is particularly likely to interfere with working memory and inhibitory control (Eysenck et al., 2007). In source memory paradigms, the use of emotional versus neutral stimuli has been shown to result in attentional changes that benefit item information, but at the expense of contextual details (Mather et al., 2006; Mitchell, Mather, Johnson, Raye & Greene, 2006). Not only can emotional arousal alter the allocation of attention, but it also has obvious autonomic effects, including increased heart rate and reduced HRV (e.g., Friedman, 2007; Hagemann et al., 2003). For older adults, the sympathetic predominance seen at rest may reflect a tonic cardiovascular state that is similar to that of chronic emotional arousal seen in clinical anxiety disorders. This sympathetically mediated but non-emotional condition also appears to disrupt finely tuned attentional allocation, as

seen in positive correlations between higher resting RPP and the source memory performance of older adults reported here.

Understanding the role of RSA is more challenging. In general, heart rate variability is inversely related to blood pressure variability (Sloan et al., 1997). To ensure adequate perfusion, and because wide fluctuations in pressure can be harmful, blood pressure is normally kept within a certain physiological range. When a transient increase in blood pressure occurs, arterial baroreflexes relax blood vessel walls (Brownley et al., 2000) and increase vagal output, reducing heart rate and contractile strength (Thames & Kontos, 1970). Because blood vessels receive only sympathetic innervation, changes in arterial stiffness are mediated sympathetically, making vagally mediated cardiac adjustments initiated by the baroreceptors critical for offsetting changes in blood pressure (e.g., Sloan, Shapiro, Bagiella, Myers & Gorman, 1999). Thus, individual differences in resting measures of RSA essentially index the capacity for parasympathetic buffering of blood pressure variability. If this capacity is reduced, then blood pressure increases may not be properly mitigated, with negative physical consequences and detrimental effects on cognitive performance.

With respect to relations between autonomic indices and task outcomes in source monitoring versus flanker tasks, our findings suggest that these tasks differed in the requirement for parasympathetic control at two levels—within-task and between-tasks. Autonomic indices were always most clearly associated with the avoidance of lure errors, but never with correct identification of study words or foils. Further, they were never linked to action slips in the flanker tasks in either group. Finding significant relationships between cardiac autonomic control and "inappropriate" attention to lures and foils (larger

LPCs) is consistent with the idea that parasympathetic control is most relevant for the avoidance of complex errors. Lures present a greater challenge than either study words or foils, requiring higher levels of controlled processing to resolve their status, and control over the tendency to ascribe them to having been "studied", on the basis of their familiarity. We speculate that the greater challenge presented by lures is also likely to increase blood pressure (cf. Wright, et al., 2005), necessitating parasympathetic cardiac adjustments in order to allow optimal controlled processing.

Our conclusion about the relevance of task demands rather than task difficulty for eliciting relationships between autonomic control variables and performance is consistent with previous research. Drawing from the same participant group as for the present study, Mathewson et al. (2008) showed significant relationships between autonomic indices (RSA and RPP) and good performance of a spatial learning task on trials that required accessing mental reconstructions of hidden mazes, but not for trials that required only passive responses to feedback. In addition, studies using HRV as a dependent variable suggest that relationships between task outcomes and HRV appear to be insensitive to the manipulation of parameters such as memory load within task (Aasman et al., 1987; Redondo & Del Valle-Inclan, 1992). In contrast, HRV is reported to be differentially sensitive to demands for active manipulation of information (e.g., Gianaros et al., 2004; Mulder, 1986; see also Wright et al., 2005).

For older adults in the current study, relatively higher resting RSA predicted better performance of the task that required executive processing. The fact that this relationship was not found for younger adults may be because sorting out the ambiguous status of lures was not difficult for this age group. They misclassified only 16% of lures,

whereas older adults who were quite capable of discriminating between previously studied words and new, never-seen foils nonetheless had considerable difficulty withholding their "target" response to lures. It is possible that the restricted range of lure errors for the young group precluded any correlations with RSA, although a significant relationship between lure errors and IBI suggested that parasympathetic influence on heart rate was also beneficial for our younger participants.

Summary

Although older adults can generally remember item information, under ordinary conditions they typically have greater difficulty making correct attributions about the source of a particular item or event. Our main goal was to ascertain whether controlled processing was more efficient in older adults whose HRV was relatively preserved, that is, in those with greater parasympathetic control and lower sympathetic drive, relative to their same age peers. This hypothesis was supported. Within the older group, better source monitoring performance was associated with slower resting heart rate (longer IBI), higher resting RSA, and lower resting RPP, suggesting that relatively preserved parasympathetic function was conducive to the performance of a task requiring top-down attentional control. A similar dynamic was reflected in the younger group, where a more relaxed resting heart rate was also associated with better performance of the source task, although this did not extend to RSA or RPP. For both younger and older adults, greater sympathetic drive appeared to be linked to inappropriate cognitive appraisal of salient but non-target stimuli, particularly lures. These relations are consistent with the idea that parasympathetic control, which declines with age, is necessary for controlling arousal in response to cognitive challenge.

Chapter 5: General Discussion

Evidence for selective decline of executive functions in late life can be found in the performance of complex tasks that involve such processes as source monitoring (e.g., Dywan & Jacoby, 1990) and spatial learning (e.g., Kirasic, Allen & Haggerty, 1992). Remembering an event, along with its context, relies on hippocampal function (e.g., Gold et al., 2006; Manns & Eichenbaum, 2006), which is particularly vulnerable to age-related decline (De Jong et al., 1999; Driscoll et al., 2003; Jack et al., 1998; Raz & Rodrigue, 2006). Because of this decline, older adults are less likely to encode or retrieve the contextual details about a remembered event (Kensinger & Schacter, 1999; Senkfor & Van Petten, 1998; Spencer & Raz, 1995) and more likely to attribute memories to sources that seem familiar and plausible but may be incorrect (e.g., Dywan & Jacoby, 1990; Jennings & Jacoby, 1997). In young adults, these operations appear to be effortless and to result in the correct attribution of sources in a fairly automatic fashion.

Older adults are also more likely than younger adults to have difficulty learning spatial relations between objects (Lövdén et al., 2005; Moffat et al., 2006) and creating allocentric maps of space (Moffat & Resnick, 2002), independent of any perceptual or motor problems, with the result that they may have trouble finding their way in familiar as well as unfamiliar environments (Chiu et al., 2004; Kirasic, 2000). During spatial navigation tasks, reduced functioning in hippocampal and extrahippocampal regions appears to be accompanied by increased activity in ACC and medial frontal cortex, suggesting a compensatory shift from medial temporal systems to more frontal, controlled processes (Gutchess et al., 2005; Moffat et al., 2006). The same principle may hold for source memory performance, given evidence of changes in functional

connectivity between the hippocampus and the rest of the brain such that connections to anterior regions are stronger and to posterior ones weaker, as compared to younger adults (Dennis et al., 2008). Results from both of these kinds of complex tasks suggest that what is learned easily and efficiently by a healthy young person may be acquired in later life with difficulty, via the use of more effortful controlled processes and different neural circuitry (e.g., Grady, Springer, Hongwanishkul, McIntosh & Winocur, 2006; Gutchess et al., 2005).

When automatic processes are less available (e.g., Moffat et al., 2007), or when tasks are difficult (e.g., Paus et al., 1998) or require working memory (Cabeza & Nyberg, 2000), activity is increased in medial prefrontal regions of the brain, particularly in ACC. ACC signals following errors alert other prefrontal brain regions to immediately increase top-down control (Botvinick et al., 2001) and change strategy to improve performance (Bartholow et al., 2005). They also provide a local history of the rewards and losses associated with recent actions (Kennerly et al., 2006). Third, error signals to prefrontal cortex (ERNs, FRNs) may also be responsible for initiating a widespread release of acetylcholine throughout the brain that focuses attention and increases cognitive control (Sarter et al., 2006). These neural alarm signals are generally attenuated in older adults, likely due to age-related decline in the availability of mesencephalic dopamine (Volkow et al., 1998), or they may reflect poor performance by this age group (Eppinger et al., 2008). If ACC error signals are too small to rouse prefrontal regions sufficiently, this may have consequences for recruiting the cholinergic system and re-asserting cognitive control, with the result that performance may not be stabilized enough to avert negative outcomes.

To meet behavioural requirements, the ACC integrates cognitive and motivational states with states of bodily arousal through its projections to subcortical autonomic control areas (Critchley et al., 2003; Critchley et al., 2005). The autonomic system comprises parasympathetic activity (associated with energy conservation, homeostatic functions, and focused attention) and sympathetic activity (associated with energy mobilization, increased emotional arousal, and preparation for action). Tasks requiring controlled processing, i.e., those with higher physiological costs (Aasman et al., 1987), would presumably be most vulnerable to age-related changes in these autonomic regulatory functions. However, parasympathetic function, so important for focussed attention, declines with age (Waddington et al., 1979), while resting sympathetic tone is normal or increased (Low, 1997).

The heterogeneity seen in many domains related to aging leads researchers to look beyond group effects and consider how individual differences in various age-sensitive physiological systems affect the behavioural outcomes of interest. In this thesis, the main focus has been on individual differences in higher order cognitive control and in autonomic influences (Berntson et al., 1994) that are associated with ACC function. We expected that behavioural, electrocortical, and phasic vagal cardiac influences would be correlated in tasks that tapped executive functioning. As well, we expected that higher levels of phasic vagal cardiac control in old age would be associated with higher levels of performance when top-down attentional control was required. The main hypothesis was that executive performance would be relatively preserved for older adults who have maintained a high level of autonomic flexibility compared to that of their peers for whom this responsivity has declined.

Relationships among behavioural, electrocortical, and cardiac measures

Behavioural performance was examined in tests of source monitoring, spatial learning, and speeded responding in relation to electrophysiological responses and cardiac autonomic control. The main issues were whether ACC would respond to error feedback in the same way in older and younger adults across tasks and difficulty levels, and whether younger and older participants with higher HRV (greater parasympathetic influence) and concomitantly lower sympathetic predominance would perform cognitively challenging tasks more successfully and efficiently. LORETA analyses of FRN activation following maze errors indicated that the neural response of older adults did not discriminate very well between positive and negative feedback in the maze-learning task. Moreover, shallow FRNs could not have been due to uncertainty about errors, since feedback was always informative and accurate. Nonetheless, despite the reduced amplitudes among older adults, relatively deeper FRNs predicted better memory performance of the largest maze for the older group. Results also indicated that increased resting RPP, a proxy for cardiac workload and thus, sympathetic influence on heart rate, was associated with less successful spatial learning and reduced electrophysiological correlates of error processing (FRNs) in older adults, suggesting less efficient performance monitoring with elevated RPP in this group. Conversely, higher RSA was associated with greater ease and more successful spatial learning performance for younger adults, suggesting that parasympathetic competence facilitated maze learning in this group.

In the source monitoring exclusion task, older adults were less able than young adults to distinguish between the familiarity associated with previously studied words and

that associated with new words that were merely repeated in the test list. However, performance did not differ between older and younger adults on a contrasting, speeded response task (Eriksen & Eriksen, 1974). With respect to source monitoring, relatively lower levels of RSA within the older group predicted a greater tendency to falsely attribute lures to the list of studied words. This indicates that although RSA was reduced, group-wise, with age, individual differences in RSA among older adults still predicted more successful source monitoring. Autonomic variables were also analyzed with respect to electrophysiological measures of attention allotted to target versus non-target information (LPCs). Low RSA and high sympathetic drive both pointed to a reduced ability to suppress the LPC response to salient non-target information. In this task, controlling the attentional response to lures on correct trials correlated with more successful avoidance of lure errors, suggesting that when electrophysiological responses to non-target lures were larger, participants had a greater tendency to process them like target information.

Thus, older adults made "attentional errors," as it were, with respect to correctly rejected lures, that seemed to forecast behavioural errors. Greater sympathetic drive was directly linked to both the allocation of attention (LPCs) during correct trials in this task and behavioural errors. Thus, for two tests of executive functioning, we have presented evidence for the association of sympathetic drive with brain responses in older adults that appeared to lead to behavioural errors. In addition, relatively higher resting RSA in older adults was conducive to more efficient information processing in both of these tasks, being related to more robust registration of errors in the spatial task (i.e., larger FRNs) and marginally to reduced attentional allocation to non-target information in the source

task (i.e., smaller LPCs). Conversely, in the Eriksen flanker task, virtually no relations were found between autonomic variables and either error-monitoring performance or ERPs.

Although the relationships differed by age and task, the model emerging from these studies highlights a special role for parasympathetic modulation of heart rate vis-à-vis complex cognition: for tasks requiring executive skills, particularly attentional control and internal monitoring or working memory, higher RSA was conducive to good performance, consistent with previous studies of attention and working memory in younger (Hansen et al., 2003; Johnsen et al., 2003; Melis & van Boxtel, 2007) and older adults (Dywan et al., submitted). However, higher RPP in the older group appeared to have a detrimental effect on performance, consistent with studies linking hypertension to poor cognitive outcomes (e.g., Elias et al., 2003; Raz et al., 2003) and long-term cognitive impairment (e.g., Kivipelto et al., 2001; Launer et al., 2000; Skoog et al., 1996). Good behavioural performance and appropriate cortical responses were positively aligned with healthy parasympathetic function and negatively aligned with unhealthy sympathetic predominance.

The fact that several significant RPP correlations were unique to the older group does not suggest that sympathetic function per se has detrimental effects on performance, but more likely, poor performance is due to the greater dependence of cardiac modulation on the sympathetic system, without the counterbalancing effect of the vagal brake (Porges, 1995a). Sympathetic transmission requires 4 seconds to peak and returns slowly to baseline because the sympathetic neurotransmitter, norepinephrine, has a relatively slow onset. Norepinephrine is also removed from cardiac tissue relatively slowly (Levy,

1993). In contrast, parasympathetic activation can slow heart rate within a single cardiac cycle (Levy, 1997) because of the fast onset and high turnover rate of acetylcholine, the parasympathetic transmitter. Because of the different pharmacokinetics of their respective neurotransmitters, changes in heart rate follow changes in parasympathetic efferent activity much more closely than do changes in sympathetic activity (Berntson, Cacioppo & Quigley, 1993). Parasympathetic activity is thus likely to be more sensitive to fast-changing cortical demands than is sympathetic activity. The age-related shift towards greater sympathetic predominance indicates that the fine-grained, efficient, high frequency, beat-to-beat control of heart rate is reduced in older adults, leaving the slower-responding and metabolically more costly system greater responsibility, as it were, for short-term cardiac regulation (Saul, 1990).

RSA capacity in young adults appeared to be beneficial for the mental construction of large mazes, and RSA capacity in older adults appeared to be critical for sorting out the status of lures and controlling the tendency to make a prepotent response. However, although sensitive to age group and specific task demands, autonomic responses in both age groups appear to be activated by the demand for executive versus automatic processing. Resting RSA was correlated with better performance in younger adults in the largest maze of the spatial learning task, whereas resting heart rate predicted test errors for older adults. Conversely, resting RSA was correlated with better performance in older adults in the source-monitoring task, whereas resting heart rate predicted source errors in the younger group. If these results are taken together, it appears that resting heart rate, which is under predominantly parasympathetic control,

significantly predicted performance for a particular age group, even when RSA did not (Low, 1997).

Relationships between individual cardiac autonomic control indices and behavioural outcomes were clearly specific to executive functions. They were more reliable in test trials of the maze task where differential learning rates affected performance outcomes, but for learn trials only in the largest mazes that is, for trials in which working memory was required in addition to guessing. Autonomic relationships were also evident in the source memory task that required the resolution of lure status and control over the tendency to attribute lures to the study list, but not in flanker task performance, which could be accomplished using information that was provided on the computer screen or in immediate memory. Even when flanker difficulty was increased, there were no relationships between either RSA or RPP and task outcomes. Similarly, Jennings and colleagues (1997) reported that task responses requiring mnemonic look-up are unique in that they will not only slow response selection but also transiently delay heartbeats, whereas other cognitive operations such as arithmetic addition will not. Furthermore, memory processes in other contexts (e.g., rehearsal) are likely to induce cardiac acceleration, rather than deceleration, due to the metabolic requirements of these processes (van der Molen, Bashore, Halliday & Callaway, 1991). Indeed working memory requirements seem to be critical for eliciting relationships between cardiac autonomic control variables and task performance (cf. Jorna, 1992; Mulder, 1986), whereas manipulating task characteristics more superficially through augmenting the visual complexity of the flanker array and increasing the speed and complexity of the response by requiring the use of the incompatible hand (cf. Jennings, van der Molen,

Brock & Somsen, 1991; Mulder & Mulder-Hajonides van der Meulen, 1973) do not.

However, it is clear that increased task difficulty can be confounded with changes in task

requirements with respect to working memory (e.g., Gianaros et al., 2004; Vincent, Craik

& Furedy, 1996).

How does parasympathetic control contribute to good performance?

Based on the extant literature, there are at least four possible mechanisms

whereby the parasympathetic system could contribute to good performance outcomes.

First, parasympathetic modulation of heart rate appears to be the main autonomic control

mechanism for buffering BP changes in response to challenging situations (Sloan et al.,

1999). Executive challenges posed by tests of working memory are associated with

changes in HRV (e.g., Aasman et al., 1987; Aasman, Wijers, Mulder & Mulder, 1988)

and blood pressure (e.g., Budge, de Jager, Hogervorst & Smith, 2002; Kuo et al., 2004).

Studies have suggested that patients with chronic hypertension are less able to

compensate for rapid changes in blood pressure and thus the brain is more vulnerable to

blood pressure fluctuations (e.g., Baron, 2001). This may have cumulative effects over

time, as seen in numerous studies linking hypertension to increased risk of cognitive

impairment (e.g., Breteler, 2000; Kivipelto et al., 2001; Launer et al., 2000; Petrovitch,

White, Izmirilian, et al., 2000; Skoog et al., 1996; Whitmer, Sidney, Claiborne Johnston

& Yaffe, 2005). The relative reduction of parasympathetic control with age may

constitute an important mechanism by which autonomic change has negative effects on

cognitive function, that is, by leaving sympathetic activation unopposed and thus

reducing the autonomic system's ability to counter rapid changes in blood pressure in

situations of challenge (Sloan et al., 1999; Van Vliet, Belforti & Montani, 2002).

Additional research is necessary to determine whether this hypothesis has sufficient explanatory power to account for the findings here and elsewhere.

Second, it has been suggested that the intrinsic physiological function of RSA is to improve the efficiency of pulmonary gas exchange (Hayano & Yasuma, 2003; Yasuma & Hayano, 2004). Due to the parasympathetic gating of heart rate reflected in RSA, heart rate increases slightly during inspiration, as oxygen is being taken in, and slows slightly during expiration, avoiding unnecessary beats when no extra oxygen is available, thereby conserving cardiac and respiratory energy (Hayano & Yasuma, 2003). By ensuring optimal brain perfusion with the least metabolic expense, RSA may provide a small physiological reserve that has subtle effects on brain perfusion. Higher levels of RSA may therefore impact positively on cognitive functioning, particularly in situations that tax working memory capacity. This physiological advantage may account for our findings, but more investigation is required before accepting it as an explanation for them.

Third, RSA may reduce the likelihood of prepotent responses (e.g., Dywan et al., 2002), by keeping sympathetic arousal in check. Parasympathetic and sympathetic autonomic activity is modulated by the Central Autonomic Network (CAN; Benarroch, 1997), which integrates information about internal bodily states, sensory information and the external environment, adjusting physiological arousal up or down as appropriate for the context (Benarroch, 1993). When the ability of the parasympathetic system to oppose sympathetic activity is reduced with age or illness, the resulting chronic autonomic state is similar to that seen in conditions of heightened emotional arousal (e.g., Thayer, Friedman & Borkovec, 1996). Being in a relatively more aroused state could increase the

predisposition to respond impulsively, without adequately sorting out the status of lures, making it harder to control the tendency to make inappropriate responses to information that is compelling but incorrect. It is possible that a state of heightened arousal is enough to explain relationships between autonomic control and performance of complex working memory tasks in older adults, but more research would be needed to establish this.

All of the above alternatives impute the benefits of RSA to mechanisms that are primarily physiological. But cardiac responses may be influenced centrally (Benarroch, 1997; Jennings et al., 1991; Thayer & Lane, 2000). For example, when a prepotent response must be held in check, "midbrain coordination of the countermanding of response execution" is reflected in phasic cardiac slowing following individual trials (Jennings et al., 1992; see also Jennings & van der Molen, 2002). In these instances, the brief lengthening of the interbeat interval that occurs does not represent a passive relaxation of heart rate, but rather the active inhibition of central representations of alternative responses, in favour of a higher priority action. It is not just motor responses, but *central representations* of various actions that are inhibited, as shown by the fact that heart rate slowing tracks the degree of stimulus rotation in mental rotation paradigms, i.e., slowing is more pronounced with greater rotations (Band & Miller, 1997), and the fact that heart rate slowing is specific to *successful* inhibition of the incorrect response in situations when instructions conflict (Jennings et al., 1992). Arguably, inhibition is integral to both of the executive function tasks used in the present studies. Cognitive operations in the source memory task include resisting prepotent tendencies to identify lures as study words in favour of more appropriate responses. In repeated test trials in the

maze task, they include consulting memory to select one correct tile from two or three equally likely tiles and ignoring the others, for each move.

Of course there is a physiological advantage to the momentary heartbeat delay as well: lengthening the interbeat interval allows the heart slightly more time to fill, so that on the next cardiac cycle, the heartbeat will be stronger and blood volume greater (Jennings & van der Molen, 2002). Because the lengthening is momentary, vagal control is implicated. (See also Obrist, 1981). However, if the vagal brake is less sensitive, due to hypertension, or if central dampening of response representations is reduced in old age so that these momentary delays do not reliably occur, then countermanding prepotent responses would be more difficult and errors more likely. Thus, the principle of neurovisceral integration (Friedman, 2007; Thayer & Lane, 2000) is clearly manifested in the inhibition of prepotent responses in tasks that require working memory.

Future directions

The present model should be considered a set of working hypotheses that need replication and further testing. Questions remain, of course. Currently, the exact mechanisms by which parasympathetic capacity exerts its beneficial effect on cognitive outcomes are not known. If they were known, they could be very helpful for the development of strategies to delay cognitive decline. The administration of medications for hypertension has been shown to increase HRV (Ylitalo, Juhani Airaksinen, Sellin & Huikuri, 1999) and to reduce the risk of long-term cognitive impairment (e.g., Forette et al., 2002; Peila et al., 2006), suggesting that artificially limiting the strength of sympathetic activation can forestall cognitive decline. Alternatively, HRV can be improved in older adults with regular exercise (e.g., Pichot et al., 2005; Sandercock et al.,

2005). This leads to a new question: Does either the artificial or natural reinstatement of parasympathetic function result in a concomitant improvement in cognitive function? It is unlikely that pharmaceutical and lifestyle solutions can reverse age-related change in autonomic control, but they may offset some of the negative effects of aging with benefits derived from improving perfusion and controlling blood pressure variability or metabolic factors such as insulin resistance (e.g., Wareham, Wong & Day, 2000). Such solutions may even promote neurogenesis in the dentate gyrus of the hippocampus (e.g., Pereira et al., 2007). Longitudinal and population studies will be needed to address these questions.

Hypertension is a strong risk factor for hippocampal atrophy (De Jong et al., 1999; Korf, White, Scheltens & al., 2004), cognitive impairment (Kilander et al., 1998; Solfrizzi et al., 2004), vascular dementia (Launer et al., 2000; Posner et al., 2002), and Alzheimer's disease (Kivipelto et al., 2001; Petrovitch et al., 2000). Vascular factors may even have a synergistic role in the development of Alzheimer-type neurodegeneration (Iadecola & Gorelick, 2003; Jellinger, 2005). Ten years ago, Brookmeyer (1998) suggested that the public health impact of delaying dementia onset by as little as 2 years would be to cut incidence rates by 25%. Physical activity in midlife (Rovio et al., 2005) and even in late life (Lytle, Vander, Pandav, Dodge & Ganguli, 2004) has been shown to reduce the risk of cognitive impairment and to delay cognitive decline by as much as 1.5 years (e.g., Weuve, Kang, Manson et al., 2004; Larson, Wang, Bowen, et al., 2006; see also Rockwood & Middleton, 2007). The magnitude of this effect is comparable to that of drugs currently available to treat progressive cognitive decline, with two important advantages: the drugs offer only symptomatic treatment, and exercise avoids their side

effects. The question of whether cognitive function can be maintained or restored by the preservation of parasympathetic predominance in autonomic control has not been answered, but in the light of estimates that the dementia cases will balloon from 4.5 million in the U.S. in 2000 to approximately 13.2 million by 2050 at present rates of population growth (Hebert, Scherr, Bienias, Bennett & Evans, 2003), attempts to answer it would be worthwhile.

Footnotes

1. Most of the older adults had been prescribed some form of blood pressure medication. However, only 1 of the 14 was taking beta-blockers, which are believed to have central nervous system effects. Because the error counts and midline ERPs for this individual were within one standard deviation of the means for the older group in all cases, these data were included in all relevant analyses. We note that some hypertension is typically found in samples within this age range (Jennings, Van der Veen & Meltzer, 2006; Mathewson et al., 2005).

2. Three younger participants completed the maze task using a keypad to respond. Their behavioural data were not significantly different from those of the rest of the younger group (one-way ANOVAs, $ps > .15$) and so were retained.

3. Because difficulty level was confounded with grid size, we reanalyzed error scores and response times after dividing them by the average error score or response time for each maze across groups. In both cases, the interaction between group and trial type remained robust (error scores, $p < .001$; completion times, $p < .01$); however, in both cases the three-way interaction with grid size was lost. Thus, although groups performed similarly on learn trials when everyone had to depend on feedback for each move and differed on test trials when differential learning rates became relevant these group differences were not exacerbated as a function of grid size.

4. The t statistic for significance in a local region is always equal to or less than the t statistic for the global test. Thus, any t statistic for a local maximum in a mid-sagittal region can never exceed the corresponding t statistic for global brain activation reported in Table 2.5.

5. Although a significant decline in acetylcholine is more typically associated with Alzheimer's disease and a significant decline in dopamine with Parkinson's disease, there is evidence that these losses may follow the initial loss of the neuroprotective benefits of

norepinephrine due to degeneration of the locus coeruleus, a major source of noradrenergic neurons in the brain (Kalinin et al., 2007; Rommelfanger & Weinshenker, 2007).

6. A version of this chapter has been published as a journal article by *Psychophysiology* (2008) with the following authors: K. J. Mathewson, J. Dywan, P. J. Snyder, W. J. Tays, and S. J. Segalowitz.

7. Although this placement was not standard for ECG recording, in most cases recordings were adequate for calculating autonomic indices. Therefore, not all analyses included exactly the same participants.

8. Respiration rates were not available in this study. It is generally desirable to demonstrate that RSA measures of heart rate variability are not influenced by respiration rate (e.g., Grossman & Taylor, 2007; Wilhelm, Grossman & Roth, 1999). However, natural respiration rates are unlikely to unduly affect RSA during recordings of resting heart rate (Berntson et al., 1997; Denver, Reed & Porges, 2007). Also, we used this as a trait-like measure of individual differences, rather than to make comparisons across conditions or phases in the experiment, so there is no question of task-related changes in breathing rates affecting our RSA measures.

9. RSA from the pre-testing rest period proved to be a significant predictor of test trial errors regardless of grid size, and also for learn trial errors in the 8×8 maze. An averaged measure of RSA (i.e., from both rest periods) was a comparable predictor of performance in most analyses. However, RSA from the post-test resting period was not (all $ps > .10$). This suggests that variance in resting RSA from the pre-testing period, reflecting trait-like differences in RSA, was integral to the relationships with performance.

10. Eppinger et al. (2008) found that if performance is equated between older and younger adults by the use of a flexible response deadline, ERNs are not reduced with age.

However, for the same task, *feedback*-related negativities (FRNs) were clearly reduced in older adults, even when performance was equated. Our results are consistent with the latter finding of Eppinger and colleagues: there was no response deadline in the maze task because responses were self-paced, and FRNs were clearly reduced in older adults.

11. As mentioned, most of the older adults had been prescribed some form of blood pressure medication. However, in the sample used for this study, only two of the 14 were taking beta-blockers. Since their data did not differ from those of the other adults and since dropping them from the analysis did not change the results in any substantial way, they were retained due to our small sample size.

12. Post-test blood pressure readings were unavailable for several young participants and one older one. Replacement of these values was done two ways before calculation of RPP. We let available pre-test readings stand in for missing post-test values. We also interpolated any missing individual post-test value from its corresponding pre-test value, using the B and constant from the regression line for pre- and post-test blood pressure readings. As there were no differences in the patterns of results, regardless of which measure was used, we report RPP data based on the simple substitutions.

References

Aasman, J., Mulder, G. & Mulder, L. J. M. (1987). Operator effort and the measurement of heart rate variability. *Human Factors, 29*, 161-170.

Aasman, J., Wijers, A. A., Mulder, G. & Mulder, L. J. M. (1988). Measuring mental fatigue in normal daily working routines. In P. A. Hancock & N. Meshkati (Eds.), *Human mental workload*. Amsterdam: North Holland.

Agelink, M. W., Klimke, A., Cordes, J., Sanner, D., Kavuk, I., Malessa, R., Kleiser, E. & Baumann, B. (2004). A functional-structural model to understand cardiac autonomic nervous system (ANS) dysregulation in affective illness and to elucidate the ANS effects of antidepressive treatment. *European Journal of Medical Research, 9*, 37-50.

Ahern, G. L., Sollers, J. J., Lane, R. D., Labiner, D. M., Herring, A. M., Weinand, M. E., Hutzler, R. & Thayer, J. F. (2001). Heart rate and heart rate variability changes in the intracarotid sodium amobarbital test. *Epilepsia, 42*(7), 912-921.

Akselrod, S. D., Gordon, U., Ubel, A. F., Shannon, D. C., Barger, C. A. & Cohen, R. J. (1981). Power spectrum analysis of heart rate fluctuation: A quantitative probe of beat-to-beat cardiovascular control. *Science, 213*, 220-222.

Amiez, C., Joseph, J. P. & Procyk, E. (2006). Reward encoding in the monkey anterior cingulate cortex. *Cerebral Cortex, 16*, 1040-1055.

Appelhans, B. M. & Luecken, L. J. (2006). Heart rate variability as an index of regulated emotional responding. *Review of General Psychology, 10*, 229–240.

Baddeley, A. D., Emslie, H. & Nimmo-Smith, I. (1992). The Speed and Capacity of Language Processing (SCOLP) Test. Bury St. Edmonds: Thames Valley Test Company.

Band, G. P. H. & Kok, A. (2000). Age effects on response monitoring in a mental-rotation task. *Biological Psychology, 51*, 201-221.

Band, G. P. H. & Miller, J. (1997). Mental rotation interferes with response preparation. *Journal of Experimental Psychology: Human Perception and Performance, 23*, 319–338.

Baron, J. C. (2001). Perfusion thresholds in human ischemia: historical perspective and therapeutic implications. *Cerebrovascular Diseases, 1 1*(suppl1), 2-8.

Bartholow, B. D., Pearson, M. A., Dickter, C. L., Sher, K. J., Fabiani, M. & Gratton, G. (2005). Strategic control and medial frontal negativity: Beyond errors and response conflict. *Psychophysiology, 42*, 33-42.

Beauchaine, T. (2001). Vagal tone, development, and Gray's motivational theory: Toward an integrated model of autonomic nervous system functioning in psychopathology. *Development and Psychopathology, 13*, 183-214.

Behrens, T. E. J., Woolrich, M. W., Walton, M. E. & Rushworth, M. F. S. (2007). Learning the value of information in an uncertain world. *Nature Neuroscience, 10*, 1214-1221.

Benarroch, E. E. (1993). The central autonomic network: Functional organization, dysfunction and perspective. *Mayo Clinic Proceedings, 68*, 988-1001.

Benarroch, E. E. (1997). The central autonomic network. In P. A. Low (Ed.), *Clinical Autonomic Disorders* (second ed.). Philadelphia, PA: Lippincott-Raven Publishers.

Bentin, S. & McCarthy, G. (1994). The effects of immediate stimulus repetition on reaction time and event-related potentials in tasks of different complexity. *Journal of Experimental Psychology*, 130–149.

Benton, D., Parker, P. Y. & Donohue, R. T. (1996). The supply of glucose to the brain and cognitive functioning. *Journal of Biosocial Science, 28*, 463-479.

Berntson, G. G., Bigger Jr., J. T., Eckberg, D. L., Grossman, P., Kaufmann, P. G., Malik, M., Nagaraja, H. M., Porges, S. W., Saul, J. P., Stone, P. H. & van der Molen, M. W. (1997). Heart rate variability: Origins, methods and interpretive caveats. *Psychophysiology, 34*, 623-648.

Berntson, G. G., Cacioppo, J. T., Binkley, P. F., Uchino, B. N., Quigley, K. S. & Fieldstone, A. (1994). Autonomic cardiac control. III. Psychological stress and cardiac response in autonomic space as revealed by pharmacological blockades. *Psychophysiology, 31*, 599-608.

Berntson, G. G., Cacioppo, J. T. & Grossman, P. (2007). Whither vagal tone? *Biological Psychology, 74*, 295-300.

Berntson, G. G., Cacioppo, J. T. & Quigley, K. S. (1991). Autonomic determinism: The modes of autonomic control, the doctrine of autonomic space, and the laws of autonomic constraint. *Psychological Review, 98*, 459-487

Berntson, G. G., Cacioppo, J. T. & Quigley, K. S. (1993). Respiratory sinus arrhythmia: Autonomic origins, physiological mechanisms, and psychophysiological implications. *Psychophysiology, 30*, 183-196.

Berntson, G. G. & Stowell, J. R. (1998). ECG artifacts and heart period variability: Don't miss a beat! *Psychophysiology, 35*, 127–132.

Bonnemeier, H., Wiegand, U. K. H., Braindes, A., Kluge, N., Katus, H. A. & Richardt, G. (2003). Circadian profile of cardiac autonomic nervous modulation in healthy subjects. *Journal of Cardiovascular Electrophysiology, 14*, 791-803.

Botvinick, M. M., Braver, T. S., Barch, D. M., Carter, C. & Cohen, J. D. (2001). Conflict monitoring and cognitive control. *Psychological Review, 108*, 624-652.

Breteler, M. M. B. (2000). Vascular involvement in cognitive decline and dementia: Epidemiologic evidence from the Rotterdam Study and the Rotterdam Scan Study. *Annals of the New York Acadamey of Sciences, 903*, 157-165.

Brookmeyer, R., Gray, S. & Kawas, C. (1998). Projections of Alzheimer's disease in the United States and the public health impact of delaying disease onset. *American Journal of Public Health, 88*, 1337-1342.

Brownley, K. A., Hurwitz, B. E. & Schneiderman, N. (2000). Cardiovascular psychophysiology. In J. T. Cacioppo & L. G. Tassinary & G. G. Berntson (Eds.), *Handbook of Psychophysiology* (2nd ed., pp. 224-264). Cambridge, U.K.: Cambridge University Press.

Budge, M. M., de Jager, C., Hogervorst, E. & Smith, A. D. (2002). Total plasma homocysteine, age, systolic blood pressure, and cognitive performance in older people. *Journal of the American Geriatrics Society, 50*, 2014-2018.

Bunge, S. A., Ochsner, K. N., Desmond, J. E., Glover, G. H. & Gabrieli, J. D. E. (2001). Prefrontal regions involved in keeping information in and out of mind. *Brain, 124*, 2074-2086.

Bush, G., Luu, P. & Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Sciences, 4*, 215-222.

Cabeza, R. & Nyberg, L. (2000). Imaging cognition: II. An empirical review of 275 PET and fMRI studies. *Journal of Cognitive Neuroscience, 12*, 1-47.

Cacioppo, J. T., Berntson, G. G., Larsen, J. T., Poehlmann, K. M. & Ito, T. A. (2000). The psychophysiology of emotion. In M. Lewis & J. M. Haviland-Jones (Eds.), *Handbook of Emotions* (2nd ed., pp. 173-191). New York, NY: The Guilford Press.

Chao, L. L. & Knight, R. T. (1997). Prefrontal deficits in attention and inhibitory control with aging. *Cerebral Cortex, 7*, 63-69.

Chiu, Y.-C., Algase, D., Whall, A., Liang, J., Liu, H.-C., Lin, K.-N., at al.(2004). Getting lost: directed attention and executive functions in early Alzheimer's disease patients. *Dementia and Geriatric Cognitive Disorders, 17*, 174-180.

Coles, M. G. H., Gehring, W. J., Gratton, G. & Donchin, E. (1991). Stimulus-response compatibility and psychophysiology. In J. Requin & G. E. Stelmach (Eds.), *Tutorials in motor neuroscience.* (pp. 27-28). New York, NY: Kluwer Academic/Plenum Publishers.

Coles, M. G. H., Scheffers, M. K. & Holroyd, C. B. (2001). Why is there an ERN/Ne on correct trials? Response representations, stimulus-related components and the theory of error-processing. *Biological Psychology, 56*, 173-189.

Critchley, H. D., Mathias, C. J., Josephs, O., O'Doherty, J., Zanini, S., Dewar, B.-K., Cipoletti, L., Shallice, T. & Dolan, R. J. (2003). Human cingulate cortex and autonomic control: Converging neuroimaging and clinical evidence. *Brain, 126*, 2139-2152.

Critchley, H. D., Tang, J., Glaser, D., Butterworth, B. & Dolan, R. J. (2005). Anterior cingulate activity during error and autonomic response. *NeuroImage, 27*, 885-895.

Crone, E. A. M., van der Veen, F. M., van der Molen, M. W., Somsen, R. J. M., van Beek, B. & Jennings, J. R. (2003). Cardiac concomitants of feedback processing. *Biological Psychology, 64*, 143-156.

Cruz-Muros, I., Afonso-Oramas, D., Abreu, P., Barroso-Chinea, P., Rodriquez, M., Gonzalez, M. C. & Hernandez, T. G. (2007). Aging of the rat mesostriatal system: Differences between the nigrostriatal and the mesolimbic compartments. *Experimental Neurology, 204*, 147-161.

de Bruijn, E. R. A., Hulstijn, W., Verkes, R. J., Ruigt, G. S. F. & Sabbe, B. G. C. (2004). Drug-induced stimulation and suppression of action monitoring in healthy volunteers. *Psychopharmacology, 177*, 151-160.

de Bruijn, E. R. A., Hulstijn, W., Verkes, R. J., Ruigt, G. S. F. & Sabbe, B. G. C. (2005). Altered response evaluation: Monitoring of late responses after admininstration of D-amphetamine. *Journal of Psychophysiology, 19*, 311-318.

De Jong, G. I., Farkas, E., Stienstra, C. M., Plass, J. R. M., Keijser, J. N., de la Torre, J. C. & Luiten, P. G. M. (1999). Cerebral hypoperfusion yields capillary damage in the hippocampal CA1 area that correlates with spatial memory impairment. *Neuroscience, 91*, 203-210.

Dehaene, S., Posner, M. I. & Tucker, D. M. (1994). Localization of a neural system for error detection and compensation. *Psychological Science, 5*, 303-305.

Dekker, J. M., Crow, R. S., Folsom, A. R., Hannan, P. J., Liao, D., Swenne, C. A. & Schouten, E. G. (2000). Low heart rate variability in a 2-minute rhythm strip predicts risk of coronary heart disease and mortality from several causes. *Circulation, 102*, 1239-1244.

Dellinger, J. A., Taylor, H. L. & Porges, S. W. (1987). Atropine sulfate effects on aviator performance and on respiratory rate period interactions. *Aviation, Space and Evironmental Medicine, 58*, 333.

DeMeersman, R. E. (1993). Aging as a modulator of respiratory sinus arrhythmia. *Journal of Gerontology: Biological Sciences, 48*, B74-B78.

DeMeersman, R. E. & Stein, P. K. (2007). Vagal modulation and aging. *Biological Psychology, 74*, 165-173.

Dennis, N. A., Hayes, S. M., Prince, S. E., Madden, D. J., Huettel, S. A. & Cabeza, R. (2008). Effects of aging on the neural correlates of successful item and source memory encoding. *Journal of Experimental Psychology: Learning, Memory and Cognition, 34,* 791-808.

Denver, J. W., Reed, S. F. & Porges, S. W. (2007). Methodological issues in the quantification of respiratory sinus arrhythmia. *Biological Psychology, 74*, 286-294.

Derrick, W. L. (1988). Dimensions of operator workload. *Human Factors, 30*, 95-110.

Derryberry, D. & Reed, M. A. (2002). Anxiety-related attentional biases and their regulation by attentional control. *Journal of Abnormal Psychology, 111*, 225–236.

Devinsky, O., Morrell, M. & Vogt, B. A. (1995). Contributions of anterior cingulate cortex to behaviour. *Brain, 118*, 279-306.

Donchin, Y., Feld, J. M. & Porges, S. W. (1985). The measurement of respiratory sinus arrhythmia during recovery from isoflurane-nitrous oxide anesthesia. *Anesthesia and Analgesia, 64*, 811.

Donkers, F. C. L., Nieuwenhuis, S. & van Boxtel, G. J. M. (2005). Mediofrontal negativies in the absence of responding. *Cognitive Brain Research, 25*, 777-787.

Donohue, R. T. & Benton, D. (1999). Cognitive functioning is susceptible to the level of blood glucose. *Psychopharmacology, 145*, 378-385.

Driscoll, I., Hamilton, D. A., Petropoulos, H., Yeo, R. A., Brooks, W. M., Baumgartner, R. N. & Sutherland, R. J. (2003). The aging hippocampus: Cognitive, biochemical and structural findings. *Cerebral Cortex, 13*, 1344-1351.

Dywan, J. & Jacoby, L. L. (1990). Effects of aging on source monitoring: Differences in susceptibility to false fame. *Psychology and Aging, 5*, 379-387.

Dywan, J., Mathewson, K. J. & Segalowitz, S. J. (submitted). Source memory and aging: A neurophysiological perspective.

Dywan, J., Segalowitz, S. J. & Arsenault, A. (2002). Electrophysiological response during source memory decisions in older and younger adults. *Brain and Cognition, 49*, 322-340.

Dywan, J., Segalowitz, S. J. & Webster, L. (1998). Source monitoring: ERP evidence for greater reactivity to nontarget information in older adults. *Brain and Cognition, 36*, 390-430.

Dywan, J., Segalowitz, S. J., Webster, L., Hendry, K. & Harding, J. (2001). ERP evidence for age-related differences in attentional allocation during a source monitoring task. *Developmental Neuropsychology, 19*, 99-120.

Elias, M. F., Elias, P. K., Sullivan, L. M., Wolf, P. A. & D'Agostino, R. B. (2003). Lower cognitive function in the presence of obesity and hypertension. *International Journal of Obesity and Related Metabolic Disorders, 27*, 260-268.

Eppinger, B., Kray, J., Mock, B. & Mecklinger, A. (2008). Better or worse than expected? Aging, learning and the ERN. *Neuropsychologia, 46*, 521-539.

Erdine, S., Ari, O., Zanchetti, A., Cifkova, R., Fagard, R., Kjeldsen, S., et al. (2006). ESH-ESC guidelines for the management of hypertension. *Herz, 31*, 331-338.

Eriksen, B. A. & Eriksen, C. W. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. *Perception and Psychophysics, 16*, 143-149.

Eysenck, M. W., Derakshan, N., Santos, R. & Calvo, M. G. (2007). Anxiety and cognitive performance: Attentional control theory. *Emotion, 7*, 336-353.

Fabes, R. A., Eisenberg, N., Karbon, M., Troyer, D. & Switzer, G. (1994). The relations of children's emotion regulation to their vicarious emotional responses and comforting behaviors. *Child Development, 65*, 1678-1693.

Falkenstein, M., Hohnsbein, J., Hoormann, J. & Blanke, L. (1990). Effects of errors in choice reaction tasks on the ERP under focused and divided attention. In C. H. M. Brunia & A. W. K. Gaillard & A. Kok (Eds.), *Psychophysiological Brain Research* (pp. 192-195). Tilburg, The Netherlands: Tilburg University Press.

Falkenstein, M., Hohnsbein, J., Hoormann, J. & Blanke, L. (1991). Effects of cross-modal divided attention on late ERP components. II. Error processing in choice reaction tasks. *Electroencephalography and Clinical Neurophysiology, 78*, 447-455.

Falkenstein, M., Hoormann, J. & Hohnsbein, J. (2001). Changes of error-related ERPs with age. *Experimental Brain Research, 138*, 258-262.

Farmer, M. E., Kittner, S. J., Abbott, R. D., Wolz, M. M., Wolf, P. A. & Whiter, L. R. (1990). Longitudinally measured blood pressure, antihypertensive medication use and cognitive performance: The Framingham Study. *Journal of Clinical Epidemiology, 43*, 475-480.

Ferrandez, A.-M. & Pouthas, V. (2001). Does cerebral activity change in middle-aged adults in a visual discrimination task? *Neurobiology of Aging, 22*, 645-657.

Fisk, G. D. & Wyss, J. M. (1997). Pressor and depressor sites are intermingled in the cingulate cortex of the rat. *Brain Research, 754*, 204-212.

Folstein, M. F., Folstein, S. E. & McHugh, P. R. (1975). "Mini-Mental State": A practical guide for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 196-198.

Forette, F., Seux, M.-L., Staessen, J. A., Lutgarde, T., at al.(2002). The prevention of dementia with anti-hypertensive treatment: New evidence from the systolic hypertension in Europe (Syst-Eur) study. *Archives of Internal Medicine, 162*, 2046-2052.

Frazier, T. W., Strauss, M. E. & Steinhauer, S. R. (2004). Respiratory sinus arrhythmia as an index of emotional response in young adults. *Psychophysiology, 41*, 75-83.

Fredericks, T. K., Choi, S. D., Hart, J., Butt, S. E. & Mital, A. (2005). An investigation of myocardial aerobic capacity as a measure of both physical and cognitive workloads. *International Journal of Industrial Ergonomics, 35*, 1097-1107.

Friedman, B. H. (2007). An autonomic flexibility-neurovisceral integration model of anxiety and cardiac vagal tone. *Biological Psychology, 74*, 185-199.

Friedman, B. H. & Thayer, J. F. (1998). Autonomic balance revisited: Panic anxiety and heart rate variability. *Journal of Psychosomatic Research, 44*, 133-151.

Gaykema, R. P., van Weeghel, R., Hersh, L. B. & Luiten, P. G. (1991). Prefrontal cortical projections to the cholinergic neurons in the basal forebrain. *Journal of Comparative Neurology, 303*, 563-583.

Gaykema, R. P. & Zabosky, L. (1996). Direct catecholaminergic– cholinergic interactions in the basal forebrain: II. Substantia nigra-ventral tegmental area projections to cholinergic neurons. *Journal of Comparative Neurology, 374*, 555-577.

Gehring, W. J., Goss, B., Coles, M. G. H., Meyer, D. E. & Donchin, E. (1993). A neural system for error detection and compensation. *Psychological Science, 4*, 385-390.

Gehring, W. J. & Knight, R. T. (2000). Prefrontal-cingulate interactions in action monitoring. *Nature Neuroscience, 3*, 516-520.

Gianaros, P. J., Salomon, K., Zhou, F., Owens, J. F., Edmundowicz, D., Kuller, L. E. & Matthews, K. E. (2005). A greater reduction in high-frequency heart rate variability to a psychological stressor is associated with subclinical coronary and aortic calcification in postmenopausal women. *Psychosomatic Medicine, 67*, 553-560.

Gianaros, P. J., Van der Veen, F. M. & Jennings, J. R. (2004). Regional cerebral blood flow correlates with heart period and high-frequency heart period variability during working memory tasks: Implications for cortical and subcortical regulation of cardiac autonomic activity. *Psychophysiology, 41*, 521-530.

Gold, J. J., Smith, C. N., Bayley, P. J., Shrager, Y., Brewer, J. B., Stark, C. E., et al., (2006). Item memory, source memory, and the medial temporal lobe: Concordant findings from fMRI and memory-impaired patients. *Proceedings of the National Academy of Sciences, 103*, 9351-9356.

Goldberger, A. L. (1996). Non-linear dynamics for clinicians: chaos theory, fractals, and complexity at the bedside. *Lancet, 347*, 1312-1314.

Goldberger, A. L. (1997). Fractal variability versus pathological periodicity: complexity loss and stereotypy in disease. *Perspectives in Biology and Medicine, 40*, 543-561.

Grady, C., Springer, M. V., Hongwanishkul, D., McIntosh, A. R. & Winocur, G. (2006). Age-related changes in brain activity across the adult lifespan. *Journal of Cognitive Neuroscience, 18*, 227-241.

Graham, F. K. & Clifton, R. K. (1966). Heart-rate change as a component of the orienting response. *Psychological Bulletin, 65*, 305-320.

Grossman, P. & Taylor, E. W. (2007). Toward understanding respiratory sinus arrhythmia: Relations to cardiac vagal tone, evolution and bioBehavioural functions. *Biological Psychology, 74*, 263-285.

Grossman, P., van Beek, J. & Wientjes, C. (1990). A comparison of three quantification methods for estimation of respiratory sinus arrhythmia. *Psychophysiology, 27*, 702-714.

Gutchess, A. H., Welsh, R. C., Hedden, T., Bangert, A., Minear, M., Liu, L. L., at al.(2005). Aging and the neural correlates of successful picture encoding: frontal activations compensate for deceased medial-temporal activity. *Journal of Cognitive Neuroscience, 17*, 84-96.

Guzzetti, S., Piccaluga, E., Casati, R., Cerutti, S., Lombardi, F., Pagani, M. & Malliani, A. (1988). Sympathetic predominance in essential hypertension: A study employing spectral analysis of heart rate variability. *Journal of Hypertension, 6*, 711-717.

Hagemann, D., Waldstein, S. R. & Thayer, J. F. (2003). Central and autonomic nervous system integration in emotion. *Brain and Cognition, 52*, 79-87.

Hajcak, G., McDonald, N. & Simons, R. F. (2003). To err is autonomic: Error-related brain potentials, ANS activity, and post-error compensatory behavior. *Psychophysiology, 40*, 895-903.

Hajcak, G., Moser, J. S., Holroyd, C. B. & Simons, D. J. (2006). The feedback-related negativity reflects the binary evalaution of good versus bad outcomes. *Biological Psychology, 71*, 148-153.

Hall, M., Vasko, R., Buysse, D., Ombayo, H., Chen, Q., Cashmere, J. D., Kupfer, D. & Thayer, J. F. (2004). Acute stress affects heart rate variability during sleep. *Psychosomatic Medicine, 66*, 56-62.

Hansen, A. L., Johnsen, B. H., Sollers, I., J. J., Stenvik, K. & Thayer, J. F. (2004). Heart rate variability and its relation to prefrontal cognitive function: The effects of training and detraining. *European Journal of Applied Physiology, 93*, 263-272.

Hansen, A. L., Johnsen, B. H. & Thayer, J. F. (2003). Vagal influence on working memory and attention. *International Journal of Psychophysiology, 48*, 263-274.

Hatanaka, N., Tokuno, H., Hamada, I., Inase, M., Ito, Y., Imanishi, M., Hasegawa, N., Akazawa, T., Nambu, A. & Takada, M. (2003). Thalamocortical and intracortical connections of monkey cingulate motor areas. *Journal of Comparative Neurology, 462*, 121-138.

Hayano, J. & Yasuma, F. (2003). Hypothesis: respiratory sinus arrhythmia is an intrinsic resting function of cardiopulmonary system. *Cardiovascular Research, 58*, 1-9.

Hayano, J., Yasuma, F., Okada, A., Mukai, S. & Fujinami, T. (1996). Respiratory sinus arrhythmia: A phenomenon improving pulmonary gas exchange and circulatory efficiency. *Circulation, 94*, 842-847.

Hebert, L. E., Scherr, P. A., Bienias, J. L., Bennett, D. A. & Evans, D. A. (2003). Alzheimer disease in the US population: Prevalence estimates using the 2000 census. *Archives of Neurology, 60*, 1119-1122.

Henderson, H., Schwartz, C., Mundy, P., Burnette, C., Sutton, S., Zahka, N. & Pradella, A. (2006). Response monitoring, the error-related negativity, and differences in social behavior in autism. *Brain and Cognition, 61*, 96-109.

Herrmann, M. J., Römmler, J., Ehlis, A.-C., Heidrich, A. & Fallgatter, A. J. (2004). Source localization (LORETA) of the error-related negativity (ERN/Ne) and positivity (Pe). *Cognitive Brain Research, 20*, 294-299.

Hillman, C. H., Belopolsky, A., Snook, E. M., Kramer, A. F. & McAuley, E. (2004). Physical activity and executive control: Implications for increased cognitive health during older adulthood. *Research Quarterly for Exercise and Sport, 75*, 176–185.

Holroyd, C. B. & Coles, M. G. H. (2002). The neural basis of human error-processing: Reinforcement learning, dopamine and the error-related negativity. *Psychological Review, 109*, 679-709.

Holroyd, C. B., Nieuwenhuis, S., Yeung, N., Nystrom, L., Mars, R. B., Coles, M. G. H. & Cohen, J. D. (2004). Dorsal anterior cingulate cortex shows fMRI response to internal and external error signals. *Nature Neuroscience, 7*, 497-498.

Hoshikawa, Y. & Yamamoto, Y. (1997). Effects of Stroop color-word conflict test on the autonomic nervous system responses. *American Journal of Physiology: Heart Circulation Physiology, 272*, H1113-1121.

Iadecola, C. & Gorelick, P. B. (2003). Converging pathogenic mechanisms in vascular and neurodegenerative dementia. *Stroke, 34*, 335-337.

Jack, J. C. R., Petersen, R. C., Xu, Y., O'Brien, P. C., Ivnik, R. J., at al.(1998). Rate of medial temporal lobe atrophy in typical aging and Alzheimer's disease. *Neurology, 51*, 993-999.

Jacoby, L. L., Bishara, A. J., Hessels, S. & Toth, J. P. (2005). Aging, subjective experience, and cognitive control: Dramatic false remembering by older adults. *Journal of Experimental Psychology: General, 134*, 131-148.

Jacoby, L. L., Kelley, C. M. & Dywan, J. (1989). Memory attributions. In H. L. Roediger III & F. I. M. Craik (Eds.), *Varieties of Memory and Consciousness: Essays in Honor of Endel Tulving.* (pp. 391-422). Hillsdale, NJ: Lawrence Erlbaum Associates, Inc.

Jacoby, L. L., Kelley, C. M. & McElree, B. (1999). The role of cognitive control: Early selection vs late correction. In S. Chaiken & Y. Trope (Eds.), *Dual process theories in social psychology* (pp. 383-400). New York, NY: Guilford.

Janowsky, J. S., Shimamura, A. P. & Squire, L. R. (1989). Source memory impairment in patients with frontal lobe lesions. *Neuropsychologia, 7*, 1043-1056.

Jellinger, K. A. (2005). Understanding the pathology of vascular cognitive impairment. *Journal of the Neurological Sciences, 229–230*, 57–63.

Jennings, J. M. & Jacoby, L. L. (1997). An opposition procedure for detecting age-related deficits in recollection: Telling effects of repetition. *Psychology and Aging, 12*, 352-361.

Jennings, J. R. & McKnight, J. D. (1994). Inferring vagal tone from heart rate variability. *Psychosomatic Medicine, 56*, 194-196.

Jennings, J. R., van der Molen, M. & Debski, K. (2003). Mental rotation delays the heart beat: Probing the central processing bottleneck. *Psychophysiology, 40*, 666-674.

Jennings, J. R. & van der Molen, M. W. (2002). Cardiac timing and the central regulation of action. *Psychological Research, 66*, 337-349.

Jennings, J. R., van der Molen, M. W. & Brock, K. (1997). Mnemonic search, but not arithmetic transformation, is associated with psychophysiological inhibition. *Journal of Experimental Psychology: Human Perception and Performance, 23*, 154-167.

Jennings, J. R., van der Molen, M. W., Brock, K. & Somsen, R. J. M. (1991). Response inhibition initiates cardiac deceleration: Evidence from a sensory-motor compatibility paradigm. *Psychophysiology, 28*, 72-85.

Jennings, J. R., van der Molen, M. W., Brock, K. & Somsen, R. J. M. (1992). On the synchrony of stopping motor responses and delaying heartbeats. *Journal of Experimental Psychology: Human Perception and Performance, 18*, 422-436.

Jennings, J. R., Van der Veen, F. M. & Meltzer, C. C. (2006). Verbal and spatial working memory in older individuals: A positron emission tomography study. *Brain Research, 1092*, 177-189.

Johnsen, B. H., Thayer, J. F., Laberg, J. C., Wrmnes, B., Raadal, M., Skaret, E., Kvale, G. & Berg, E. (2003). Attentional and physiological characteristics of patients with dental anxiety. *Anxiety Disorders, 17*, 75-87.

Johnson, M. K. (2005). The relation between source memory and episodic memory: Comment on Siedlecki et al. (2005). *Psychology and Aging, 20*, 529-531.

Jorna, P. G. A. M. (1992). Spectral analysis of heart rate and psychological state: A review of its validity as a workload index. *Biological Psychology, 34*, 237-257.

Kaasinen, V., Vilkman, H., Hietala, J., Nagren, K., Helenius, H., Olsson, H., at al.(2000). Age-related dopamine D2/D3 receptor loss in extrastriatal regions of the human brain. *Neurobiology of Aging, 21*, 683-688.

Kalinin, S., Gavrilyuk, V., Polak, P. E., Vasser, R., Zhao, J., Heneka, M. T. & Feinstein, D. L. (2007). Noradrenaline deficiency in brain increases B-amyloid plaque burden in an animal model of Alzheimer's disease. *Neurobiology of Aging, 28*, 1206-1214.

Katona, P. G. & Jih, F. (1975). Respiratory sinus arrhythmia: Noninvasive measure of parasympathetic control. *Journal of Applied Physiology, 39*, 801-805.

Kennedy, D. O. & Scholey, A. B. (2000). Glucose administration, heart rate and cognitive performance: effects of increasing mental effort. *Psychopharmacology, 149*, 63-71.

Kennerly, S. W., Walton, M. E., Behrens, T. E. J., Buckley, M. J. & Rushworth, M. F. S. (2006). Optimal decision-making and the anterior cingulate cortex. *Nature Neuroscience, 9*, 940-947.

Kensinger, E. A. & Schacter, D. (1999). When true memories suppress false memories: Effects of aging. *Cognitive Neuropsychology, 16*, 399-415.

Kilander, L., Nyman, H., Boberg, M., Hansson, L. & Lithell, H. (1998). Hypertension is related to cognitive impairment : A 20-year follow-up of 999 men. *Hypertension, 31*, 780-786.

Kim, D. H., Lipsitz, L. A., Ferrucci, L., Varadhan, R., Guralnik, J. M., Carlson, M. C., Fleisher, L. A., Fried, L. P. & Chaves, P. H. M. (2006). Association between reduced heart rate variability and cognitive impairment in older disabled women in the community: Women's Health and Aging Study 1. *Journal of the American Geriatric Society, 54*, 1751-1757.

Kirasic, K. C. (2000). Age differences in adults' spatial abilities, learning environmental layout, and wayfinding behavior. *Spatial Cognition and Computation, 2*, 117-134.

Kirasic, K. C., Allen, G. L. & Haggerty, D. (1992). Age-related differences in adults' macrospatial cognitive processes. *Experimental Aging Research, 18*, 33-39.

Kivipelto, M., Helkala, E. L., Laakso, M. P., Hanninen, T., Hallikainen, M., Alheinin, K., at al.(2001). Midlife vascular risk factors and Alzheimer's disease in later life: A longitudinal, population-based study. *British Medical Journal, 322*, 1447-1451.

Kok, A. (2000). Age-related changes in involuntary and voluntary attention as reflected in components of the event-related potentials (ERP). *Biological Psychology, 54*, 107-143.

Korf, E. S., White, L. R., Scheltens, P., at al.(2004). Midlife blood pressure and the risk of hippocampal atrophy. *Hypertension, 44*, 29-34.

Kuo, H. K., Sorond, F., Iloputaife, I., Gagnon, M., Milberg, W. & Lipsitz, L. A. (2004). Effects of blood pressure on cognitive function in elderly persons. *Journal of Gerontology: Medical Sciences, 59A*, 1191-1194.

Lacey, J. I. (1967). Somatic response patterning and stress: Some revisions of activation theory. In M. H. Appley & R. Trumbell (Eds.), *Psychological Stress: Issues in Research* (pp. 4-44). New York, NY: Academic Press.

Larson, E. B., Wang, L., Bowen, J. D., McCormick, W. C., Teri, L., Crane, P. & Kukull, W. (2006). Exercise is associated with reduced risk for incident dementia among persons 65 years of age and older. *Annals of Internal Medicine, 144*, 73-81.

Launer, L., Ross, G. W., Petrovich, H., Masaki, K., Foley, D., White, L. R. & Havlik, J. R. (2000). Midlife blood pressure and dementia: the Honolulu–Asia aging study. *Neurobiology of Aging, 21*, 49-55.

Levy, M. N. (1990). Autonomic interactions in cardiac control. *Annals of the New York Acadamey of Sciences, 601*, 209-221.

Levy, M. N. (1993). Assessment of beat-by-beat control of heart rate by the autonomic nervous system: molecular biology techniques are necessary, but not sufficient. *Journal of Cardiovascular Electrophysiology, 4*, 183-193.

Levy, M. N. (1997). Neural control of cardiac function. *Bailliere's Clinical Neurology, 6*, 227-244.

Liao, D., Cai, J., Barnes, R. W., Tyroler, H. A., Rautaharju, P., Holme, I. & Heiss, G. (1996). Association of cardiac autonomic function and the development of hypertension. *American Journal of Hypertension, 9*, 1147-1156.

Lindmark, S., Lönn, L., Wiklund, U., Tufvesson, M., Olsson, T. & Eriksson, J. W. (2005). Dysregulation of the autonomic nervous system can be a link between visceral adiposity and insulin resistance. *Obesity Research, 13*, 717-728.

Loftus, E. F. (1975). Leading questions and the eyewitness report. *Cognitive Neuropsychology, 7*, 560-572.

Lövdén, M., Schellenbach, M., Grossman-Hutter, B., Krüger, A. & Lindenberger, U. (2005). Environmental topography and postural control demands shape aging-associated decrements in spatial navigation performance. *Psychology and Aging, 20*, 683-694.

Low, P. A. (1997). The effect of aging on the autonomic nervous system. In P. A. Low (Ed.), *Clinical Autonomic Disorders* (second ed.). Philadelphia: Lippincott-Raven Publishers.

Lyness, J. M. & Porges, S. W. (1985). *Psychophysiological responses of type A and B men with and without coronary disease*. Unpublished manuscript.

Lytle, M. E., Vander, B. J., Pandav, R., Dodge, H. H. & Ganguli, M. (2004). Exercise level and cognitive decline: the MoVIES project. *Alzheimer Disease and Associated Disorders, 18*, 57-64.

Manns, J. R. & Eichenbaum, H. (2006). Evolution of declarative memory. *Hippocampus, 16*, 795-808.

Mars, R. B., de Bruijn, E. R. A., Hulstijn, W., Miltner, W. H. R. & Coles, M. G. H. (2004). What if I told you: "You were wrong"? Brain potentials and Behavioural adjustments elicited by feedback in a time-estimation task. In M. Ullsperger & M. Falkenstein (Eds.), *Errors, Conflicts and the Brain. Current Opinions on Performance Monitoring* (pp. 129-134). Dresden: Sächsiches Digitaldruck Zentrum GmbH.

Masi, C. M., Hawkley, L. C., Rickett, E. M. & Cacioppo, J. T. (2007). Respiratory sinus arrhythmia and diseases of aging: Obesity, diabetes mellitus, and hypertension. *Biological Psychology, 74*, 212-223.

Mather, M., Johnson, M. K. & De Leonardis, D. M. (1999). Stereotype reliance in source monitoring: Age differences and neuropsychological test correlates. *Cognitive Neuropsychology, 16*, 437-458.

Mather, M., Mitchell, K. J., Raye, C. L., Novak, D. L., Greene, E. J. & Johnson, M. K. (2006). Emotional arousal can impair feature binding in working memory. *Journal of Cognitive Neuroscience, 18*, 614-625.

Mathewson, K. J., Dywan, J., Snyder, P. J., Tays, W. J. & Segalowitz, S. J. (in preparation). Aging and autonomic control and in a spatial learning task.

Mathewson, K. J., Dywan, J. & Segalowitz, S. J. (2005). Brain bases of error-related ERPs as influenced by age and task. *Biological Psychology, 70*, 88-104.

Mathewson, K. J., Dywan, J., Snyder, P. J., Tays, W. J. & Segalowitz, S. J. (2008). Aging and electrocortical response to error feedback during a spatial learning task. *Psychophysiology, 45*, 936-948.

Matsunaga, W., Isobe, K. & Shirokawa, T. (2006). Involvement of neurotrophic factors in aging of noradrenergic innervations in hippocampus and frontal cortex. *Neuroscience Research, 54*, 313-318.

Matthews, S. C., Paulus, M. P., Simmons, A. N., Nelesen, R. A. & Dimsdale, J. E. (2004). Functional subdivisions within anterior cingulate cortex and their relationship to autonomic nervous system function. *NeuroImage, 22*, 1151-1156.

Melis, C. & van Boxtel, A. (2007). Autonomic physiological response patterns related to intelligence. *Intelligence, 35*, 471-487.

Mell, T., Heekerena, H. R., Marschnera, A., Wartenburger, I., Villringera, A. & Reischies, F. M. (2005). Effect of aging on stimulus-reward association learning. *Neuropsychologia, 43*, 554-563.

Merritt, M. M., Bennett, G. G., Williams, R. B., Sollers, I., J. J. & Thayer, J. F. (2004). Low educational attainment, John Henryism, and cardiovascular reactivity to and recovery from personally relevant stress. *Psychosomatic Medicine, 66*, 49-55.

Middleton, H. C., Sharma, A., Agouzoul, D., Sahakian, B. J. & Robbins, T. W. (1999). Contrasts between the cardiovascular concomitants of tests of planning and attention. *Psychophysiology, 36*, 610-618.

Miller, E. K. & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience, 24*, 167-202.

Milner, B. (1965). Visually guided maze learning in man: Effects of bilateral hippocampal, bilateral frontal and unilateral cerebral lesions. *Neuropsychologia, 3*, 317-338.

Miltner, W. H. R., Braun, C. H. & Coles, M. G. H. (1997). Event-related brain potentials following incorrect feedback in a time-estimation task: evidence for a "generic" neural system for error detection. *Journal of Cognitive Neuroscience, 9*, 788-798.

Mitchell, K. J., Mather, M., Johnson, M. K., Raye, C. L. & Greene, E. J. (2006). A functional magnetic resonance imaging investigation of short-term source and item memory for negative pictures. *NeuroReport, 17*, 1543-1548.

Moffat, S. D., Elkins, W. & Resnick, S. M. (2006). Age differences in the neural systems supporting human allocentric spatial navigation. *Neurobiology of Aging, 27*, 965-972.

Moffat, S. D., Kennedy, K. M., Rodrigue, K. M. & Raz, N. (2007). Extrahippocampal contributions to age differences in human spatial navigation. *Cerebral Cortex, 17*, 1274-1282.

Moffat, S. D. & Resnick, S. M. (2002). Effects of age on virtual environment place navigation and allocentric cognitive mapping. *Behavioural Neuroscience, 116*, 851-859.

Monroe, R. G. & French, G. N. (1961). Left ventricular pressure-volume relationships and myocardial oxygen consumption in the isolated heart. *Circulation Research, 9*, 362-373.

Movius, H. L. & Allen, J. J. B. (2005). Cardiac vagal tone, defensiveness and motivational style. *Biological Psychology, 68*, 147-162.

Mulder, G. (1986). The concept and measurement of mental effort. In G. R. J. Hockey & A. W. K. Gaillard & M. G. H. Coles (Eds.), *Energetics and human information processing*. Dordrecht: Martinus Nijhoff.

Mulder, G. & Mulder-Hajonides van der Meulen, W. R. E. H. (1973). Mental load and the measurement of heart rate variability. *Ergonomics, 16*, 69-83.

Müller, S. V., Möller, J., Rodriguez-Fornells, A. & Münte, T. F. (2005). Brain potentials related to self-generated and external information used for performance monitoring. *Clinical Neurophysiology, 116*, 63-74.

Munro, G. E. S., Dywan, J., Harris, G. T., McKee, S., Unsal, A. & Segalowitz, S. J. (2007). ERN varies with degree of psychopathy in an emotion discrimination task. *Biological Psychology, 76*, 31-42.

Murphy, K. J., West, R., Armilio, M. L., Craik, F. I. M. & Stuss, D. T. (2007). Word-list-learning performance in younger and older adults: Intra-individual performance variability and false memory. *Aging, Neuropsychology, and Cognition, 14*, 70-94.

Nakai, S., Matsunaga, W., Isobe, K. & Shirokawa, T. (2006). Age-dependent interactive changes in serotonergic and noradrenergic cortical axon terminals in F344 rats. *Neuroscience Research, 54*, 220-229.

Nelson, R. R., Gobel, F., Jorgensen, C. R., Wang, K., Wang, Y. & Taylor, H. L. (1974). Hemodynamic predictors of myocardial oxygen consumption during static and dynamic exercise. *Circulation, 50*, 1179-1189.

Newman, M. C. & Kazniak, A. W. (2000). Spatial memory and aging: performance on a human analog of the Morris water maze. *Aging, Neuropsychology, and Cognition, 7*, 86-93.

Nieuwenhuis, S., Aston-Jones, G. & Cohen, J. D. (2005). Decision-making, the P3 and the locus-coeruleus and the norepinephrine system. *Psychological Bulletin, 131*, 510-532.

Nieuwenhuis, S., Ridderinkhof, K. R., Talsma, D., Coles, M. G. H., Kok, A. & van der Molen, M. (2002). A computational account of altered error-processing in older age: Dopamine and the error-related negativity. *Cognitive, Affective and Behavioural Neuroscience, 2*, 19-36.

Nieuwenhuis, S., Slagter, H. A., von Geusau, N. J. A., Heslenfeld, D. J. & Holroyd, C. B. (2005). Knowing good from bad: Differential activation of human cortical areas by positive and negative outcomes. *European Journal of Neuroscience, 21*, 3161-3168.

Obrist, P. A. (1981). *Cardiovascular psychophysiology: a perspective.* New York, NY; Plenum Press.

Obrist, P. A., Webb, R. A., Sutterer, J. R. & Howard, J. L. (1970). The cardiac-somatic relationship: Some reformulations. *Psychophysiology, 6*, 569-587.

Oliveira, F. T. P., McDonald, J. J. & Goodman, D. (2007). Performance monitoring in anterior cingulate is not all error-related: Expectancy deviation and the representation of action-outcome associations. *Journal of Cognitive Neuroscience, 19*, 1994-2004.

Ota, M., Yasuno, F., Ito, H., Seki, C., Nozaki, S., Asada, T., et al., (2006). Age-related decline of dopamine synthesis in the living human brain measured by positron emission tomography with L-[B-11C]DOPA. *Life Sciences, 79*, 730-736.

Pailing, P. E. & Segalowitz, S. J. (2004). The error-related negativity as a state and trait measure: Motivation, personality, and ERPs in response to errors. *Psychophysiology, 41*, 84-95.

Pailing, P. E. & Segalowitz, S. J. (2004). The effects of uncertainty in error-monitoring on associated ERPs. *Brain and Cognition, 56*, 215-233.

Park, S. B., Lee, B. C. & Jeong, K. S. (2007). Standardized tests of heart rate variability for autonomic function tests in healthy Koreans. *International Journal of Neuroscience, 117*, 1707-1717.

Pascual-Marqui, R. D., Esslen, M., Kochi, K. & Lehmann, D. (2002). Functional imaging with low resolution brain electromagnetic tomography (LORETA): a review. *Methods & Findings in Experimental & Clinical Pharmacology, 24C*, 91-95.

Paus, T., Koski, L., Caramanos, Z. & Westbury, C. (1998). Regional differences in the effects of task difficulty and motor output on blood flow response in the human anterior cingulate cortex: A review of 107 PET activation studies. *NeuroReport, 9*, R37-R47.

Peila, R., White, L. R., Masaki, K., Petrovich, H. & Launer, L. (2006). Reducing the risk of dementia: Efficacy of long-term treatment of hypertension. *Stroke, 37*, 1165-1170.

Pereira, A. C., Huddleston, D. E., Brickman, A. M., Sosunuv, A. A., Hen, R., McHann, G. M., et al. (2007). An in vivo correlate of exercise-induced neurogenesis in the adult dentate gyrus. *Proceedings of the National Academy of Sciences, 104*, 5638-5643.

Petrovitch, H., White, L. R., Izmirilian, G., at al.(2000). Midlife blood pressure and neuritic plaques, neurofibrillary tangles and brain weight at death: The Honolulu-Asia Aging Study. *Neurobiology of Aging, 21*, 57-62.

Pichot, V., Roche, F., Denis, C., Garet, M., Duverney, D., Costes, F. & Barthélémy, J.-C. (2005). Interval training in elderly men increases both heart rate variability and baroreflex activity. *Clinical Autonomic Research, 15*, 107-115.

Pietrzak, R. H., Cohen, H. & Snyder, P. J. (2007). Learning efficiency and error monitoring in normal aging: An investigation using a novel hidden maze learning test. *Archives of Clinical Neuropsychology, 22*, 235-245.

Pitzalis, M. V., Mastropasqua, F., Massari, F., Forleo, C., Di Maggio, M. & Passantino, A. (1996). Short- and long-term reproducibility of time and frequency domain heart rate variability measurements in normal subjects. *Cardiovascular Research, 32*, 226-233.

Polich, J. (2007). Updating P300: An integrative theory of P3a and P3b. *Clinical Neurophysiology, 118*, 2128-2148.

Polich, J. & Criado, J. R. (2006). Neuropsychology and neuropharmacology of P3a and P3b. *International Journal of Psychophysiology, 60*, 172-185.

Porges, S. W. (1985). Method and apparatus for evaluating rhythmic oscillations in aperiodic physiological response systems. United States.

Porges, S. W. (1986). Respiratory sinus arrhythmia: Physiological basis, quantitative methods, and clinical implications. In P. Grossman & K. Janssen & D. Vaitl (Eds.), *Cardiorespiratory and cardiosomatic psychophysiology*. New York, NY: Plenum Press.

Porges, S. W. (1992). Autonomic regulation and attention. In B. A. Campbell & H. Hayne & R. Richardson (Eds.), *Attention and information processing in infants and adults: Perspectives from human and animal research*. Hillsdale, NJ: Lawrence Erlbaum Associates, Publishers.

Porges, S. W. (1995a). Cardiac vagal tone: A physiological index of stress. *Neuroscience and BioBehavioural Reviews, 19*, 225-233.

Porges, S. W. (1995b). Orienting in a defensive world: Mammalian modifications of our evolutionary heritage: A poly-vagal theory. *Psychophysiology, 32*, 301-318.

Porges, S. W. (2001). The polyvagal theory: Phylogenetic substrates of a social nervous system. *International Journal of Psychophysiology, 42*, 123-146.

Porges, S. W. (2003). The polyvagal theory: Phylogenetic contributions to social behavior. *Physiology and Behavior, 79*, 503-513.

Porges, S. W., Arnold, W. R. & Apfeldorf, M. (1973). *Attentional performance and heart rate variability in aged subjects*. Unpublished manuscript.

Porges, S. W., Doussard-Roosevelt, J. A., Portales, A. L. & Seuss, P. E. (1994). Cardiac vagal tone: Stability and relation to difficultness in infants and three-year-olds. *Developmental Psychobiology, 27*, 289-300.

Porges, S. W., McCabe, P. M. & Yongue, B. G. (1982). Respiratory-heart rate interactions: Psychophysiological implications for pathophysiology and behaviour. In J. T. Cacioppo & R. Petty (Eds.), *Perspectives in Cardiovascular Psychophysiology* (pp. 223-264). New York, NY: Guilford.

Porges, S. W. & Raskin, D. C. (1969). Respiratory and heart rate components of attention. *Journal of Experimental Psychology, 81*, 497-503.

Posner, H. B., Tang, M. X., Luchsinger, J., Lantigua, R., Stern, Y. & Mayeux, R. (2002). The relationship of hypertension in the elderly to AD, vascular dementia, and cognitive function. *Neurology, 58*, 1175-1181.

Rajah, M. N. & D'Esposito, M. (2005). Region-specific changes in prefrontal function with age: A review of PET and fMRI studies on working and episodic memory. *Brain, 128*, 1964-1983.

Raz, N. (2000). Aging of the brain and its impact on cognitive performance: Integration of structural and functional findings. In F. I. M. Craik & T. A. Salthouse (Eds.), *Handbook of Aging and Cognition*. Mahwah, NJ: Erlbaum.

Raz, N. & Rodrigue, K. M. (2006). Differential aging of the brain: Patterns, cognitive correlates and modifiers. *Neuroscience and BioBehavioural Reviews, 30*, 730-748.

Raz, N., Rodrigue, K. M. & Acker, J. D. (2003). Hypertension and the brain: Vulnerability of the prefrontal regions and executive functions. *Behavioural Neuroscience, 117*, 1169-1180.

Rechlin, T., Weis, M. & Claus, D. (1994). Heart rate variability in depressed patients and differential effects of paroxetine and amitriptyline on cardiovascular autonomic functions. *Pharmacopsychiatry, 27*, 124-128.

Redondo, J. & Del Valle-Inclan, F. (1992). Decrements in heart rate variability during mnemonic search. *International Journal of Psychophysiology, 13*, 29-35.

Reeves, S., Bench, C. & Howard, R. (2002). Ageing and the nigrostriatal dopaminergic system. *International Journal of Geriatric Psychiatry, 17*, 358-370.

Ridderinkhof, K. R., Ullsperger, M., Crone, E. A. M. & Nieuwenhuis, S. (2004). The role of the medial frontal cortex in cognitive control. *Science, 306*, 443-447.

Robbins, M. A., Elias, M. F., Elias, P. K. & Budge, M. M. (2005). Blood pressure and cognitive function in an African-American and a Caucasian-American sample: The Maine-Syracuse Study. *Psychosomatic Medicine, 67*, 707-714.

Robinson, B. F. (1967). Relation of heart rate and systolic blood pressure to the onset of pain in angina pectoris. *Circulation, 35*, 1073-1083.

Rockwood, K. & Middleton, L. (2007). Physical activity and the maintenance of cognitive function. *Alzheimer's and Dementia, 3*, S38-S44.

Rommelfanger, K. S. & Weinshenker, D. (2007). Norepinephrine: The redheaded stepchild of Parkinson's Disease. *Biochemical Pharmacology, 74*, 177-190.

Rottenberg, J. (2007). Cardiac vagal control in depression: A critical analysis. *Biological Psychology, 74*, 200-211.

Rovio, S., Kareholt, I., Helkala, E. L., Viitanen, M., Winblad, B., Tuomilehto, J., at al.(2005). Leisure-time physical activity at midlife and the risk of dementia and Alzheimer's disease. *Lancet Neurology, 4*, 705-711.

Rushworth, M. F. S., Walton, M. E., Kennerly, S. W. & Bannerman, D. M. (2004). Action sets and decisions in the medial frontal cortex. *Trends in Cognitive Sciences, 8*, 410-417.

Sack, M., Hopper, J. W. & Lamprecht, F. (2004). Low respiratory sinus arrhythmia and prolonged psychophysiological arousal in posttraumatic stress disorder: Heart rate dynamics and individual differences in arousal regulation. *Biological Psychiatry, 55*, 284-290.

Salthouse, T. A. (1996). The processing speed theory of adult age differences. *Psychological Review, 103*, 403-428.

Sandercock, G. R. H., Bromley, P. D. & Brodie, D. A. (2005). Effects of exercise on heart rate variability: Inferences from meta-analysis. *Medicine and Science in Sports Exercise, 37*, 433-439.

Sarter, M., Gehring, W. J. & Kozak, R. (2006). More attention must be paid: the neurobiology of attentional effort. *Brain Research Reviews, 51*, 145-160.

Saul, J. P. (1990). Beat-to-beat variations of heart rate reflect modulation of cardiac autonomic outflow. *News in Physiological Sciences, 5*, 32-37.

Scheffers, M. K. & Coles, M. G. H. (2000). Performance monitoring in a confusing world: error-related brain activity, judgments of response accuracy, and types of errors. *Journal of Experimental Psychology: Human Perception and Performance, 26*, 141-151.

Schneider, W., Dumais, S. T. & Schiffrin, R. M. (1984). Automatic and controlled processing and attention. In R. Parasuraman & D. R. Davies (Eds.), *Varieties of Attention*. New York, NY: Plenum.

Scholey, A. B., Harper, S. & Kennedy, D. O. (2001). Cognitive demand and blood glucose. *Physiology and Behavior, 73*, 585-592.

Schultz, S. K., O'Leary, D. S., Ponto, L. L. B., Watkins, G. L., Hichwa, R. D. & Andreasen, N. C. (1999). Age-related changes in regional cerebral blood flow among young to midlife adults. *NeuroReport, 10,* 2493-2496.

Schwaber, J. S., Kapp, B. S. & Higgins, G. A. (1980). The origin and extent of direct amygdala projections to the region of the dorsal motor nucleus of the vagus and the nucleus of the solitary tract. *Neuroscience Letters, 20,* 15-20.

Seely, A. J. E. & Macklem, P. T. (2004). Complex systems and the teachnology of variability analysis. *Critical Care, 8,* R367-R384.

Segalowitz, S. J. (1999). ERP-Score Analysis Program. St. Catharines, Ontario: Brock University.

Senkfor, A. J. & Van Petten, C. (1998). Who said what? An event-related potential investigation of source and item memory. *Journal of Experimental Psychology: Learning, Memory and Cognition, 24,* 1005-1025.

Shidara, M. & Richmond, B. J. (2002). Anterior cingulate: Single neuronal signals related to degree of reward expectancy. *Science, 296,* 1709-1711.

Shima, K. & Tanji, J. (1998). Role for cingulate motor area cells in voluntary movement selection based on reward. *Science, 282,* 1335-1338.

Singh, D., Vinod, K., Saxena, S. C. & Deepak, K. K. (2006). Spectral evaluation of aging effects on blood pressure and heart rate variations in healthy subjects. *Journal of Medical Engineering & Technology, 30,* 145-150.

Skoog, I., Lernfelt, B., Landahl, S., Palmertz, B., Andreasson, L. A., Nilsson, L., Persson, G., A., O. & Svanborg, A. (1996). 15-year longitundinal study of blood pressure and dementia. *Lancet, 347,* 1141-1145.

Sloan, R. P., De Meersman, R. E., Shapiro, P. A., Bagiella, E., Kuhl, J. P., Zion, A. S., Paik, M. & Myers, M. M. (1997). Cardiac autonomic control is inversely related to blood pressure variability responses to psychological challenge. *American Journal of Physiology, 272,* H2227-H2232.

Sloan, R. P., Shapiro, P. A., Bagiella, E., Myers, M. M. & Gorman, J. M. (1999). Cardiac autonomic control buffers blood pressure variability responses to challenge: A psychophysiologic model of coronary artery disease. *Psychosomatic Medicine, 61,* 58-68.

Smiley, J. F., Subramanian, M. & Mesulam, M. M. (1999). Monoaminergic–cholinergic interactions in the primate basal forebrain. *Neuroscience, 93*, 817-829.

Snyder, P. J., Worth, J., Giordani, B., Caveney, A. F., Feltner, D. & Maruff, P. (2005). A method for determining the magnitude of change across different cognitive functions in clinical trials: The effects of acute administration of two different doses of alprazolam. *Human Psychopharmacology, 20*, 263-273.

Solfrizzi, V., Panza, F., Colacicco, A. M., D'Introno, A., Capurso, C., Torres, F., at al.(2004). Vascular risk factors, incidence of MCI, and rates of progression to dementia. *Neurology, 63*, 1882-1891.

Somsen, R. J. M., van der Molen, M. W., Jennings, J. R. & van Beek, B. (2000). Wisconsin card sorting in adolescents: Analysis of performance, response times and heart rate. *Acta Psychologia, 104*, 227-257.

Spencer, W. D. & Raz, N. (1994). Memory for facts, source, and context: Can frontal lobe dysfunction explain age-related differences? *Psychology and Aging, 9*, 149-159.

Spencer, W. D. & Raz, N. (1995). Differential effects of aging on memory for content and context: A meta-analysis. *Psychology and Aging, 10*, 527-539.

Spyer, K. M. (1994). Central mechanisms contributing to cardiovascular control. *Journal of Physiology, 474*, 1-19.

Takayama, S., Sakura, H., Katsumori, K., Wasada, T. & Iwamoto, Y. (2001). A possible involvement of parasympathetic neuropathy on insulin resistance in patients with type 2 diabetes. *Diabetes Care, 24*, 968-969.

Ter Horst, G. J. & Postema, F. (1997). Forebrain parasympathetic control of heart activity: Retrograde transneuronal viral labeling in rats. *American Journal of Physiology, 273*, H2926-H2930.

Terreberry, R. R. & Neafsey, N. E. (1987). The rat medial frontal cortex projects directly to autonomic regions of the brainstem. *Brain Research Bulletin, 19*, 639-649.

Thames, M. D. & Kontos, H. A. (1970). Mechanisms of baroreceptor-induced changes in heart rate. *American Journal of Physiology, 218*, 251-256.

Thayer, J. F., Friedman, B. H. & Borkovec, T. D. (1996). Autonomic characteristics of generalized anxiety disorder and worry. *Biological Psychiatry, 39*, 255-266.

Thayer, J. F. & Lane, R. D. (2000). A model of neurovisceral integration in emotion regulation and dysregulation. *Journal of Affective Disorders, 61*, 201-216.

Udupa, K., Sathyaprabha, T. N., Thirthalli, J., Kishore, K. R., Lavekar, G. S., Raju, T. A. & Gangadhar, B. N. (2007). Alteration of cardiac autonomic functions in patients with major depression: A study using heart rate variability measures. *Journal of Affective Disorders, 100*, 137-141.

Umetani, K., Singer, D. H., McCraty, R. & Atkinson, M. (1998). Twenty-four hour time domain heart rate variability and heart rate: Relations to age and gender over nine decades. *Journal of the American College of Cardiology, 31*, 593-601.

Vaidya, J. G., Paradiso, S., Boles Ponto, L. L., McCormick, L. M. & Robinson, R. G. (2007). Aging, grey matter, and blood flow in the anterior cingulate cortex. *NeuroImage, 37*, 1346-1354.

van der Kooy, K. G., van Hout, H. P. J., van Marwijk, H. W. J., de Haan, M., Stehouwer, C. D. A. & Beekman, A. T. F. (2006). Differences in heart rate variability between depressed and non-depressed elderly. *International Journal of Geriatric Psychiatry, 21*, 147-150.

van der Molen, M. W., Bashore, T. R., Halliday, R. & Callaway, E. (1991). Chronopsychophysiology: Mental chronometry augmented by psychophysiological time markers. In J. R. Jennings & M. G. H. Coles (Eds.), *Handbook of Cognitive Psychophysiology: Central and Autonomic Nervous System Approaches* (pp. 9-179). Chichester, England: Wiley.

van der Molen, M. W., Somsen, R. J. M. & Orlebeke, J. F. (1985). The rhythm of the heart beat in information processing. In P. K. Ackles & J. R. Jennings & M. G. H. Coles (Eds.), *Advances in Psychophysiology* (Vol. 1, pp. 1-88). Greenwich, CT: JAI Press.

van Veen, V. & Carter, C. (2002). The timing of action-monitoring processes in the anterior cingulate cortex. *Journal of Cognitive Neuroscience, 14*, 593-602.

Van Vliet, B. N., Belforti, F. & Montani, J. P. (2002). Baroreflex stabilization of the double (pressure-rate) product at 0.05 Hz in conscious rabbits. *American Journal of Physiology: Regulatory, Integrative and Comparative Physiology, 282*, R1746–R1753.

Vincent, A., Craik, F. I. M. & Furedy, J. J. (1996). Relations among memory performance, mental workload and cardiovascular responses. *International Journal of Psychophysiology, 23*, 181-198.

Vogt, B. A., Berger, G. R. & Derbyshire, S. W. G. (2003). Structural and functional dichotomy of human mid-cingulate cortex. *European Journal of Neuroscience, 18*, 3134-3144.

Volkow, N. D., Gur, R. C., Wang, G.-J., Fowler, J. S., Moberg, P. J., Ding, Y.-S., Hitzemann, R., Smith, G. & Logan, J. (1998). Association between decline in brain dopamine activity with age and cognitive and motor impairment in healthy individuals. *American Journal of Psychiatry, 155*, 344-349.

Volkow, N. D., Logan, J., Fowler, J. S., Wang, G.-J., Gur, R. C., Wong, C., Felder, C., Gatley, S. J., Ding, Y.-S., Hitzemann, R. & Pappas, N. (2000). Association between age-related decline in brain dopamine activity and impairment in frontal and cingulate metabolism. *American Journal of Psychiatry, 157*, 75-80.

Waddington, J. L., MacCulloch, M. J. & Sambrooks, J. E. (1979). Resting heart rate variability in man declines with age. *Experientia, 35*, 1197-1198.

Walton, M. E., Croxson, P., Behrens, T. E. J., Kennerly, S. W. & Rushworth, M. F. S. (2007). Adaptive decision making and value in the anterior cingulate cortex. *NeuroImage, 36*, T142-T154.

Walton, M. E., Devlin, J. T. & Rushworth, M. F. S. (2004). Interactions between decision making and performance monitoring within prefrontal cortex. *Nature Neuroscience, 7*, 1259-1265.

Wareham, N. J., Wong, M.-Y. & Day, N. E. (2000). Glucose intolerance and physical inactivity: the relative importance of low habitual activity energy expenditure and cardiorespiratory fitness. *American Journal of Epidemiology, 152*, 132-139.

Wennerblom, B., Lurje, L., Solem, J., Tygesen, H., Udén, M., Vahisalo, R. & Hjalmarson, A. (2000). Reduced heart rate variability in ischemic heart disease is only partially caused by ischemia. An HRV study before and after PTCA. *Cardiology, 94*, 146-151.

Weuve, J., Kang, J. H., Manson, J. E., Breteler, M. M. B. & Ware, J. H. (2004). Physical activity, including walking, and cognitive function in older women. *Journal of the American Medical Association, 292*, 1454-1461.

Whalen, P. J., Bush, G., McNally, R. J., Wilhelm, S., McInerney, S. C., Jenike, M. A. & Rauch, S. L. (1998). The emotional counting Stroop paradigm: A functional magnetic resonance imaging probe of the anterior cingulate affective division. *Biological Psychiatry, 44*, 1219-1228.

Whitmer, R. A., Sidney, S., Claiborne Johnston, S. & Yaffe, K. (2005). Midlife cardiovascular risk factors and risk of dementia in late life. *Neurology, 64*, 277-281.

Wilhelm, F. H., Grossman, P. & Roth, W. T. (1999). Analysis of cardiovascular regulation. *Biomedical Sciences Instrumentation, 35*, 135-140.

Wilding, E. L. & Rugg, M. D. (1997). Event-related potentials and the recognition memory exclusion task. *Neuropsychologia, 35*, 119-128.

Wright, C. E., Kunz-Ebrecht, S. R., Iliffe, S., Foese, O. & Steptoe, A. (2005). Physiological correlates of cognitive functioning in an elderly population. *Psychoneuroendocrinology, 30*, 826-838.

Yasuma, F. & Hayano, J. (2004). Respiratory sinus arrhythmia: Why does the heartbeat synchronize with respiratory rhythm? *CHEST, 125*, 683-690.

Yeung, N., Holroyd, C. B. & Cohen, J. D. (2005). ERP correlates of feedback and reward processing in the presence and absence of response choice. *Cerebral Cortex, 15*, 535-544.

Yeung, N. & Sanfey, A. G. (2004). Independent coding of reward magnitude and valence in the human brain. *Journal of Neuroscience, 24*, 6258-6264.

Ylitalo, A., Juhani Airaksinen, K. E., Sellin, L. & Huikuri, H. V. (1999). Effects of combination antihypertensive therapy on baroreflex sensitivity and heart rate variability in systemic hypertension. *American Journal of Cardiology, 83*, 885-889.

Yoshida, W. & Ishii, S. (2006). Resolution of uncertainty in prefrontal cortex. *Neuron, 50*, 781-789.

Zigmond, A. S. & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica, 67*, 361-370.

Table 2.1. *Mean Number of Errors (SD) for Younger and Older Participants as a Function of Trial Type and Maze Level. N = 19 younger, 14 older.*

		Maze Level			Means
		4 × 4	6 × 6	8 × 8	
Learn Trials					
	Younger	4.61 (.89)	12.14 (1.60)	18.53 (2.93)	**11.76 (.35)**
	Older	5.72 (1.04)	13.04 (1.77)	19.75 (4.23)	**12.83 (.41)**
Test Trials					
	Younger	1.16 (.82)	4.29 (2.36)	5.97 (4.30)	**3.81 (.76)**
	Older	3.03 (1.55)	9.22 (4.19)	13.97 (7.28)	**8.74 (.88)**

Note: Marginal means (standard errors) are in bold.

Table 2.2. *Mean Completion Times (SD) for Younger and Older Participants as a Function of Trial Type and Maze Level. N = 19 younger, 7 older.*

		Maze Level			Means
		4 × 4	6 × 6	8 × 8	
Learn Trials					
	Younger	25.81 (5.9)	53.38 (11.7)	78.25 (15.2)	**52.48 (2.7)**
	Older	32.83 (9.9)	67.51 (16.6)	97.41 (17.8)	**65.92 (4.1)**
Test Trials					
	Younger	14.76 (3.2)	29.62 (5.1)	41.18 (9.4)	**28.52 (1.8)**
	Older	24.41 (5.4)	48.78 (14.9)	67.56 (10.2)	**46.92 (2.7)**

Note: Marginal means (standard errors) are in bold.

Table 2.3. *Peak FRN Amplitudes (SD) in Microvolts During the Maze Learning Task as a Function of Group, Site, Trial Type, and Maze Level.*

Level	Site	Learn Trials		Test Trials	
		Younger	Older	Younger	Older
4 × 4	Fz	-2.45 (2.08)	1.44 (2.52)	-1.63 (3.30)	-.24 (1.49)
	FCz	-1.19 (2.00)	1.68 (2.77)	-.52 (3.38)	-.20 (2.42)
	Cz	.31 (3.49)	1.34 (2.98)	.64 (4.60)	-.20 (3.03)
		- 1.11 (.66)	**1.48 (.84)**	**-.51 (.82)**	**-.21 (1.0)**
6 × 6	Fz	-1.62 (2.25)	1.80 (.93)	-1.07 (2.10)	2.96 (1.27)
	FCz	-.02 (2.63)	2.79 (1.73)	-.22 (2.47)	3.58 (1.51)
	Cz	1.35 (4.11)	2.54 (2.22)	.56 (4.41)	3.10 (1.93)
		-.10 (.63)	**2.38 (.81)**	**-.24 (.59)**	**3.21 (.75)**
8 × 8	Fz	-1.65 (2.13)	1.75 (1.53)	-1.34 (2.43)	1.68 (1.16)
	FCz	-.69 (2.64)	2.19 (2.11)	-1.12 (4.41)	2.45 (1.98)
	Cz	1.01 (4.08)	2.09 (2.20)	.22 (5.66)	2.21 (1.97)
		-.44 (.66)	**2.01 (.84)**	**-.75 (.91)**	**2.11 (1.2)**

Note: The FRN was scored as the lowest peak between 280-400 ms post-feedback for both age groups. Marginal means (standard errors) are in bold.

Table 2.4. *Peak Feedback P3 Amplitudes (SD) in Microvolts During the Maze Learning Task as a Function of Group, Site, Trial Type, and Maze Level.*

Level	Site	Learn Trials		Test Trials	
		Younger	Older	Younger	Older
4 × 4	Fz	2.00 (2.58)	3.22 (2.17)	3.51 (3.62)	2.42 (2.19)
	FCz	3.93 (3.15)	4.45 (1.95)	6.21 (3.45)	3.51 (1.97)
	Cz	5.49 (3.66)	4.90 (2.65)	8.37 (4.76)	4.15 (2.32)
		3.81 (.62)	**4.19 (.79)**	**6.03 (.73)**	**3.36 (.93)**
6 × 6	Fz	2.82 (2.09)	4.35 (1.65)	3.03 (2.36)	4.55 (1.02)
	FCz	4.46 (2.81)	5.53 (1.12)	5.44 (3.03)	5.46 (1.32)
	Cz	5.98 (3.90)	5.44 (1.98)	7.02 (3.54)	5.18 (2.11)
		4.42 (.60)	**5.11 (.76)**	**5.16 (.53)**	**5.06 (.68)**
8 × 8	Fz	2.72 (1.98)	3.72 (2.16)	3.14 (2.95)	3.49 (1.18)
	FCz	4.38 (2.74)	4.61 (1.58)	5.57 (3.04)	4.76 (1.07)
	Cz	5.58 (3.61)	4.67 (1.62)	7.32 (4.47)	4.98 (1.61)
		4.23 (.55)	**4.33 (.70)**	**5.34 (.67)**	**4.41 (.86)**

Note: Average P3 amplitudes were calculated from 360-460 ms post-feedback for younger adults and 400-520 ms for older adults. Marginal means (standard errors) are in bold.

Table 2.5. *Comparisons of Whole Scalp Activation based on Low Resolution Electromagnetic Tomography (LORETA) for Error versus Correct Trials for FRNs and P3s for Each Group, Maze Level, and Trial Type.*

Level	Trial Type	FRN (Error vs Correct)		P3 (Error vs Correct)	
		Younger	Older	Younger	Older
4 × 4	Learn	7.18*** (4.28)	3.09 (4.70)	7.77*** (4.07)	8.22*** (5.08)
	Test	4.59*** (3.41)	4.86 (5.31)	9.07*** (3.60)	6.63** (4.84)
6 × 6	Learn	6.22** (4.55)	7.20* (5.96)	8.86*** (4.02)	9.72** (5.47)
	Test	8.29*** (3.95)	6.43 (6.64)	12.60*** (3.64)	8.47** (5.93)
8 × 8	Learn	7.18*** (4.41)	3.67 (4.53)	9.12*** (3.83)	5.61* (4.66)
	Test	7.83*** (3.65)	4.18 (4.27)	9.90*** (3.45)	7.91*** (4.52)

Note: $* = p < .05$, $** = p < .01$, $*** = p < .001$. Significance indicates that the t-value associated with error relative to correct feedback was larger than the critical t-value. Activation was measured at the time point of peak amplitude for each individual at Fz for the FRN, and Cz for the P3. Critical t-values for each analysis are in brackets.

Table 2.6. *Results of Hierarchical Regression Analyses Predicting Mean Number of Errors as a Function of Age Group and FRN Amplitude for Each Maze Level and Trial Type.*

Level	Model	Learn Trials				Test Trials			
		$R^2\Delta$	F	df	sr^2	$R^2\Delta$	F	df	sr^2
4 × 4	Group	.30	10.80***	25	.30*	.39	17.57***	28	.39***
	FRN	.13	5.51*	24	.05 .13*	.01	.37	27	.34** .01
	G × FRN	<.01	.11	23	.05 .13 <.01	.05	2.17	26	.33** .03 .05
6 × 6	Group	.12	3.10	23	.12	.33	10.74**	22	.33**
	FRN	.22	7.45*	22	<.01 .22*	<.01	.04	21	.18* <.01
	G × FRN	.03	.82	21	.03 <.01 .03	.01	.32	20	.06 .01 .01
8 × 8	Group	.09	2.59	25	.09	.33	13.12**	27	.33**
	FRN	.06	1.75	24	.01 .06	.11	4.89*	26	.05 .11*
	G × FRN	.05	1.59	23	.01 .03 .05	.25	20.04***	25	<.01 .14** .25***

Note. * $= p < .05$, ** $= p < .01$, *** $= p < .001$

sr^2 represents the unique variance accounted for by the specific variable relative to other variables in the equation in predicting error rate.

Table 2.7. *Summary of Means (SD) for Errors, Completion Times, FRN Amplitudes at Fz, and P3 Amplitudes at Cz, by Trial Type and Group.*

Trial Type		Mean Errors	Time (ms)	FRN_{max} (μV)	$P3_{max}$ (μV)
	Younger				
Learn	4 × 4	4.61 (0.89)	25.81 (5.9)	-2.45 (2.08)	5.49 (3.66)
	6 × 6	12.14 (1.60)	53.38 (11.7)	-1.62 (2.25)	5.98 (3.90)
	8 × 8	18.53 (2.93)	78.25 (15.2)	-1.65 (2.13)	5.58 (3.61)
Test	4 × 4	1.16 (.82)	14.76 (3.2)	-1.63 (3.30)	8.37 (4.76)
	6 × 6	4.29 (2.36)	29.62 (5.1)	-1.07 (2.10)	7.02 (3.54)
	8 × 8	5.97 (4.30)	41.18 (9.4)	-1.34 (2.43)	7.32 (4.47)
	Older				
Learn	4 × 4	5.72 (1.04)	32.83 (9.9)	1.44 (2.52)	4.90 (2.65)
	6 × 6	13.04 (1.77)	67.51 (16.6)	1.80 (0.93)	5.44 (1.98)
	8 × 8	19.75 (4.23)	97.41 (17.8)	1.75 (1.53)	4.67 (1.62)
Test	4 × 4	3.03 (1.55)	24.41 (5.4)	-0.24 (1.49)	4.15 (2.32)
	6 × 6	9.22 (4.19)	48.78 (14.9)	2.96 (1.27)	5.18 (2.11)
	8 × 8	13.97 (7.28)	67.56 (10.2)	1.68 (1.16)	4.98 (1.61)

Table 3.1. *Results of Hierarchical Regression Analyses Predicting Mean Number of Learn-Trial Errors as a Function of Group and RSA or RPP for Each Maze Level.*

Level		RSA					RPP			
	Model	$R^2\Delta$	F	df	sr^2	Model	$R^2\Delta$	F	df	sr^2
4 × 4	Group	.23	8.57**	28	.23**	Group	.18	5.50*	25	.18*
	RSA	.09	3.37	27	.10 .09	RPP	.04	1.19	24	.09 .04
	G × RSA	<.01	.01	26	.01 <.01 <.01	G × RPP	.01	.43	23	.01 <.01 .01
6 × 6	Group	.06	1.89	28	.06	Group	.02	.60	25	.02
	RSA	.02	.72	27	.03 .02	RPP	<.01	<.01	24	.02 <.01
	G × RSA	.04	1.09	26	.05 .02 .04	G × RPP	.02	.49	23	.01 .02 .02
8 × 8	Group	<.01	.02	28	<.01	Group	.01	.27	25	.01
	RSA	.23	8.03**	27	.03 .23**	RPP	.24	7.78**	24	.01 .24**
	G × RSA	.02	.58	26	.03 .07 .02	G × RPP	.17	6.84*	23	.18* .06 .17*

Note. $* = p < .05$, $** = p < .01$

sr^2 represents the unique variance accounted for by the specific variable relative to other variables in the equation in predicting error rate.

Table 3.2. *Results of Hierarchical Regression Analyses Predicting Mean Number of Test-Trial Errors as a Function of Group and RSA or RPP for Each Maze Level.*

Level		RSA					RPP			
	Model	$R^2\Delta$	F	df	sr^2	Model	$R^2\Delta$	F	df	sr^2
4 × 4	Group	.33	13.65**	28	.33**	Group	.34	12.94**	25	.34**
	RSA	.10	4.71*	27	.15* .10*	RPP	.01	.22	24	.25** .01
	G × RSA	< .01	< .01	26	.02 .01 < .01	G × RPP	.15	6.67*	23	.10* .11* .15*
6 × 6	Group	.31	12.35**	28	.31**	Group	.31	11.10**	25	.31**
	RSA	.10	4.70*	27	.13* .10*	RPP	.03	.98	24	.19* .03
	G × RSA	< .01	.11	26	< .01 .02 < .01	G × RPP	.14	6.37*	23	.10* .09 .14*
8 × 8	Group	.27	10.16**	28	.27**	Group	.33	12.09**	25	.33**
	RSA	.10	4.31*	27	.11* .10*	RPP	.04	1.61	24	.19* .04
	G × RSA	.01	.23	26	< .01 .03 .01	G × RPP	.13	5.99*	23	.09 .08 .13*

Note. * $= p < .05$, ** $= p < .01$

sr^2 represents the unique variance accounted for by the specific variable relative to other variables in the equation in predicting error rate.

Table 3.3. *Results of Hierarchical Regression Analyses Predicting FRN Amplitude as a Function of Group and RSA for Each Maze Level and Trial Type.*

Level	Model	Learn Trials $R^2\Delta$	F	df	sr^2	Test Trials $R^2\Delta$	F	df	sr^2
4 × 4	Group	.36	14.35***	26	.36***	.03	.78	26	.03
	RSA	.05	2.06	25	.20** .05	.12	3.35	25	<.01 .11
	G × RSA	.01	.30	24	.05 <.01 <.01	.09	2.81	24	.08 .15* .09
6 × 6	Group	.43	15.93**	21	.43***	.55	24.39***	20	.55***
	RSA	.07	2.73	20	.30** .07	<.01	.03	19	.50*** <.01
	G × RSA	<.01	.04	19	.02 .01 <.01	.01	.47	18	.10 <.01 .01
8 × 8	Group	.30	10.01**	23	.30**	.39	16.21***	25	.39***
	RSA	.05	1.60	22	.13* .05	.01	.37	24	.30** .01
	G × RSA	.03	.99	21	<.01 .05 .03	<.01	.05	23	.04 <.01 <.01

Note. * = $p < .05$, ** = $p < .01$, *** = $p < .001$
sr^2 represents the unique variance accounted for by the specific variable relative to other variables in the equation in predicting error rate.

Table 3.4. *Results of Hierarchical Regression Analyses Predicting FRN Amplitude as a Function of Group and RPP for Each Maze Level and Trial Type.*

Level	Model	Learn Trials $R^2\Delta$	F	df	sr^2	Test Trials $R^2\Delta$	F	df	sr^2
4 × 4	Group	.40	14.72**	22	.40**	.05	1.03	22	.05
	RPP	< .01	.01	21	.31** < .01	.25	7.44*	21	< .01 .25*
	G × RPP	.02	.72	20	.05 .02 .02	.08	2.38	20	.07 .18* .08
6 × 6	Group	.45	13.65**	17	.45**	.54	18.94***	16	.54***
	RPP	.05	1.70	16	.32** .05	.01	.16	15	.49*** < .01
	G × RPP	< .01	.02	15	.01 .01 < .01	.01	.18	14	< .01 < .01 < .01
8 × 8	Group	.35	10.00**	19	.35**	.40	13.96**	21	.40**
	RPP	< .01	.07	18	.26* < .01	.06	2.33	20	.29** .06
	G × RPP	< .01	.09	17	.02 < .01 < .01	.01	.16	19	< .01 < .01 < .01

Note. * = $p < .05$, ** = $p < .01$, *** = $p < .001$

sr^2 represents the unique variance accounted for by the specific variable relative to other variables in the equation in predicting error rate.

Table 3.5. *Pearson r Correlations Between Autonomic Indices and Mean Error Rates on Learn and Test Trials as a Function of Maze Level and Group.*

Autonomic Index	Maze Level	Group Younger	Older
RSA (Learn Trials)	4 × 4	-.31	-.35
	6 × 6	.06	-.37
	8 × 8	-.56*	-.40
RSA (Test Trials)	4 × 4	-.43†	-.36
	6 × 6	-.51*	-.31
	8 × 8	-.51*	-.28
RPP (Learn Trials)	4 × 4	.20	.29
	6 × 6	-.11	.17
	8 × 8	.38	.80**
RPP (Test Trials)	4 × 4	-.24	.55†
	6 × 6	-.05	.59*
	8 × 8	.05	.58*

Note. † = $p < .08$, * = $p < .05$, ** = $p < .01$

Table 4.1. *Mean Proportion (SD) of Items Judged to be Study Words ("Yes" Responses) in the Source Memory Task as a Function of Group. N = 16 younger, 14 older.*

Group		Word Type		
		Study	Lure	Foil
	Younger	.65 (.14)	.16 (.08)	.04 (.03)
	Older	.64 (.10)	.48 (.20)	.10 (.07)

Table 4.2. *Mean Response Times (SD) from Correct Trials in the Source Memory Task as a Function of Group and Word Type. N = 5 younger, 8 older.*

Group		Word Type		
		Study (ms)	Lure (ms)	Foil (ms)
	Younger	851 (320)	943 (366)	1114 (633)
	Older	983 (263)	858 (172)	1075 (302)

Table 4.3. *Results of Hierarchical Regression Analyses Predicting Behavioural Responses in the Source Memory Task as a Function of Group and IBI.*

Model	Word Type	$R^2\Delta$	F	df	sr^2
Group	Study	.01	.12	24	.01
IBI		.04	.87	23	.03 .04
G × IBI		.13	3.30	22	.11 .16 .13
Group	Lures	.55	28.97***	24	.54***
IBI		.18	15.78**	23	.73*** .18**
G × IBI		.02	1.68	22	.07* < .01 .02
Group	Foils	.17	4.95*	24	.16*
IBI		.05	1.31	23	.21* .05
G × IBI		.02	3.60	22	.16* .06 .11

Note. $* = p < .05$, $** = p < .01$, $*** = p < .001$
sr^2 represents the unique variance accounted for by the specific variable relative to other variables in the equation in predicting error rate.

Table 4.4. *Results of Hierarchical Regression Analyses Predicting Behavioural Responses in the Source Memory Task as a Function of Group and RSA.*

Model	Word Type	$R^2\Delta$	F	df	sr^2
Group	Study	.03	.54	21	.02
RSA		.01	.14	20	< .01 .01
G × RSA		.10	2.26	19	.08 .11 .10
Group	Lures	.57	27.70***	21	.57***
RSA		.14	9.10**	20	.14** .14**
G × RSA		.06	5.20*	19	.12** .01 .06*
Group	Foils	.18	4.56*	21	.18*
RSA		.09	2.37	20	.02 .09
G × RSA		.10	2.84	19	.12 .04 .10

Note. $* = p < .05$, $** = p < .01$, $*** = p < .001$

sr^2 represents the unique variance accounted for by the specific variable relative to other variables in the equation in predicting error rate.

Table 4.5. *Results of Hierarchical Regression Analyses Predicting Behavioural Responses in the Source Memory Task as a Function of Group and RPP.*

Model	Word Type	$R^2\Delta$	F	df	sr^2
Group	Study	.02	.42	24	.02
RPP		.01	.11	23	.01 .01
G × RPP		< .01	.01	22	< .01 < .01 < .01
Group	Lures	.58	32.62***	24	.58***
RPP		.12	9.04**	23	.38*** .12**
G × RPP		.04	3.51	22	.01 .01 .04
Group	Foils	.18	5.20*	24	.18*
RPP		< .01	.09	23	.15 < .01
G × RPP		.03	.86	22	.01 .02 .03

Note. * = $p < .05$, ** = $p < .01$, *** = $p < .001$

sr^2 represents the unique variance accounted for by the specific variable relative to other variables in the equation in predicting error rate.

Table 4.6. *Pearson r Correlations between Autonomic Indices and Behavioural Responses in the Source Memory Task as a Function of Word Type and Group.*

Autonomic Index	Word Type	Group	
		Younger	Older
IBI	Study	.45	-.24
	Lures	-.64**	-.68*
	Foils	.23	-.46
RSA	Study	.18	-.19
	Lures	-.16	-.79**
	Foils	.14	-.52
RPP	Study	-.07	-.07
	Lures	.37	.67*
	Foils	-.24	.20

Note. $* = p < .05$, $** = p < .01$

Table 4.7. *Peak Parietal Stimulus-Locked LPC Amplitudes (SD) in Microvolts Associated with Different Word Types (Study, Lure, Foil) in the Source Memory Task as a Function of Group. N = 11 younger, 9 older.*

		Word Type		
Group		Study (μV)	Lure (μV)	Foil (μV)
	Younger	1.09 (.75)	.60 (.73)	.32 (.62)
	Older	.19 (.62)	.44 (1.31)	.30 (1.16)

Table 4.8. *Results of Hierarchical Regression Analyses Predicting Parietal LPC Amplitude Associated with Previously Studied Words, Familiar Lures, and Foils in the Source Memory Task as a Function of Group and RSA.*

Model	Word Type	$R^2\Delta$	F	df	sr^2
Group	Study	.38	9.81**	16	.38**
RSA		.06	1.68	15	.42** .06
G × RSA		< .01	.08	14	.05 .02 < .01
Group	Lures	.02	.29	16	.02
RSA		.36	8.53*	15	.21* .37*
G × RSA		.05	1.23	14	.01 < .01 .05
Group	Foils	.01	.15	16	.01
RSA		.27	5.53*	15	.14 .27*
G × RSA		.07	1.40	14	.02 .01 .07

Note. $* = p < .05$, $** = p < .01$
sr^2 represents the unique variance accounted for by the specific variable relative to other variables in the equation in predicting error rate.

Table 4.9. *Results of Hierarchical Regression Analyses Predicting Parietal LPC Amplitude Associated with Previously Studied Words, Familiar Lures, and Foils in the Source Memory Task as a Function of Group and RPP.*

Model	Word Type	$R^2\Delta$	F	df	sr^2
Group	Study	.27	5.90*	16	.27*
RPP		< .01	.05	15	.18 < .01
G × RPP		< .01	.01	14	< .01 < .01 < .01
Group	Lures	< .01	.07	16	< .01
RPP		.52	16.44**	15	.18* .52**
G × RPP		.03	.95	14	.06 < .01 .03
Group	Foils	< .01	.01	16	< .01
RPP		.25	5.04*	15	.06 .25*
G × RPP		.11	2.32	14	.13 .03 .11

Note. * = $p < .05$, ** = $p < .01$

sr^2 represents the unique variance accounted for by the specific variable relative to other variables in the equation in predicting error rate.

Table 4.10. *Pearson r Correlations between Autonomic Variables and Electrocortical Response (LPC) to Test Words in the Source Memory Task as a Function of Word Type and Group.*

Autonomic Index	Word Type	Group	
		Younger	Older
RSA	Study	-.27	-.17
	Lures	-.35	-.69†
	Foils	-.22	-.58
RPP	Study	-.02	-.11
	Lures	.71*	.75*
	Foils	.17	.67

Note. † = $p < .06$; * = $p < .05$

Table 4.11. *Mean Proportion Correct (SD) in the Congruent and Incongruent Conditions of the Standard Flanker Task as a Function of Group. N = 19 younger, 20 older.*

		Error Type	
		Incongruent	Congruent
Group			
	Younger	.91 (.08)	.94 (.04)
	Older	.90 (.05)	.94 (.04)

Table 4.12. *Mean Response Times (SD) to Correct Trials in the Congruent and Incongruent Conditions of the Standard Flanker Task as a Function of Group. N = 19 younger, 20 older.*

Group		Error Type	
		Incongruent (ms)	Congruent (ms)
	Younger	460 (66)	422 (63)
	Older	562 (76)	517 (76)

Table 4.13. *Peak ERN Amplitudes (SD) in Microvolts During the Standard Flanker Task as a Function of Group and Site. N = 18 younger, 18 older.*

Group		Site	ERN Amplitude
	Younger	Fz	-4.61 (4.73)
		FCz	-6.92 (6.26)
		Cz	-7.11 (6.00)
		Pz	-2.62 (4.15)
			-5.31 (1.26)
	Older	Fz	.49 (6.39)
		FCz	.14 (6.71)
		Cz	-.09 (6.27)
		Pz	.78 (4.25)
			.33 (1.26)

Note: *Marginal means (standard errors) are in bold.*

Table 4.14. *Mean Proportion Correct (SD) in the Difficult Flanker Task for Younger Adults as a Function of Condition and Block. N = 19.*

Condition	Block	Proportion Correct
Congruent	1	.90 (.06)
Stimulus Incongruent	1	.91 (.07)
Response Incongruent	1	.81 (.08)
		.87 (.02)
Congruent	2	.91 (.06)
Stimulus Incongruent	2	.92 (.08)
Response Incongruent	2	.82 (.10)
		.89 (.02)

Note: Marginal means (standard errors) are in bold.

Table 4.15. *Mean Response Times (SD) from Correct Trials in the Difficult Flanker Task for Younger Adults as a Function of Condition and Block. N = 19.*

Condition	Block	Response Time (ms)
Congruent	1	450 (55)
Stimulus Incongruent	1	470 (42)
Response Incongruent	1	517 (70)
		479 (12)
Congruent	2	418 (57)
Stimulus Incongruent	2	441 (53)
Response Incongruent	2	489 (69)
		449 (13)

Note: *Marginal means (standard errors) are in bold.*

Table 4.16. *Peak ERN Amplitudes (SD) in Microvolts During the Difficult Flanker Task for Younger Adults as a Function of Site. N = 15.*

Site	Block	ERN Amplitude
Fz	1	-3.84 (3.56)
FCz	1	-4.63 (3.24)
Cz	1	-4.05 (2.81)
Pz	1	-.29 (2.57)
		-3.20 (.70)
Fz	2	-4.33 (3.82)
FCz	2	-6.10 (4.33)
Cz	2	-5.47 (4.44)
Pz	2	-1.15 (1.87)
		-4.27 (.81)

Note: Marginal means (standard errors) are in bold.

Groton Maze Learning Test:
4 x 4 grid

Start ▐■➡

Finish ⬅■

Error! Go back one. Try again.

Success!

(Repeat x 2)
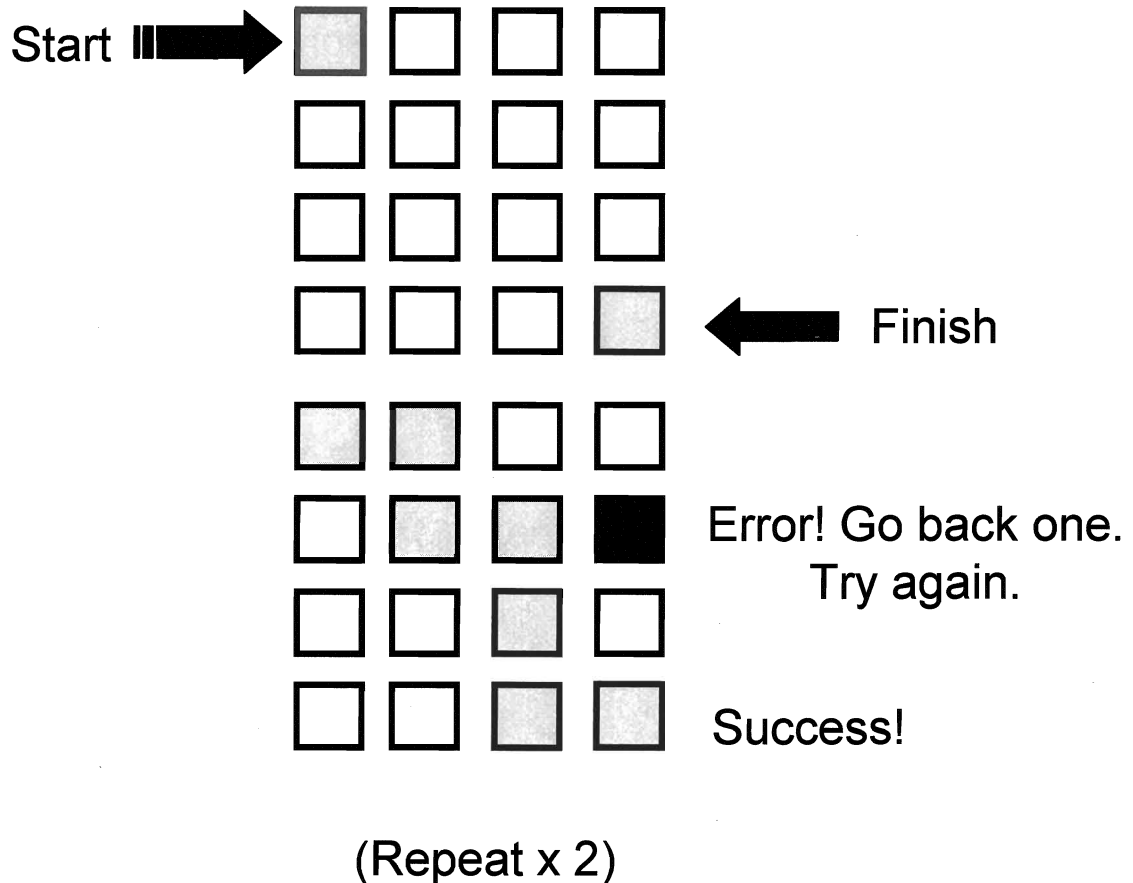
Figure 2.1. Depiction of the maze task. Tiles that have turned green (here shown in grey) indicate that a correct choice has been made. Tiles that have turned red (here shown in black) indicate an error.
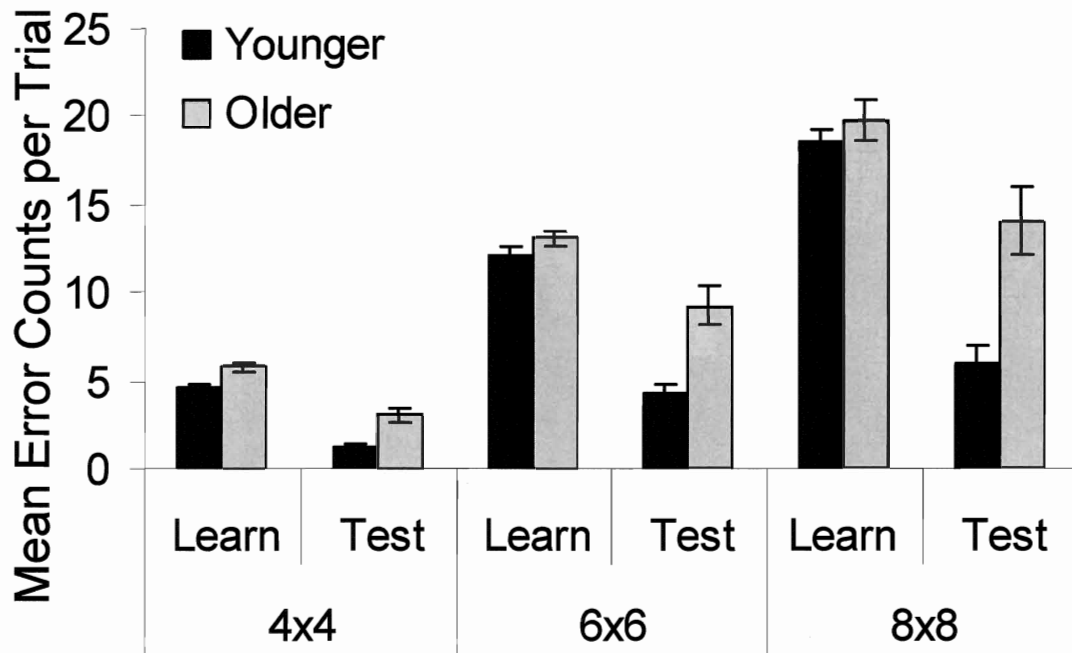
Figure 2.2. Mean accuracy rates for the maze task as a function of maze level, trial type, and group.
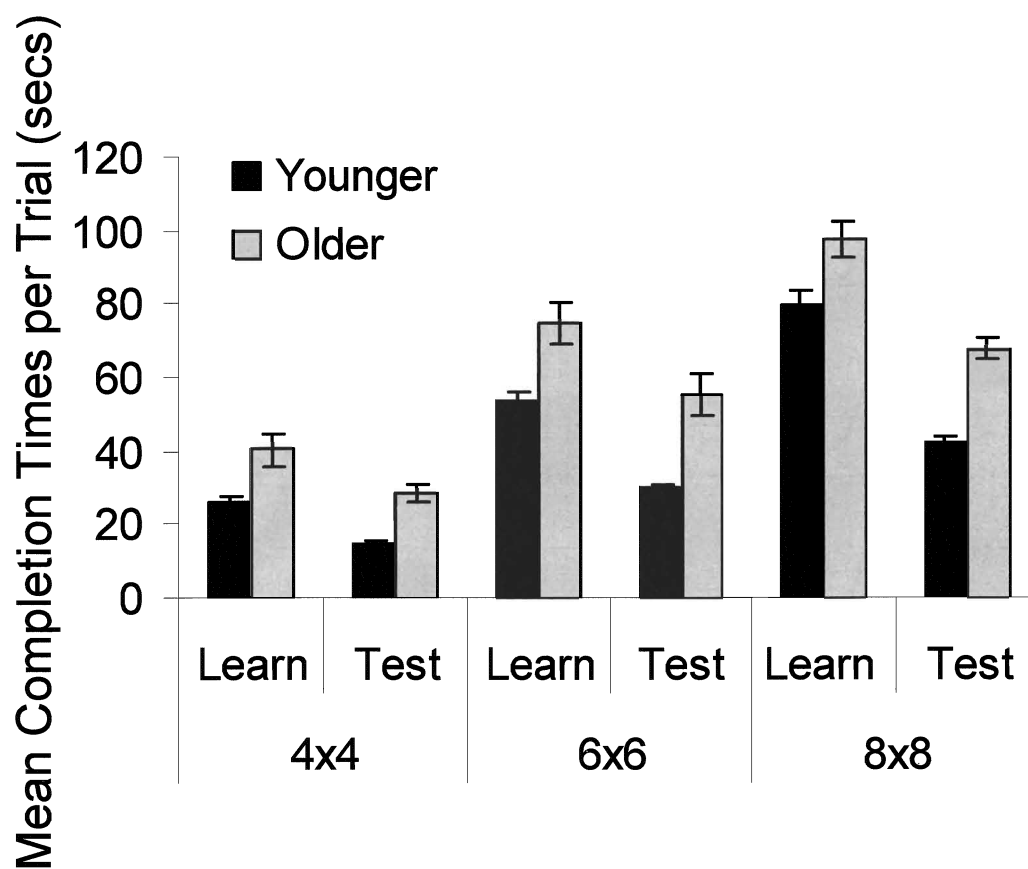
Figure 2.3. Mean completion times for the maze task as a function of maze level, trial type, and group.
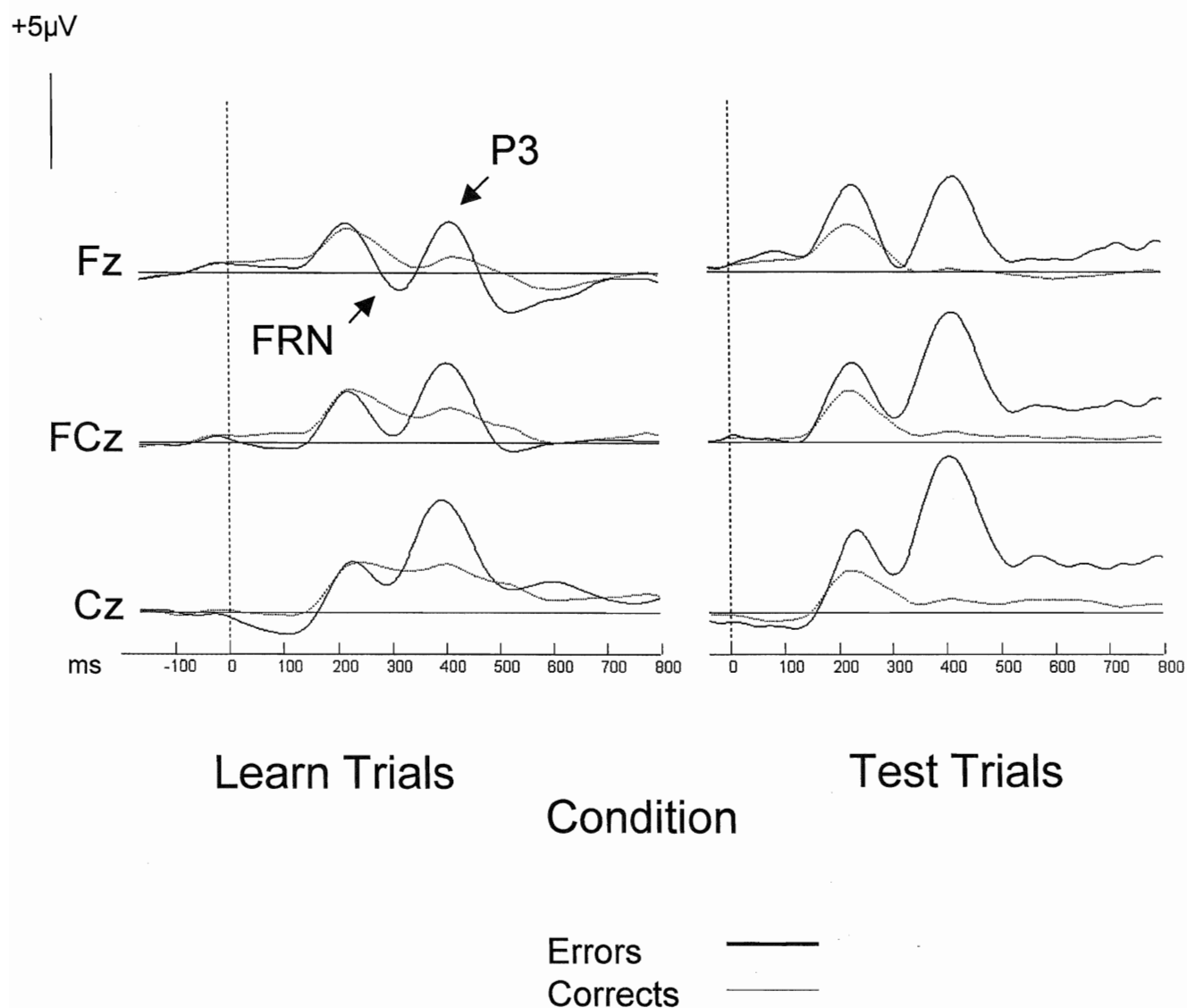
Figure 2.4. Averaged ERP waveforms from error and correct trials for younger adults in learn and test conditions collapsed across 8 unique mazes at the 4 x 4 maze level.

Older Adults (4 x 4 Maze)
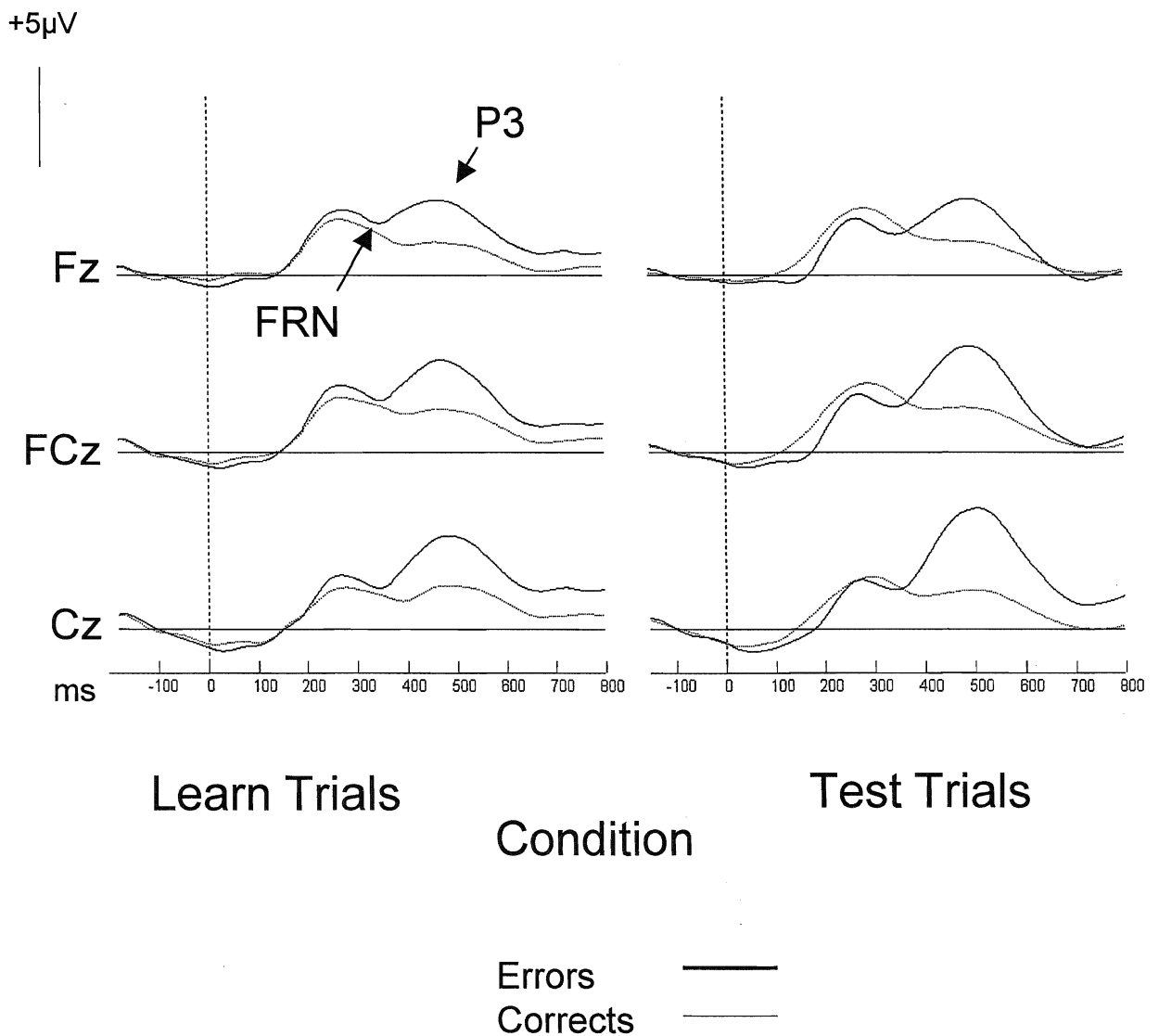
Figure 2.5. Averaged ERP waveforms from error and correct trials for older adults in learn and test conditions collapsed across 8 unique mazes at the 4 x 4 maze level.

Learn Trials (4 x 4 Grids)
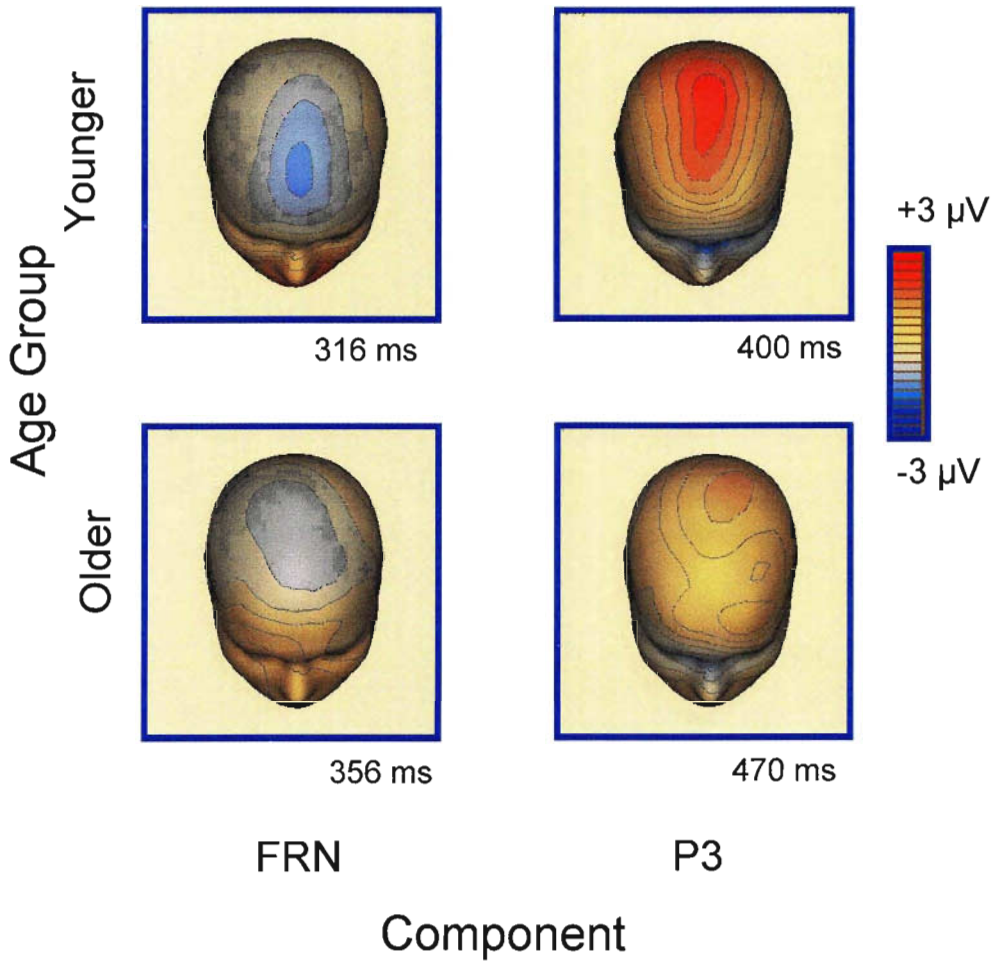
Figure 2.6. Topographies of the FRN and feedback P3 on error trials of the 4 × 4 maze in the learn condition, as a function of group.

Test Trials (4 x 4 Grids)
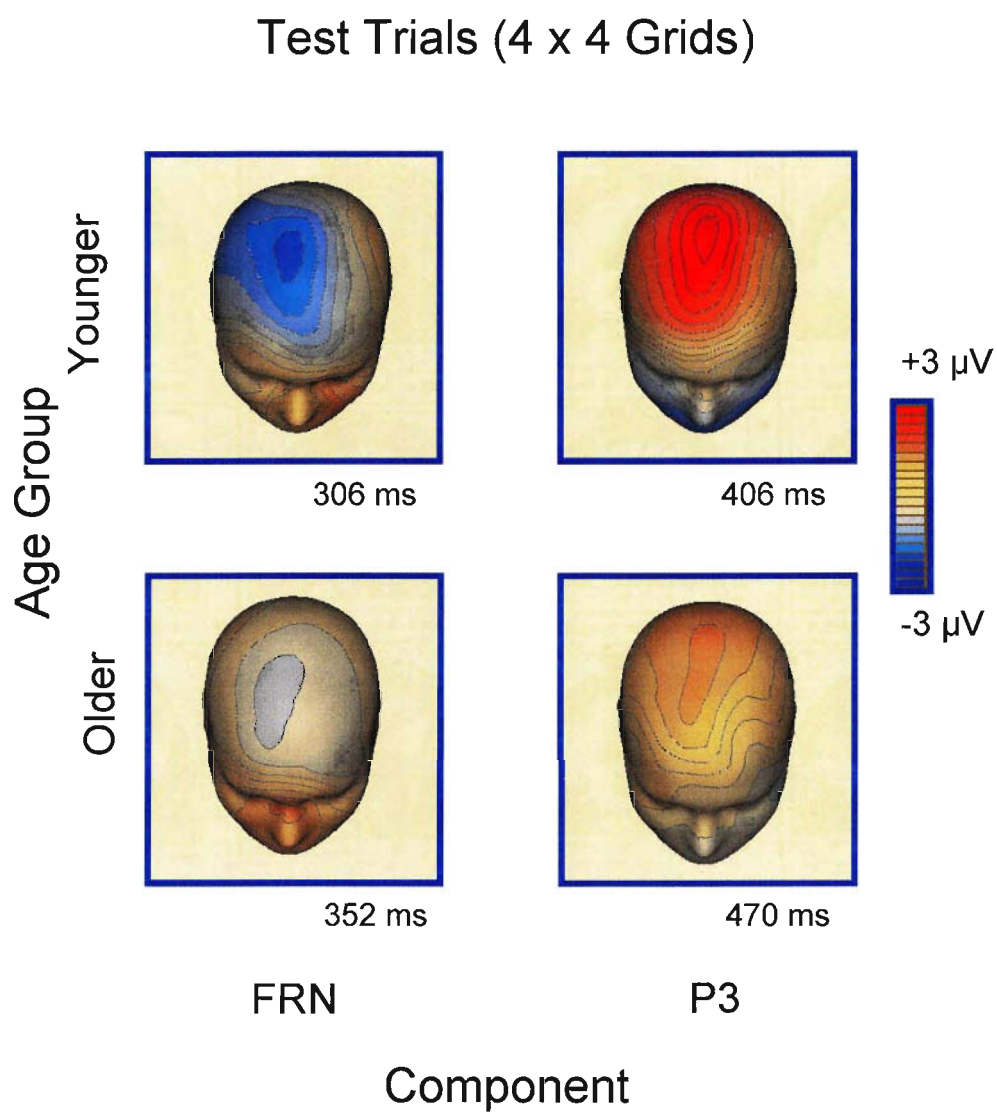
Figure 2.7. Topographies of the FRN and feedback P3 on error trials of the 4 × 4 maze in the test condition, as a function of group.

FRN

Figure 2.8. Graphical representation of LORETA *t* statistics comparing FRN activation, as a function of maze level, trial type and group. T-values are ndicated above each figure. The asterisk indicates that the t-statistic for the maximum difference in this medial region exceeds the critical t-value for significance.

Figure 2.9. Graphical representation of LORETA *t* statistics comparing P3 activation, as a function of maze level, trial type and group. T-values are ndicated above each figure. The asterisk indicates that the t-statistic for the maximum difference in this medial region exceeds the critical t-value for significance.
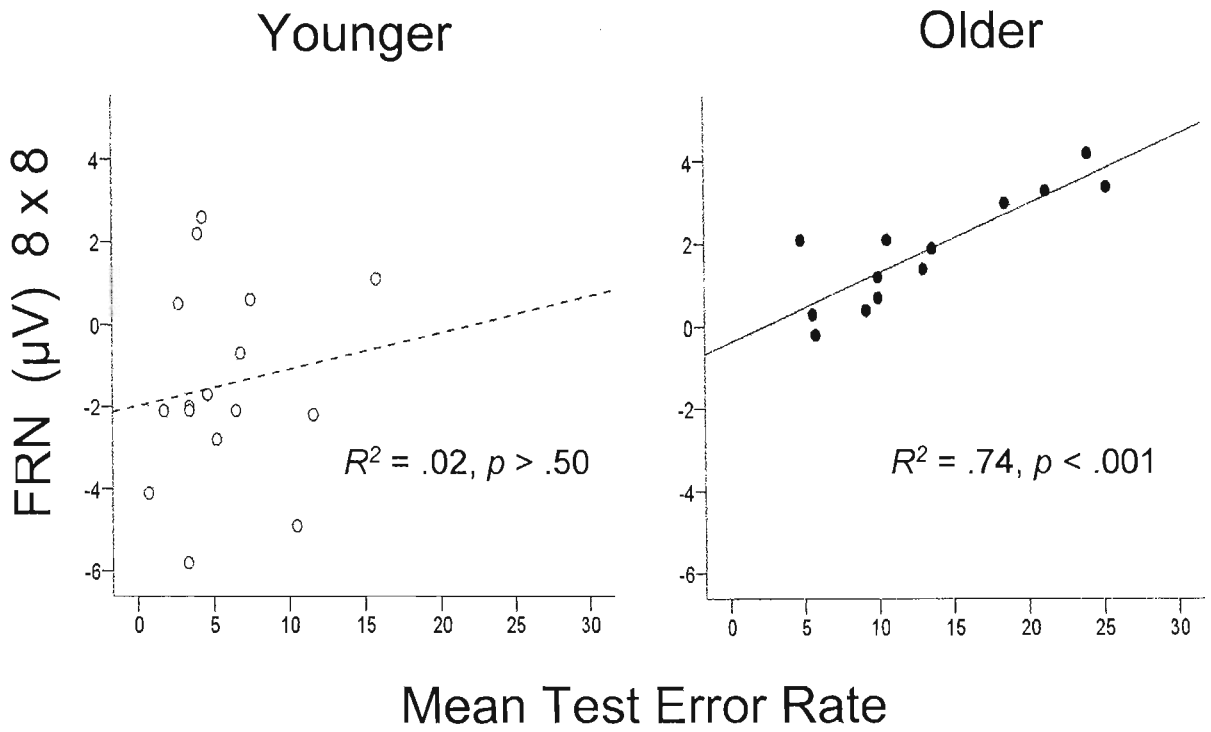
Figure 2.10. Relations of FRN amplitude to the mean number of test-trial errors in the 8 × 8 maze, as a function of group.
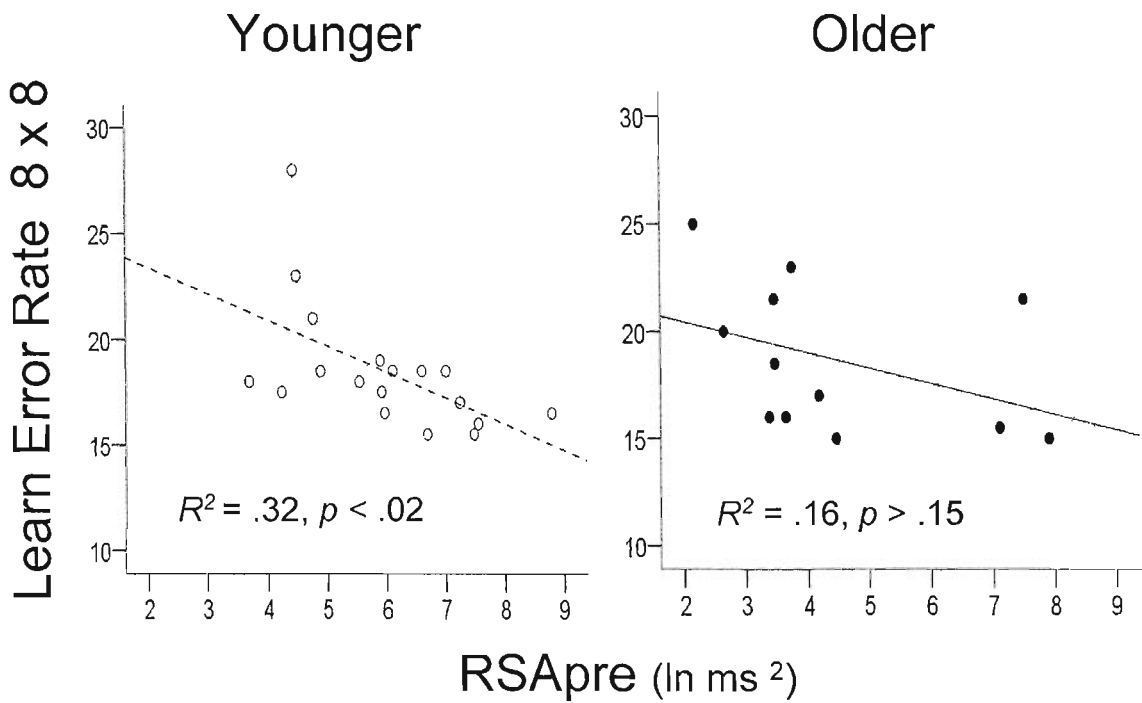
Figure 3.1. Relation of resting RSA to the mean number of learn-trial errors in the 8 x 8 maze, as a function of group.
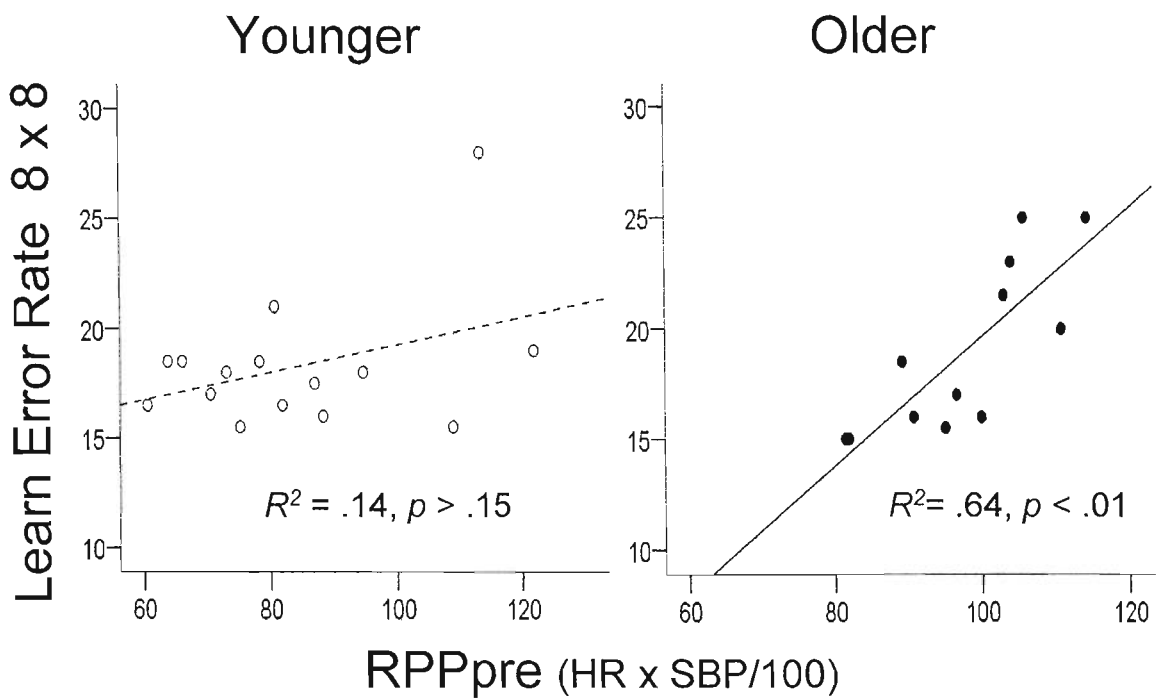
Figure 3.2. Relation of resting RPP to the mean number of learn-trial errors in the 8 x 8 maze, as a function of group.

Younger Adults

$R^2 = .18, p < .08$ (4 x 4)

$R^2 = .26, p < .04$ (6 x 6)

$R^2 = .26, p < .04$ (8 x 8)

Test Error Rate

RSApre (ln ms ^{2})
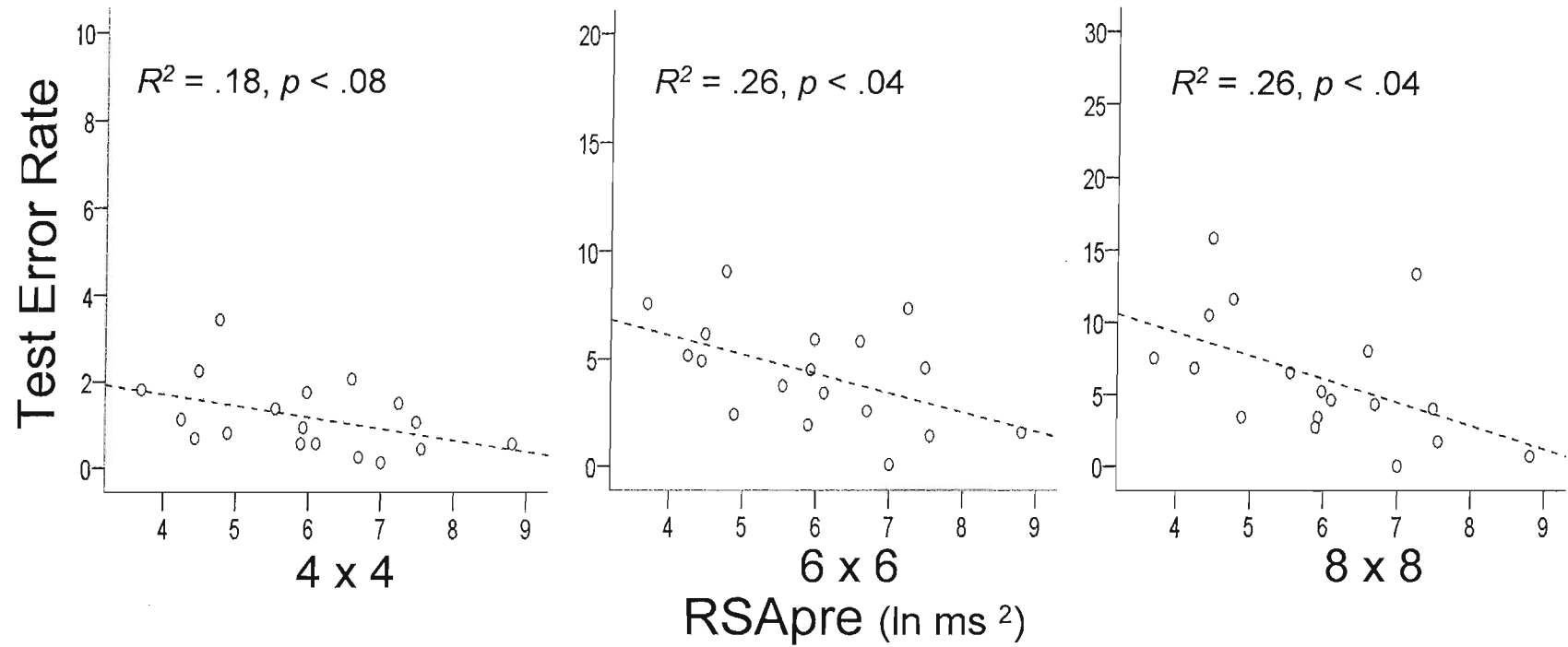
Figure 3.3. Correlations between resting RSA and mean number of test-trial errors as a function of maze level for younger adults.

Older Adults
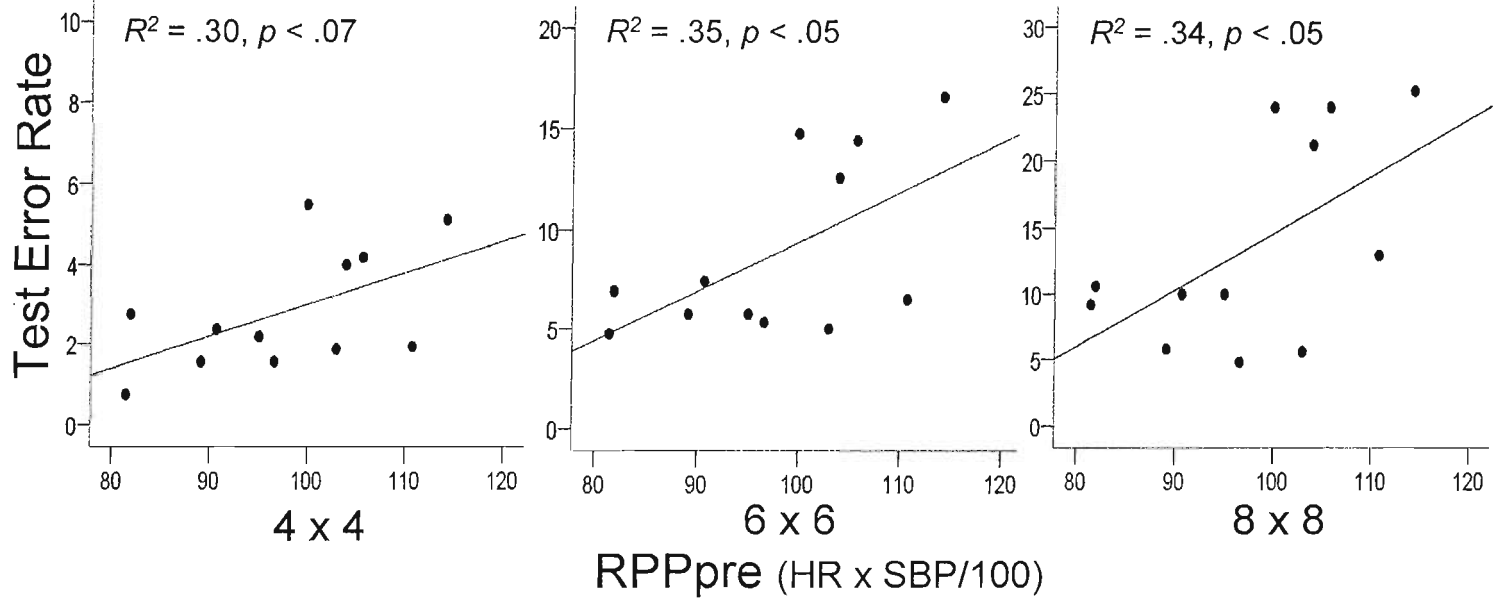
Figure 3.4. Correlations between resting RPP and mean number of test-trial errors as a function of maze level for older adults.
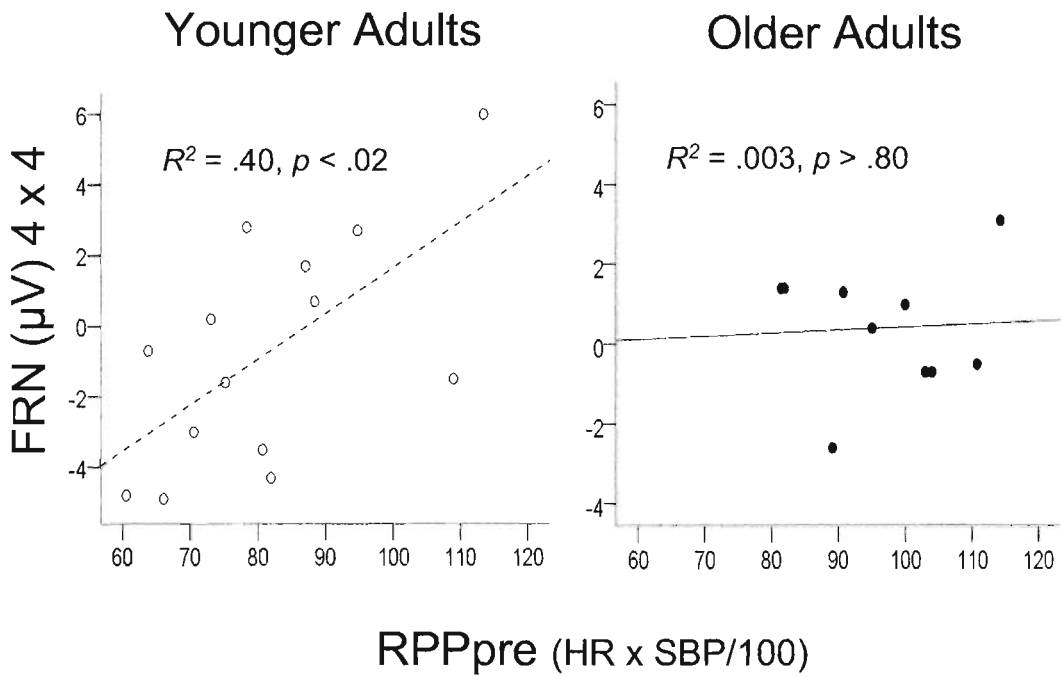
Figure 3.5. Correlations between resting RPP and FRN amplitude following test trial errors in the 4 x 4 maze by group.

Source Memory Task
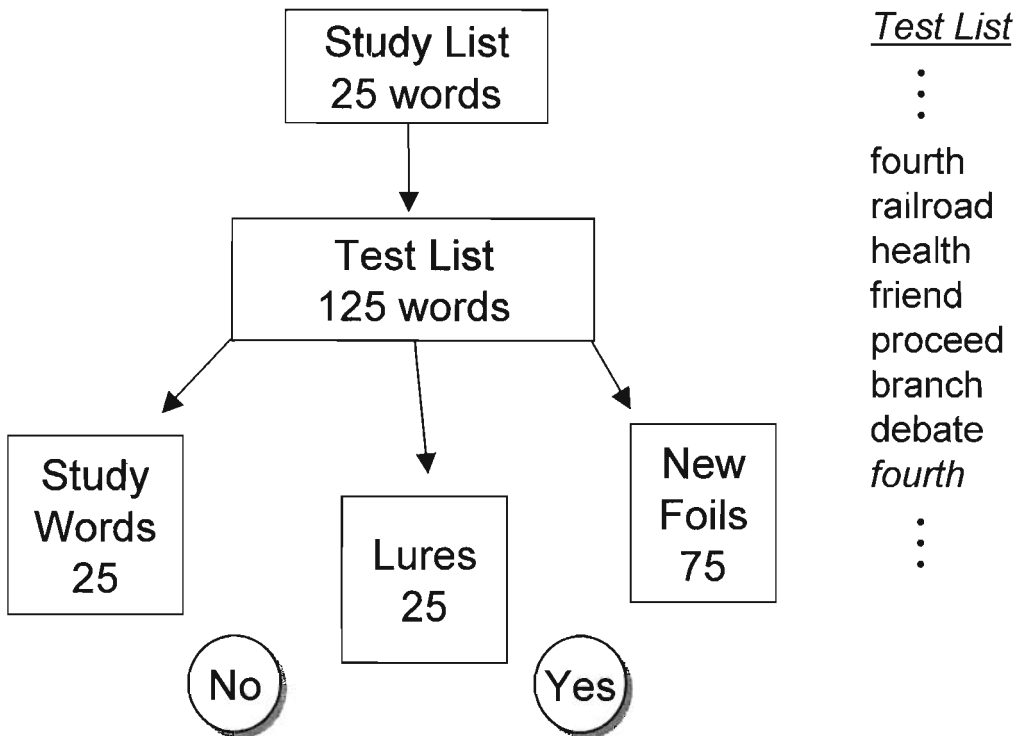
Figure 4.1. Depiction of the source memory task. Participants press "Yes" for a test word that appeared in the study list and "No" for any other word. Lures are repeated new words in the test list.
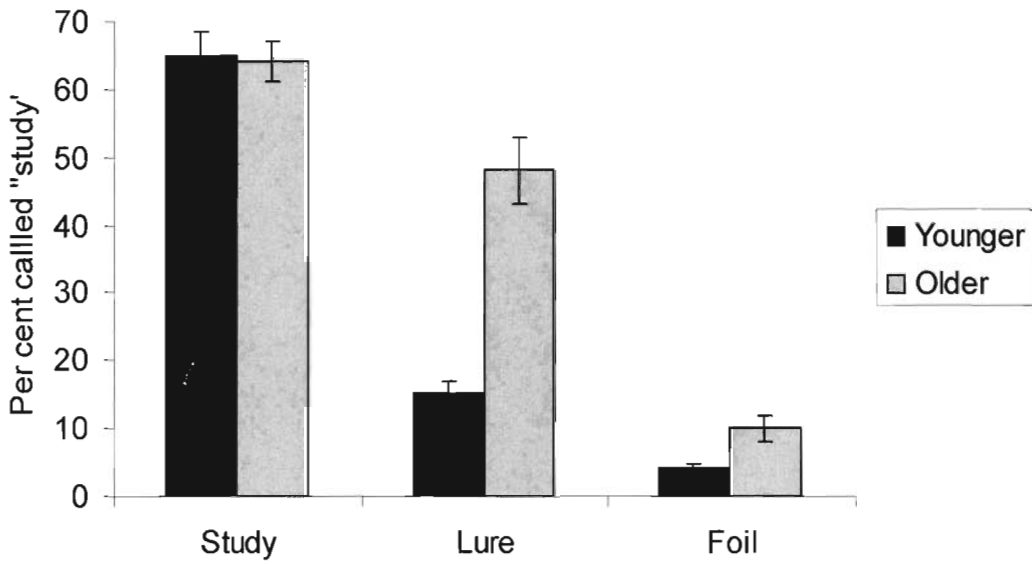
Figure 4.2. Mean percentage of words judged to be from the study list as a function of word type and group in the source memory task.
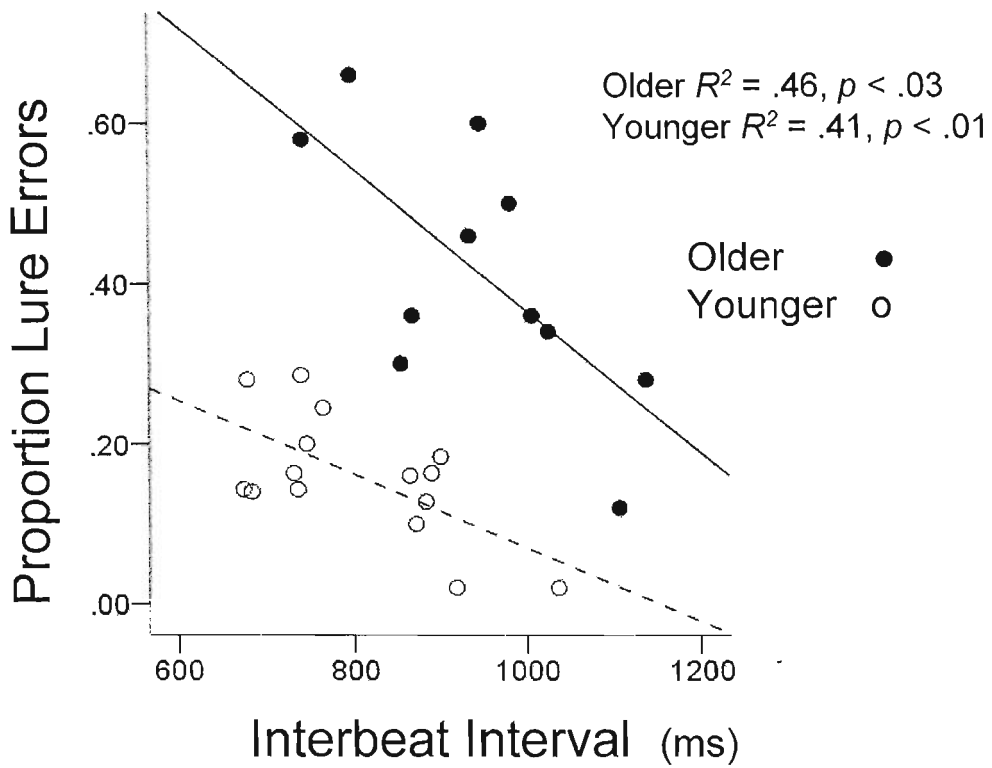
Figure 4.3. Relations between resting IBI and the proportion of lure errors in the source memory task by age group.
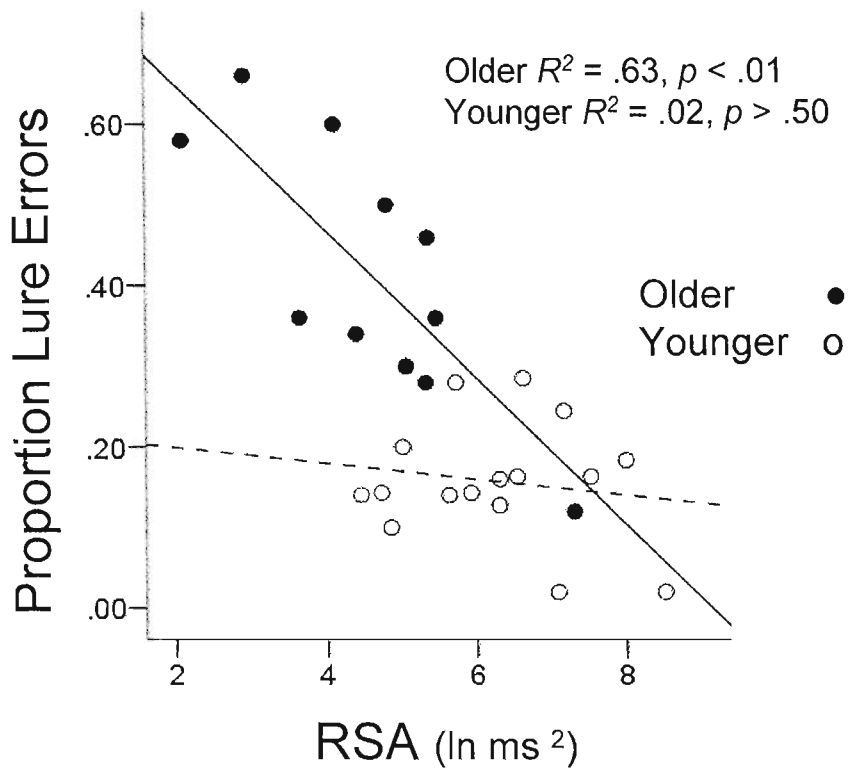
Figure 4.4. Relations between resting RSA and the proportion of lure errors in the source memory task by age group.
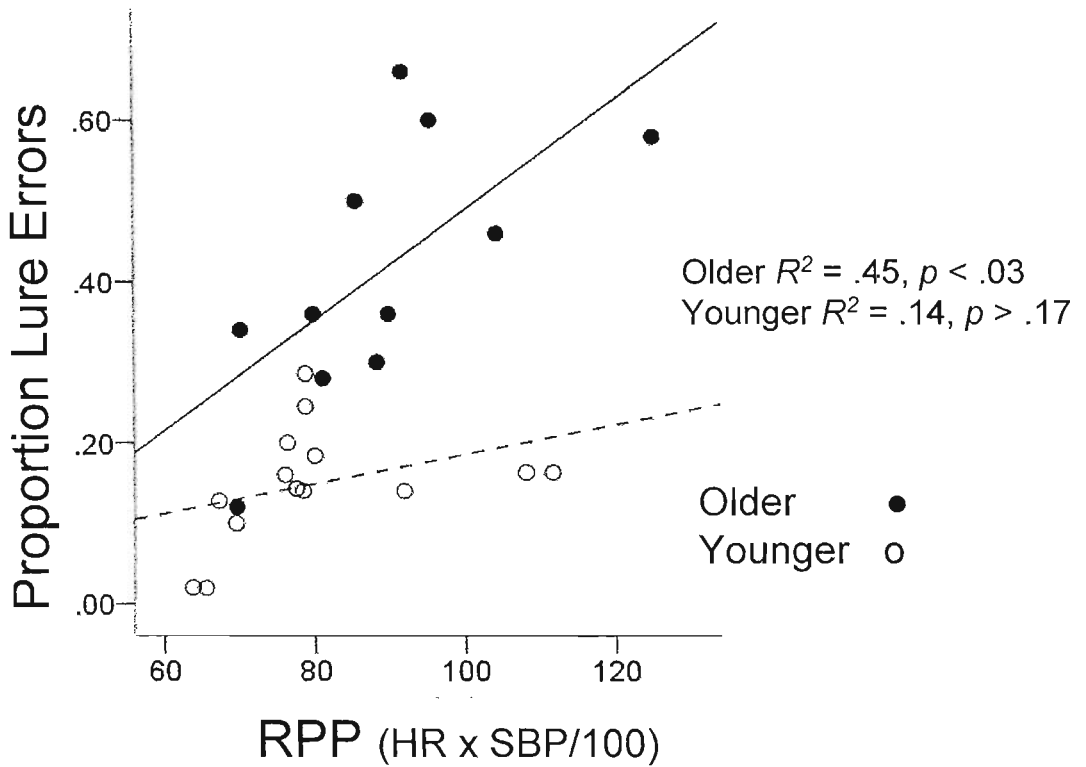
Figure 4.5. Relations between resting RPP and the proportion of lure errors in the source memory task by age group.
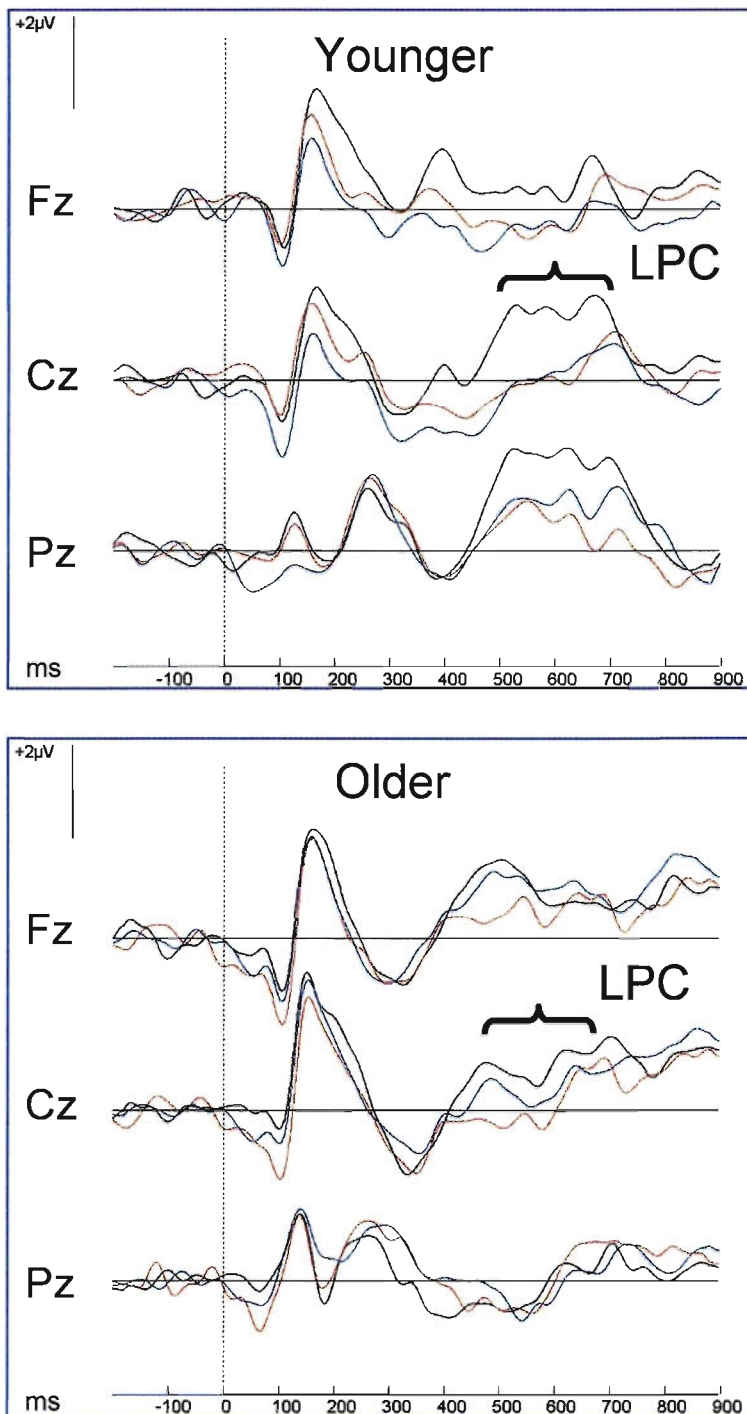
Figure 4.6. Grand-average stimulus-locked ERPs elicited by study words, lures and foils during the source memory task for younger (n = 10) and older adults (n = 8). Correct trials.
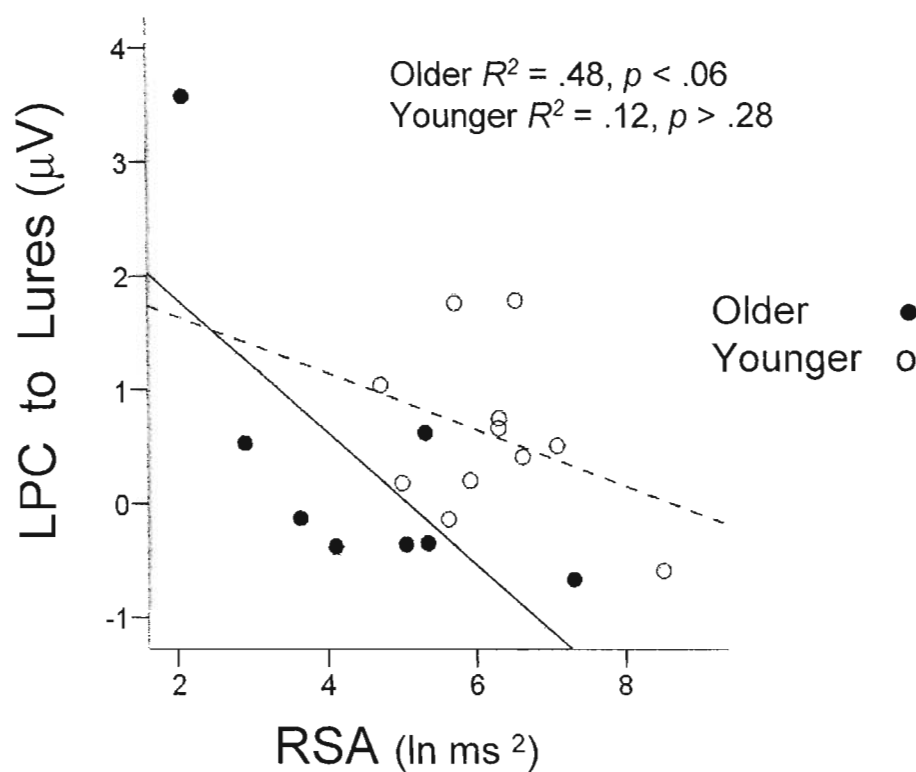
Figure 4.7. Relations between resting RSA and LPC to lures in the source memory task by group.
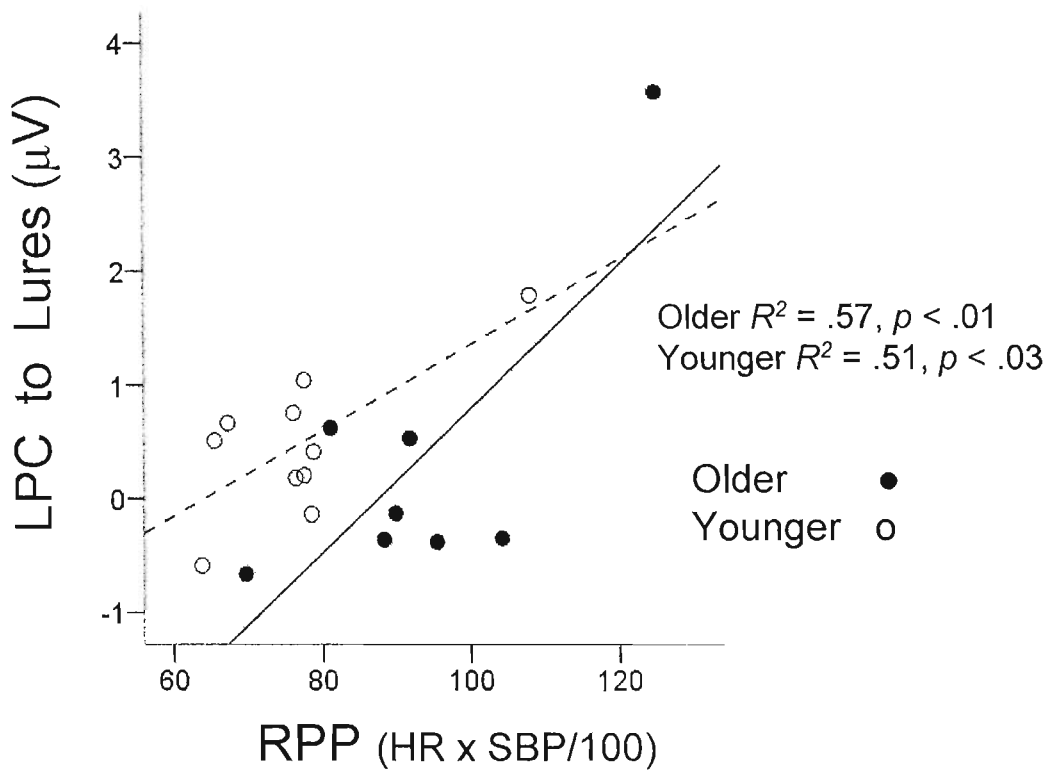
Figure 4.8. Relations between resting RPP and LPC to lures in the source memory task by group.
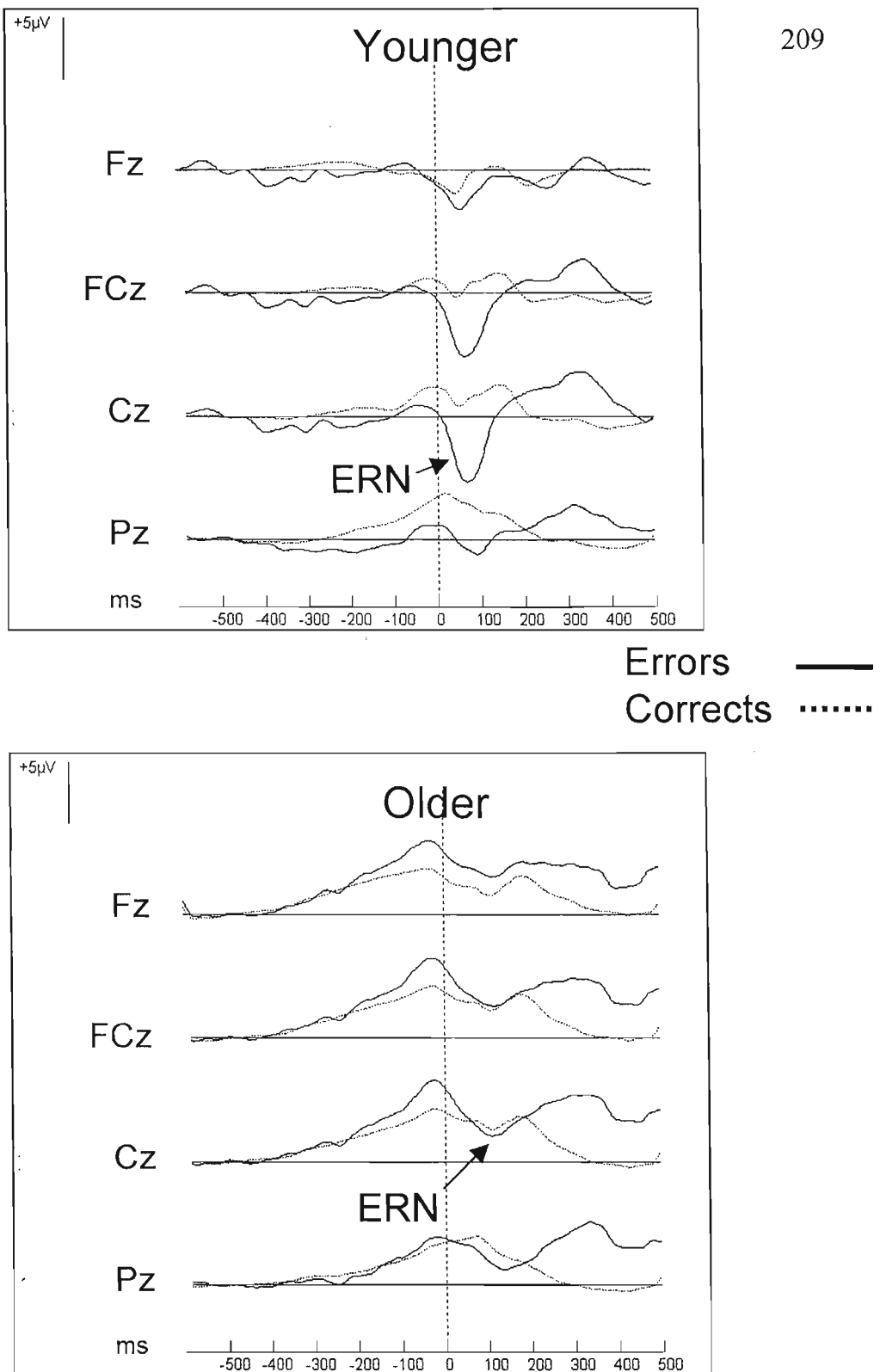
Figure 4.9. Grand-average response-locked ERPs elicited by correct
and incorrect responses in the standard letter flanker task for younger
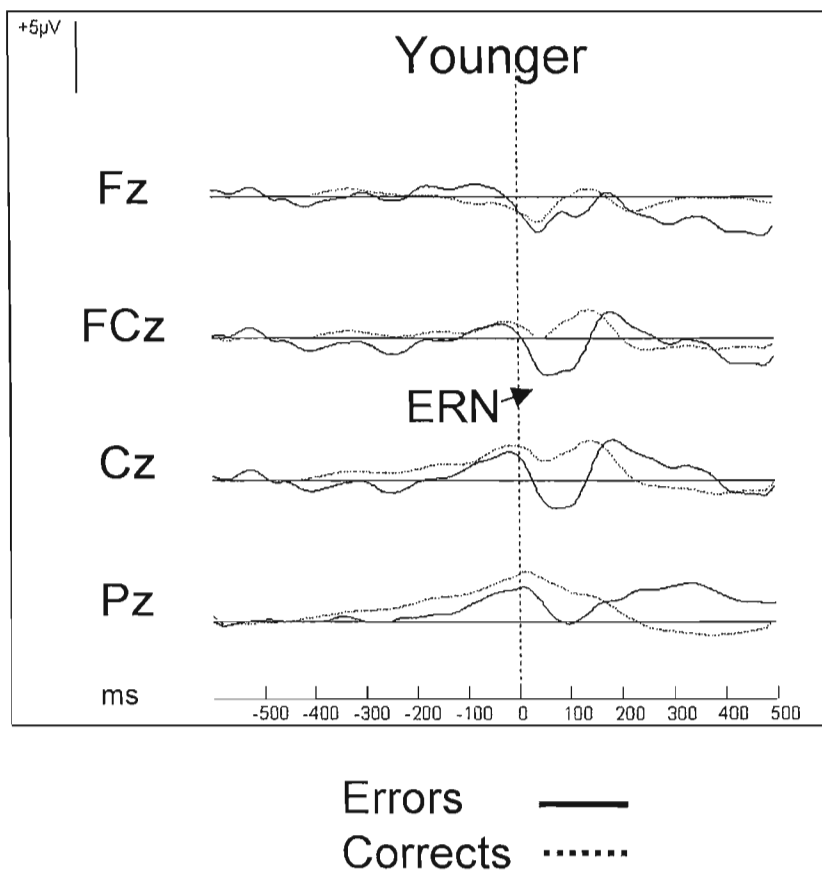(n = 18) and older adults (n = 16).

Figure 4.10. Grand-average response-locked ERPs elicited by correct and incorrect responses in the difficult letter flanker task for younger adults. (n =18)

Appendix A

Brock University
Senate Research Ethics Board

Extensions 3943/3035, Room AS 302

DATE: February 3, 2004

FROM: Joe Engemann, Chair

Senate Research Ethics Board (REB)

TO: Jane Dywan, Psychology

Karen Matthewson

William Tays

FILE: **03-285 Matthewson/Tays**

TITLE: **The ability to control error response in low and high attention demanding tasks**

The Brock University Research Ethics Board has reviewed the above research proposal.

DECISION: Accepted as Clarified

This project has been approved for the period of **February 3, 2004** to **August 31, 2005** subject to full REB ratification at the Research Ethics Board's next scheduled meeting. The approval may be extended upon request. *The study may now proceed.*

Please note that the Research Ethics Board (REB) requires that you adhere to the protocol as last reviewed and approved by the REB. The Board must approve any modifications before they can be implemented. If you wish to modify your research project, please refer to www.BrockU.CA/researchservices/forms.html to complete the appropriate form *REB-03 (2001) Request for Clearance of a Revision or Modification to an Ongoing Application.*

Adverse or unexpected events must be reported to the REB as soon as possible with an indication of how these events affect, in the view of the Principal Investigator, the safety of the participants and the continuation of the protocol.

If research participants are in the care of a health facility, at a school, or other institution or community organization, it is the responsibility of the Principal Investigator to ensure that the ethical guidelines and approvals of those facilities or institutions are obtained and filed with the REB prior to the initiation of any research protocols.

The Tri-Council. Policy Statement requires that ongoing research be monitored. A Final Report is required for all projects, with the exception of undergraduate projects, upon completion of the project. Researchers with projects lasting more than one year are required to submit a Continuing Review Report annually. The Office of Research Services will contact you when this form *REB-02 (2001) Continuing Review/Final Report* is required.

Please quote your REB file number on all future correspondence.

Deborah VanOosten, Research Ethics Officer
Brock University
Office of Research Services
500 Glenridge Avenue
St. Catharines, Ontario, Canada L2S 3A1
phone: (905)688-5550, ext. 3035   **fax:** (905)688-0748
email: deborah.vanoosten@brocku.ca
http://www.brocku.ca/researchservices/humanethics.html

Health and Medical History Questionnaire (Check all that apply) Study: _____
Subject ID code: _____ Age: _____ Gender: _____ Date:_____

Item	Past	Continuing problem/relevant details
Vision Problems		
Hearing Problems		
Problems with Language (speech, word finding, stuttering)		
Serious Headaches		
Special Problems with Reading		
Special Problems with Arithmetic or Number Skills		
General Fatigue		
Chronic Fatigue Syndrome		
Mono, Epstein Barr, HIV, or other long-lasting virus		
Serious Accident		
Head Injury/Concussion		
Loss of Consciousness		
Fainting or Dizziness		
Seizure Disorder (Epilepsy)		
Major Surgery (recent, last few years)		
Recent Major Stress (e.g., death in family/health concerns, in last year)		
Problems with appetite/eating (eating more or less than required)		
Asthma/serious allergies		
Arthritis/rheumatism or other movement/motor problems		
Paralysis/numbness		
Autoimmune Disorders (e.g., Lupus, Multiple Sclerosis)		
Serious Infections/Fevers (e.g., Tuberculosis)		
Diabetes		
Heart Disease/irregularities		

Hypertension (High Blood Pressure)		
High Cholesterol/triglycerides		
Chronic Obstructive Lung Disease		
Disease/dysfunction of major organs (e.g., liver, kidneys)		
Problems with attention or concentration (e.g., ADD)		
Problems with activity level (hyperactivity)		
Problems with mood (Depression/Anxiety)		
Other Psychiatric problems		
Problems with sleep (e.g., falling asleep, frequent or early waking)		
Other serious disease/health concerns (e.g., cancer; chronic pain)		

Medications
Are you taking any prescribed or over-the-counter medications?

Medication	Purpose

Use of Stimulants/Suppressants
(0 = none; 1 = v. light; 2 = light to moderate; 3 = moderate; 4 = moderate to high; 5 = high)

caffeine (coffee, tea, chocolate, soft drinks)	
alcohol (beer, wine, liquor)	
Nicotine	
recreational or mood altering drugs (soft, e.g., marijuana)	
Recreational -- harder drugs (e.g., cocaine)	

General Health Practices:

Exercise (how strenuous, how often?)	
Diet (healthy choices? How consistent?)	

Appendix C

NAME: _____ **HADS** DATE: _____

This questionnaire is designed to help identify how you feel. Read each question and check the response which comes closest to have you have been feeling in the past few weeks. Don't take too long on any one question; your immediate reaction to each item is what is of interest.

1) I feel tense or "wound up":
   Most of the time _____
   A lot of the time _____
   Time to time, occasionally _____
   Not at all _____

2) I feel as if I am slowed down:
   Nearly all the time _____
   Very often _____
   Sometimes _____
   Not at all _____

3) I still enjoy the things I used to enjoy:
   Definitely as much _____
   Not quite so much _____
   Only a little _____
   Hardly at all _____

4) I get a sort of frightened feeling like "butterflies" in the stomach:
   Not at all _____
   Occasionally _____
   Quite often _____
   Very often _____

5) I get a sort of frightened feeling, as if something awful is about to happen:
   Very definitely and quite badly _____
   Yes, but not too badly _____
   A little, but it doesn't worry me _____
   Not at all _____

6) I have lost interest in my appearance:
   Definitely _____
   I don't as much care as I should _____
   I may not take quite as much care _____
   I take just as much care as ever _____

7) I can laugh and see the funny side of things:
   As much as I always could _____
   Not quite so much now _____
   Definitely not so much now _____
   Not at all _____

8) I feel restless as if I have to be on the move:
   Very much indeed _____
   Quite a lot _____
   Not very much _____
   Not at all _____

9) Worrying thoughts go through my mind:
   A great deal of the time _____
   A lot of the time _____
   From time to time, not too often _____
   Only occasionally _____

10) I look forward with enjoyment to things:
   As much as I ever did _____
   Rather less than I used to _____
   Definitely less than I used to _____
   Hardly at all _____

11) I feel cheerful:
   Not at all _____
   Not often _____
   Sometimes _____
   Most of the time _____

12) I get sudden feelings of panic:
   Very often indeed _____
   Quite often _____
   Not very often _____
   Not at all _____

13) I can sit at ease and feel relaxed:
   Definitely _____
   Usually _____
   Not often _____
   Not at all _____

14) I can enjoy a good book, radio, or TV programme:
   Often _____
   Sometimes _____
   Not often _____
   Very seldom _____

Mini-Mental State Examination (MMSE)
(Instructions for the administration of the MMSE
have been provided on the reverse)

Patient's Name _____   Date _____

Rated by _____

Maximum Score	Score	
		ORIENTATION
5	____	What is the (year) (season) (date) (day) (month)?
5	____	Where are we: (province) (country) (town or city) (hospital) (floor)?
		REGISTRATION
3	____	Name 3 common objects (e.g., "apple," "table," "penny"). Take 1 second to say each. Then ask the patient to repeat all 3 after you have said them. Give 1 point for each correct answer. Then repeat them until he/she learns all 3. Make a maximum of 6 trials. Count trials and record. Trials: ____
		ATTENTION AND CALCULATION
5	____	Spell "world" backwards. The score is the number of letters in correct order (D_L_R_O_W_). [Note: Instead of "world", the following may be used — subtract 7 from 100 and keep subtracting 7 from the result until you tell him/her to stop.]
		RECALL
3	____	Ask for the 3 objects repeated above. Give 1 point for each correct answer. [Note: Recall cannot be tested if all 3 objects were not remembered during registration.]
		LANGUAGE
2	____	Name a "pencil," and a "watch." (2 points)
1	____	Repeat the following: "No ifs, ands, or buts." (1 point)
3	____	Follow a 3-stage command: "Take a paper in your right hand, fold it in half, and put it on the floor." (3 points)
		READ AND OBEY THE FOLLOWING:
1	____	Close your eyes. (1 point)
1	____	Write a sentence. (1 point)
1	____	Copy the following design. (1 point)

No construction problem

Total Score ____

Instructions for Administration of Mini-Mental State Examination (MMSE)

Orientation

1. Ask for the date. Then ask specifically for parts omitted, e.g., "Can you also tell me what season it is?" Score one point for each correct answer.
2. Ask in turn: "Can you tell me the name of this hospital?" (town, country, etc.) Score one point for each correct answer.

Registration

Ask the patient if you may test his/her memory. Then say the names of 3 unrelated objects, clearly and slowly, about one second for each. After you have said all 3, ask the patient to repeat them. This first repetition determines his/her score (0-3) but keep saying them until he/she can repeat all 3, up to 6 trials. If all 3 are not eventually learned, recall cannot be meaningfully tested.

Attention and Calculation

Ask the patient to spell the word "world" backwards. The score is the number of letters in correct order (e.g., DLROW=5; DLRW=4; DLW=3; OW=2; LDRWO=1).

Alternative: Ask the patient to subtract 7 from 100, stopping after 5 subtractions (93, 86, 79, 72, 65). The score is 1 point for each correct answer.

Recall

Ask the patient if he/she can recall the 3 words you previously asked him/her to remember. Score 0-3.

Language

Naming: Show the patient a wristwatch and ask him/her what it is. Repeat for pencil. Score 0-2.

Repetition: Ask the patient to repeat the sentence after you. Allow only one trial. Score 0 or 1.

3-stage command: Give the patient a piece of plain blank paper and repeat the command. Score 1 point for each part correctly executed.

Reading: On a blank piece of paper print the sentence, "Close your eyes," in letters large enough for the patient to see clearly. Ask him/her to read it and do what it says. Score 1 point only if he/she actually closes his/her eyes.

Writing: Give the patient a blank piece of paper and ask him/her to write a sentence for you. Do not dictate a sentence; it is to be written spontaneously. It must contain a subject and verb and be sensible. Correct grammar and punctuation are not necessary.

Copying: On a clean piece of paper, draw intersecting pentagons, each side about 1 in., and ask him/her to copy it exactly as it is. All 10 angles must be present and 2 must intersect to score 1 point. Tremor and rotation are ignored.

Appendix E

**The Speed
and Capacity
of Language-Processing Test**

Thames Valley
Test Company

The Spot-the-Word Test   Version B

This is a test of your knowledge of words. You
will be asked to decide which of two items, such
as 'bread' and 'glot', is a real word and which is an
invented item; 'bread', of course, is the real word.

Each of the pairs of items below contains one real
word and one nonsense word, invented so as to look
like a word but having no meaning. Please tick the
item in each pair that you think is the real word.
Some will be common words, most will be uncom-
mon and some very rarely used. If you are unsure,
guess, you will probably be right more often than
you think.

Before you begin the main test try the following.

Practice

kitchen	–	harrick
puma	–	laptess
plorinum	–	levity
cuticle	–	andrinand
flonty	–	xylophone
craxent	–	sofa

Are there any questions?

slank — chariot

lentil — glotex

stamen — dombus

loba — comet

pylon — stroin

scrapten — flannel

fender — ullus

ragspur — joust

milliary — mantis

sterile — palth

proctive — monotheism

glivular — stallion

intervantation — rictus

byzantine — chloriant

monologue — rufine

elegy — festant

malign — vago

exonize — gelding

bulliner — trireme

visage — hyperlistic

froin — oratory

meridian — phillidism

grottle — strumpet

equine — psynomy

baggalette — riposte

valance — plesmoid

introvert — vinadism

penumbra — rubiant

breen — malinger

gammon — unterried

coracle – prestasis

paramour – imbulasm

dallow – octaroon

fleggary – carnation

liminoid – agnostic

naquescent – plinth

thole – leptine

crattish – reform

wraith – stribble

metulate – pristine

pauper – progotic

aurant – baleen

palindrome – lentathic

hedgehog – mordler

prassy – ferret

torbate – drumlin

texture – disenrupted

isomorphic – thassiary

fremoid – vitriol

farrago – gesticity

minidyne – hermeneutic

pusality – chaos

devastate – prallage

peremptory – paralepsy

chalper – camera

roster – falluate

scaline – accolade

methagenate – pleonasm

drobble – infiltrate

mystical – harreen

Appendix F

Aging 04
Maze Task Instructions

4 by 4
-"This next task involves learning a hidden route through a maze. This first maze is made
up of 16 squares arranged in a 4 by 4 pattern. You will start in the top left-hand corner
and your goal is to find the path to the bottom right-hand corner. The maze will look
something like this (Show page). -"In order to move from the start to the end, you will
use the arrow keys. Just press the button that points in the direction that you need to go
in. You can only move to any square that is to the left, right, above or below the square
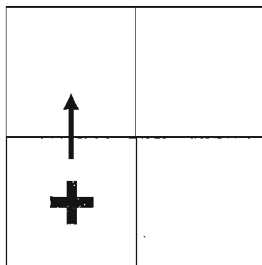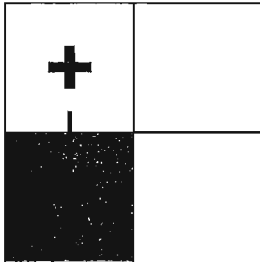you are currently on."   *You cant go off the grid*
Note: Start, end & directions.   *or move diagonally.*
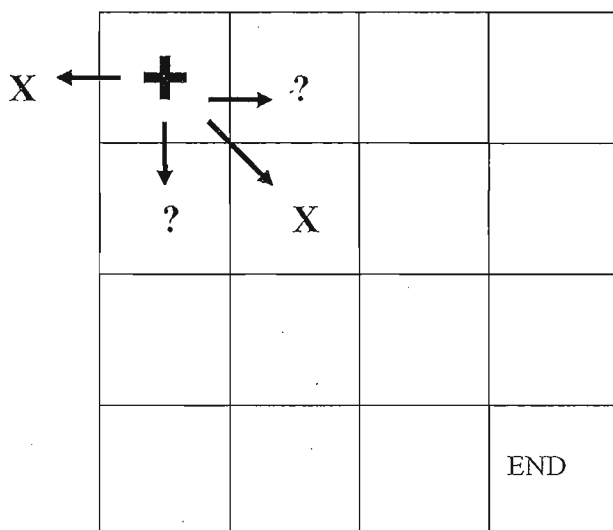
"Since the correct path is hidden you will get feedback every time you make a move. Use
this feedback to try and learn the whole correct path from start to finish.   If you make a
correct move, the box you've moved to will change to green (then a green cross). If you
make a mistake the box you've moved to will go red (then a red cross). If you make a
mistake, just go back to the square you were at to get back on the right path. Once you've
moved you will have to wait a short moment before making your next move." (Show next
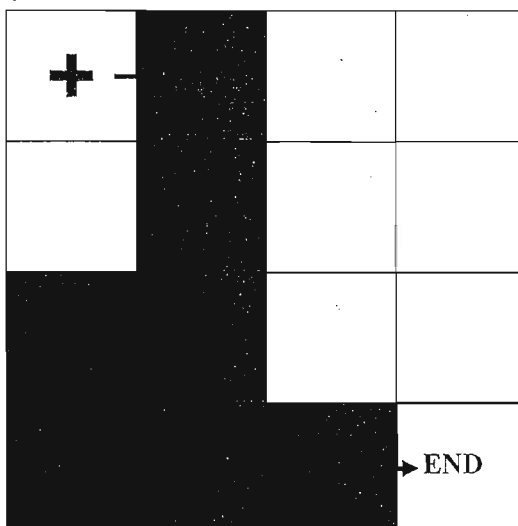page)
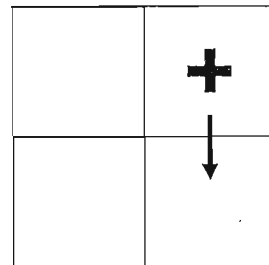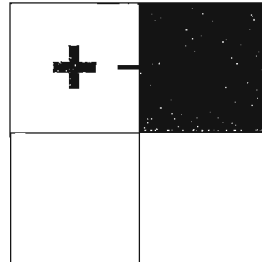
-"The path goes from block to block in irregular paths. There is only one correct path in each display and the path will never cross over itself. Here is what an example path might look like if you could see all the right moves:"

Note: "You would have to follow the path exactly as shown, going in the directions the arrows are pointing. There are no shortcuts"

Task Instrucitons:

-"You will get 8, '4 by 4' mazes to do. The first time you go through it you will just be guessing where to go. But try to remember the right path so you don't have to guess as much on the next run through the maze. You will go through each of these small '4 by 4' mazes three times. Once to learn it and then twice to see if you can remember the right way. Don't expect to be able to remember the mazes on the first time through, just try your best and guess when you need to."

"After we have finished the 8, '4 by 4' mazes we will do some larger more difficult mazes. Any questions? Ready" (Start 4 by 4 mazes)

6 by 6 Mazes:

-"The next set we will do has 36 squares arranged '6 by 6'. All the same rules apply. This will be harder then the last set so just try your best to get through the maze in the fewest steps and guess when you need to. There are 4 of these mazes and you will have a chance to do each of them 4 times. The first trial is to start learning the way through and this time you will have 3 chances to try and remember the correct path. Any questions?" (Start task)

8 by 8 Maze:

-"Now we will do the final set of mazes which are '8 by 8' or 64 squares large. This will be quite difficult but just try your best. All the same rules apply as before. You will do 2 different mazes and will do them each 5 times. One trial to try and learn the maze and four trials to try and remember where the correct path was. Any questions?" (Start task)

Appendix G

Instructions to Participants: *Day 1*-Karen& Bill, March 2004

1. Baseline heart rate/Pre: (Aging04_S#_01HRpre) **Please rest quietly for a few minutes, with your eyes open, looking at the computer screen. Just relax and feel free to blink as needed.**

[Change EEG files now].

2. a) Lag Part A: Study Phase: (Aging04_S#_01LagA).
Use merged version of LagA, combining study and test list in one file.

You are going to see some words appear one at a time on the computer screen. This is the 'study list'. I want you to read each word out loud and try to remember each word in case you should see it later.

b) Lag A: Test Phase:
[Set up red cards at either side of pt's monitor: Study on one side, Others on the other side].

Now you are going to view another list of words. In this list you will see some words from the study list and you'll see some new words. You don't need to say theme this time. What I want you to do is press the _____ key whenever you see a word form the study list. Now, some of the new words may repeat, but don't worry about that. Your job is to look for the old words, the ones from the study list. Whenever you see a word from the study list, press the _____ key. For all of the other words, press the _____ key. Please try to withhold your blink until after you have made your decision and hit the appropriate key.
So, if you see a word from the study list, show me which key you will press. _____ (Watch them.) **That's right. If you see a word that was** *not* **from the study list, show me which key you will press. _____ Right again. Do you have any questions?**

[Change EEG files now].

3. Easier Flanker Task (Flanker A): (Aging04_S#_01FlankA)
[Set up red cards at either side of monitor: H on one side, S on other].

Now we will do a different task. You will see a string of 5 letters on the screen. Your task is to identify the centre letter in the string.
If it is an H, press the _____ key. On the other hand, if it is an S, press the _____ key.
(Show examples on 4 cards: HHHHH, SSSSS, SSHSS, HHSHH).
If you saw this, which key would you press? _____
If you saw this, which key would you press? _____
If you saw this, which key would you press? _____
If you saw this, which key would you press? _____

The letter strings will appear and disappear rather quickly and there is quite a number of them. If you make a mistake, don't worry, keep going with the new strings as they appear on the screen.

There will be two pauses to let you "catch your breath/clear your head" . When they occur, just rest until the letter strings start again.
Again, please try to blink lightly and try not to blink at exactly the moment when you make your response.
Do you have any questions?
Once again, if the centre letter is an H, which key do you press? If it is an S, which key do you press?

[Change EEG files now].

4. a) Lag B: Study Phase: Aging04_S#_01LagB

Now we are going to repeat the first task but with new words. Again you will see some words appear one at a time on the computer screen. This is a brand new 'study list'. Please read each word out loud and try to remember these words for later.

b) Lag B: Test Phase: [Set up red cards again: Study, Other].

Now you are going to view another list of words. In this next list you'll see words from the second study list and new words you haven't seen yet today. As before, your job is to hit the _____ key whenever you see a study word. For all of the other words, which are *not* from the new study list, press the _____ key. Please try to withhold your blink until after you have made your decision and hit the appropriate key.
So, if you see a word from the study list, show me which key you will press. That's right. If you see a word that was not from this study list, show me which key you will press. _____ Right. If you see a study word, which key? _____ Right. Do you have any questions?

[Change EEG files now].

5. Break—juice, muffin, water, orange juice, tea, cookies, granola bars. You might want to close your eyes for a minute or two, to give them a rest.

6. Difficult Flanker Task: (HHPHH, SSXSS; Aging04_S#_01FlankBi).
[Set up red cards on either side of monitor: H, P on one side, S, X on other].

Now we will do another letter task that is similar to one you did before. You will see a string of 5 letters on the screen, as before. Again, your task is to identify the centre letter in the string. This time, if it is an H *or* a P, press the _____ key with your ____hand. If it is an S *or* an X, press the _____ key with your ____ hand.
(Show examples on 6 cards: HHHHH, SSSSS, HHPHH SSXSS, HHXHH, SSPSS).
If you saw this, which key would you press? _____
If you saw this, which key would you press? _____
If you saw this, which key would you press? _____
If you saw this, which key would you press? _____
If you saw this, which key would you press? _____

If you saw this, which key would you press? _____

Again, if you make a mistake, don't worry, keep going with the new strings as they appear on the screen.
There will be one pause. When it happens, just rest until the letter strings start again.
This letter task is shorter than the last letter task you did.
Do you have any questions?
Please try, as best you can, not to blink at exactly the moment when you make your response.
Once again, if the centre letter is an H or P, which key do you press? That's right. If it is an S or X, which key do you press? Right.

[Change EEG files now].

7. a) Lag L Study Phase: (Aging04_S#_session1LagL)

Ok, now you will see a new study list on the screen. Just read each word out loud, and try to remember it in case you come across it later.

b) Lag L: Test Phase: [Set up red cards again: Study, Other].

Now some more words will be presented on the screen. Please press the ____ key whenever you see a *study* word. For all of the *other* words, press the ____ key. Please try to withhold your blink until after you have hit the appropriate key.

[Change EEG files now].

8. . Difficult Flanker Task: (HHPHH, SSXSS; Aging04_S#_01FlankBBii).
[Set up H,P, and S,X cards on either side of monitor].

Now we will do another letter task that is the same as the last one you did.

You will see a string of 5 letters on the screen, as before. Again, your task is to identify the centre letter in the string. If it is an H *or* a P, press the ____ key with your ____ hand. If it is an S *or* an X, press the ____ key with your ____ hand.

[Only if necessary, show examples on 6 cards: HHHHH, SSSSS, HHPHH SSXSS, HHXHH, SSPSS).
If you saw this, which key would you press? _____
If you saw this, which key would you press? _____
If you saw this, which key would you press? _____
If you saw this, which key would you press? _____
If you saw this, which key would you press? _____
If you saw this, which key would you press? _____]

Again, if you make a mistake, don't worry, keep going with the new strings as they appear

on the screen. This letter task is the shorter one.

Once again, if the centre letter is an H or P, which key do you press? That's right. If it is an S or X, which key do you press? Right.

[Change EEG files now].

9. a) Lag M: Study Phase: (Aging04_S#_01LagM)

Now we are beginning the last task for today. I will show you one more study list. Again you will see some words appear one at a time on the computer screen. I want you to read the words out loud and try to remember them in case you see them again later.

b) Lag M: Test Phase: [Set up red cards: Study, Others].

This is the very last list of words. Please press the ____ key whenever you see a study word. For all of the other words, which are *not* from that study list, press the ____ key. It is important not to miss any study words if you can help it.

[Change EEG files now].

10. Baseline heart rate/Post: Aging04_S#_01HRpost.

Please rest quietly for a few minutes, with your eyes open, looking at the computer screen. Just relax and feel free to blink as needed.

[Stop recording].