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Socioaffective senescence in the rhesus monkey (Macaca mulatta)

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Abstract

Older adults (> 65 years old) make up an ever-growing percentage of the global human population. This demographic shift is among the most pressing public health concerns of our time due to the unique health challenges that older adults face. Although aging is clearly detrimental to some aspects of physical health and mental ability, relatively less work has evaluated how aging impacts social and affective (socioaffective) processing, despite the important role these two fundamental aspects of our lives play in determining our health and wellbeing. The existing literature shows the somewhat paradoxical finding that aspects of people's socioaffective processing *improve* with age—though in whom and for what reasons remain an open question. Understanding sources of variation in socioaffective aging trajectories will help promote wellbeing for those who are most in need. Although most research on socioaffective aging to date has taken place in humans, adopting a comparative approach will illuminate novel psychological, physiological, and social mechanisms through which changes to socioaffective processing occur and speak to the evolutionary origins of such changes. Here, I investigate how aspects of socioaffective processing differs across the lifespan in rhesus monkeys (*Macaca mulatta*), which share key features of human developmental neurobiology, physiology, and social behaviors. In Chapter 1, I evaluate age-related differences in visual attention towards faces of conspecifics ranging in affective content to test the hypothesis that aging influences how monkeys process affective stimuli. Consistent with work in humans, I find that while middle-aged animals display robust biases in visual attention towards threatening faces, aged animals show no such bias, suggesting phylogenetically conserved mechanisms of age-related threat avoidance. Chapter 2 evaluates age-related differences in monkeys' autonomic nervous system responsivity towards social stimuli and finds age-related disruption to how the parasympathetic nervous system of aged monkeys responds to such socioaffective stimuli. These disruptions to the parasympathetic nervous system may specifically serve as a driving force behind changes so primate social behavior in aging. Finally, Chapter 3 adopts a large-scale lifespan approach to assess how features of infant monkeys' behaviors and social environments predict risks mortality rates across 20 years of follow-up. We find infant reactivity and social environments predict morality rates across their lives, with adolescence and old age being particularly sensitive windows of development. Together, these investigations speak to the important role social and affective processing plays in health and wellbeing throughout the primate lifespan and how age-related changes in psychosocial processing and behaviors may serve to promote longevity.

In loving memory of Raymond Thomas Santistevan

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Introduction

Older adults (> 65 years old) make up an ever-growing percentage of the global population (United Nations, 2020). This demographic shift is among the most pressing public health concerns of our time due to the unique health challenges that older adults face. Although aging clearly has negative impacts on some aspects of physical and mental health, including increased incidence of disease (for review Chatterji et al., 2015) and decline in “cognitive” processes such as memory and control of attention (for review Levy, 1994), relatively less work has evaluated how aging impacts social and affective (socioaffective) processing. Understanding how our social connections and affective experiences are influenced by aging is critical given the important role these two fundamental aspects of our lives play in determining our health and wellbeing. That is, loneliness (Holt-Lunstad et al., 2010), depression (Pratt et al., 2016), and anxiety (Meier et al., 2016; Miloyan et al., 2016; Pratt et al., 2016) are associated with increased mortality rates even in younger adults and the negative consequence of these conditions are amplified in aging (Fiske et al., 2009; Schulz et al., 2000; Steptoe et al., 2013). Investigations into how environmental, social, psychological, and physiological processes interact in aging are therefore necessary for promoting wellbeing in an aging world.

Past studies of socioaffective processing in aging reveal the somewhat paradoxical finding that, on average, many aspects of people’s lives *improve* with age. For example, studies demonstrate age-related improvement in momentary affective experiences from middle to old age (e.g., Burr et al., 2021; Carstensen et al., 2011; Petrican et al., 2014; Thomas et al., 2016; for a review see Charles & Carstensen, 2010), older adults steadily prune their social networks to contain only meaningful social connections (Bruine de Bruin et al., 2020; Fung, Carstensen, et al., 2001; Fung, Lai, et al., 2001), and older adults display age-related information processing biases towards positive and away from negative affective information (for a review see Carstensen & DeLiema, 2018, meta-analysis see Reed et al., 2014). These improvements in affective processing continue, on average, until people reach approximately 80 years of age, after which trajectories flatten or reverse course (Graham et al., 2020; Joiner et al., 2018). The mechanisms supporting age-related changes to socioaffective processing are debated and numerous theoretical frameworks attempt to explain how and why changes to behavior arise in aging (e.g., Carstensen et al., 1999; Charles, 2010; Kuehn et al., 2018; Labouvie-Vief et al., 2010; Luong et al., 2015; Mendes, 2010). Below, I briefly highlight three prevalent frameworks of the psychology of aging as theoretical background into mechanisms thought to drive age-related changes to socioaffective processing.

Socioemotional selectivity theory (Carstensen et al., 1999; Carstensen & DeLiema, 2018) hypothesizes that the perception of time plays an integral role in determining how people select and pursue socioaffective goals. The theory claims that “knowledge seeking” social motives (e.g., behaviors that may benefit an individual in the distant future, such as exploration or learning) are inversely related to “emotional” social motives (behaviors which are agnostic towards the distant future and prioritize optimizing current emotional experiences and wellbeing). Further, the theory claims the relative importance of “knowledge seeking” and “emotional” goals shifts as a function of an individual’s inferred time left alive, or time left in a particular social setting (e.g., *time horizons*). Specifically, when an individual’s inferred time horizon is distant—as is the case for healthy adolescents and young-to-middle-aged adults—such individuals preferentially engage in knowledge seeking behaviors. When time horizons shrink—as for aging or terminally ill individuals—socioemotional selectivity theory predicts that an individual’s motivation will become biased towards maximizing more immediate hedonic socioemotional experiences (Carstensen et al., 1999; Carstensen & DeLiema, 2018).

Maturational dualism (Mendes, 2010) is a complimentary model and hypothesizes that the ability to sense physiological signals arising from the body (*interoception*) is compromised in aging and that decline in interoceptive ability drives age-related changes in social behavior. That is, as far back as James (1884), scholars in affective science have hypothesized that emotions arise in part through interoceptive processes (e.g., Barrett, 2017; Damasio et al., 1996; Russell, 2003; Schachter et al., 1962). According to Mendes (2010), if interoceptive ability is compromised with age (for which there is some evidence; see Khalsa, Rudrauf, &

Tranel, 2009; Murphy, Geary, Millgate, Catmur, & Bird, 2018 Mikkelson et al, 2019), or if the nature of interoceptive signals changes, so too will our affective experiences and social behaviors.

A third theoretical framework—the Strengths and Vulnerabilities Integration (SAVI) model (Charles, 2010)—incorporates aspects of each of these models. SAVI proposes that emotional wellbeing later in life is determined by balancing age-related strengths in socioaffective processing (e.g., older adults are thought to have improved emotion regulation strategies, however see Isaacowitz, 2022) and physiological vulnerabilities. According to this model, older adults typically report improved wellbeing because they employ strategies that have been learned across their lives to avoid negative or vulnerable settings; however, if they are unable to avoid these settings, they may actually be worse at affective and emotional regulation.

Although these frameworks are for the most part complementary, they focus on what Tinbergen (1963) and Mayr (1993) categorize as *proximate* causal explanations of behavior. That is, existing studies of aging in humans answer questions like: how does socioemotional processing develop across a person's life? What are the biological and psychological mechanisms through which changes in socioaffective processing occur? The study of humans alone cannot, however, speak to what Tinbergen and Mayr refer to as *ultimate* (evolutionary) explanations. Ultimate explanations speak to the evolutionary origins of age-related changes to socioaffective behaviors and are concerned with assessing how such behaviors confer fitness advantages and thus arose through natural selection. Asking ultimate questions can illuminate proximate causes because if features of socioaffective aging trajectories are preserved across phylogeny they may be due to shared features of biological senescence (e.g., changes to the brain and/or the body) in the species that are compared.

Research in rhesus monkeys (*Macaca mulatta*) may prove especially useful for simultaneously testing hypotheses about the evolutionary origins of age-related changes to socioaffective processing and informing proximate mechanisms through which changes to socioaffective processing occur. Rhesus monkeys may also serve as an animal model in which mechanistic questions about human health and disease of aging can be asked and treatments and interventions for such diseases developed. Rhesus monkeys have shorter lifespans compared to people (with a median lifespan in the wild of approximately 15 years; Hoffman et al., 2010; and up to 25 in captivity; Colman et al., 2009), mature at a rate that is 3-4 times faster than humans, reaching "adulthood" and sexual maturity around 3.5-5 years of age (Plant et al., 2005) and old age around 18 years of age (Fooden, 2000), and share key features of human neurobiology, physiology, and development (Kolk & Rakic, 2022; Laubach et al., 2018; Phillips et al., 2014; Preuss & Wise, 2022). That said, despite a rich history of studying the effects of aging on cognition in this species (Baxter, 2001; Upright & Baxter, 2021), there is a severe dearth of investigations into how social and affective processing differs across monkeys' lifespans—and the studies that do are not directly comparable to those typically used in human studies of socioaffective aging (for a review Machanda & Rosati, 2020). The studies that constitute my dissertation address this limitation by using methods directly comparable to those in humans to test psychological and evolutionary hypotheses as to the origins of and mechanisms through which changes to social and affective processing arise.

Overview

The experiments in the first chapter test for age-related differences in visual attention towards faces of conspecifics of varying affective content (e.g., threatening faces vs. neutral faces). In humans, there is substantial evidence that younger adults possess biases in visual attention towards negative facial stimuli but, interestingly, that this bias diminishes with age in a pattern called the age-related *positivity effect* (for a review see Carstensen & DeLiema, 2018, and a meta-analysis see Reed et al., 2014). Whether or not this age-related positivity effect exists in nonhuman primates is unknown and the mechanisms through which the effect emerges is debated. Results of this study help to inform the evolutionary and psychological origins of age-related changes to visual processing of psychosocial stimuli.

The second chapter evaluates how age impacts monkeys' autonomic nervous system (ANS) response patterns to socioaffective content. Despite what intuition may suggest, there is substantial variation in reported age-related differences in ANS responsivity to socioaffective stressors, with some evidence for increases and other evidence for decreases in reactivity with age (for a review Hotta & Uchida, 2010). Understanding the sources of variation in physiological responding in aging is important as an inability to adapt to physiological challenges carries potentially deadly consequences for aged organisms. The content of this chapter serves to uncover potential sources of this variation and inform evolutionary hypothesis regarding how and why changes to ANS responding occur in aging.

The final chapter adopts a large-scale lifespan perspective to evaluate how aspects of biology, behavior, and social environment in infant monkeys predicts mortality rates across twenty years of follow-up. This research is important for understanding and characterizing socioaffective aging trajectories in rhesus monkeys, generally, and for informing critical developmental windows in which adversity may impact survival of primates specifically.

References

Barrett, L. F. (2017). The theory of constructed emotion: An active inference account of interoception and categorization. *Social Cognitive and Affective Neuroscience*, *12*(1), 1–23. https://doi.org/10.1093/scan/nsw154

Baxter, M. G. (2001). Cognitive Aging in Nonhuman Primates. In P. R. Hoff & C. V. Mobbs (Eds.), *Functional Neurobiology of Aging* (pp. 407–419). Academic Press.

Bruine de Bruin, W., Parker, A. M., & Strough, J. (2020). Age differences in reported social networks and well-being. *Psychology and Aging*, *35*(2), 159.

Burr, D. A., Castrellon, J. J., Zald, D. H., & Samanez-Larkin, G. R. (2021). Emotion dynamics across adulthood in everyday life: Older adults are more emotionally stable and better at regulating desires. *Emotion*, *21*(3), 453.

Carstensen, L. L., & DeLiema, M. (2018). The positivity effect: A negativity bias in youth fades with age. *Current Opinion in Behavioral Sciences*, *19*, 7–12. https://doi.org/10.1016/j.cobeha.2017.07.009

Carstensen, L. L., Isaacowitz, D. M., & Charles, S. T. (1999). Taking Time Seriously: A Theory of Socioemotional Selectivity. *American Psychologist*, 17.

Carstensen, L. L., Turan, B., Scheibe, S., Ram, N., Ersner-Hershfield, H., Samanez-Larkin, G. R., Brooks, K. P., & Nesselroade, J. R. (2011). Emotional experience improves with age: Evidence based on over 10 years of experience sampling. *Psychology and Aging*, *26*(1), 21.

Charles, S. T. (2010). Strength and vulnerability integration: A model of emotional well-being across adulthood. *Psychological Bulletin*, *136*(6), 1068–1091. https://doi.org/10.1037/a0021232

Charles, S. T., & Carstensen, L. L. (2010). Social and emotional aging. *Annual Review of Psychology*, *61*, 383–409.

Chatterji, S., Byles, J., Cutler, D., Seeman, T., & Verdes, E. (2015). Health, functioning, and disability in older adults—Present status and future implications. *The Lancet*, *385*(9967), 563–575.

Colman, R. J., Anderson, R. M., Johnson, S. C., Kastman, E. K., Kosmatka, K. J., Beasley, T. M., Allison, D. B., Cruzen, C., Simmons, H. A., Kemnitz, J. W., & Weindruch, R. (2009). Caloric Restriction Delays Disease Onset and Mortality in Rhesus Monkeys. *Science*, *325*(5937), 201–204. https://doi.org/10.1126/science.1173635

Damasio, A. R., Everitt, B. J., & Bishop, D. (1996). The Somatic Marker Hypothesis and the Possible Functions of the Prefrontal Cortex. *Philosophical Transactions: Biological Sciences*, *351*(1346,), 1413–1420.

Fiske, A., Wetherell, J. L., & Gatz, M. (2009). Depression in Older Adults. *Annual Review of Clinical Psychology*, *5*(1), 363–389. https://doi.org/10.1146/annurev.clinpsy.032408.153621

Fooden, J. (2000). Systematic review of the rhesus macaque, Macaca mulatta (Zimmermann, 1780) / Jack Fooden. In *Systematic review of the rhesus macaque, Macaca mulatta (Zimmermann, 1780) / Jack Fooden.* Field Museum of Natural History,. https://doi.org/10.5962/bhl.title.7192

Fung, H. H., Carstensen, L. L., & Lang, F. R. (2001). Age-related patterns in social networks among European Americans and African Americans: Implications for socioemotional selectivity across the life span. *The International Journal of Aging and Human Development*, *52*(3), 185–206.

Fung, H. H., Lai, P., & Ng, R. (2001). Age differences in social preferences among Taiwanese and Mainland Chinese: The role of perceived time. *Psychology and Aging*, *16*(2), 351.

Graham, E. K., Weston, S. J., Gerstorf, D., Yoneda, T. B., Booth, T., Beam, C. R., Petkus, A. J., Drewelies, J., Hall, A. N., Bastarache, E. D., Estabrook, R., Katz, M. J., Turiano, N. A., Lindenberger, U., Smith, J., Wagner, G. G., Pedersen, N. L., Allemand, M., Spiro, A., … Mroczek, D. K. (2020). Trajectories of Big Five Personality Traits: A Coordinated Analysis of 16 Longitudinal Samples. European Journal of Personality, 34(3), 301–321. https://doi.org/10.1002/per.2259

Hoffman, C. L., Higham, J. P., Mas-Rivera, A., Ayala, J. E., & Maestripieri, D. (2010). Terminal investment and senescence in rhesus macaques (Macaca mulatta) on Cayo Santiago. *Behav Ecol*, *21*(5), 972–978. https://doi.org/10.1093/beheco/arq098

Holt-Lunstad, J., Smith, T. B., & Layton, J. B. (2010). Social relationships and mortality risk: A meta-analytic review. *PLoS Medicine*, *7*(7), e1000316.

Hotta, H., & Uchida, S. (2010). Aging of the autonomic nervous system and possible improvements in autonomic activity using somatic afferent stimulation: Aging of the autonomic nervous system. *Geriatrics & Gerontology International*, *10*, S127–S136. https://doi.org/10.1111/j.1447-0594.2010.00592.x

James, W. (1884). What is an Emotion? *Mind*, *9*(34), 188–205.

Joiner, R. J., Bergeman, C. S., & Wang, L. (2018). Affective experience across the adult lifespan: An accelerated longitudinal design. Psychology and Aging, 33(3), 399.

Kolk, S. M., & Rakic, P. (2022). Development of prefrontal cortex. *Neuropsychopharmacology*, *47*(1), 41–57. https://doi.org/10.1038/s41386-021-01137-9

Kuehn, E., Perez-Lopez, M. B., Diersch, N., Döhler, J., Wolbers, T., & Riemer, M. (2018). Embodiment in the aging mind. *Neuroscience and Biobehavioral Reviews*, *86*(January 2017), 207–225. https://doi.org/10.1016/j.neubiorev.2017.11.016

Labouvie-Vief, G., Grühn, D., & Studer, J. (2010). *Dynamic integration of emotion and cognition: Equilibrium regulation in development and aging.*

Laubach, M., Amarante, L. M., Swanson, K., & White, S. R. (2018). What, If Anything, Is Rodent Prefrontal Cortex? *Eneuro*, *5*(5), ENEURO.0315-18.2018. https://doi.org/10.1523/ENEURO.0315-18.2018

Levy, R. (1994). Aging-associated cognitive decline. Working Party of the International Psychogeriatric Association in collaboration with the World Health Organization. *International Psychogeriatrics*, *6*(1), 63–68.

Luong, G., Rauers, A., & Fingerman, K. L. (2015). *The multifaceted nature of late-life socialization: Older adults as agents and targets of socialization.*

Machanda, Z. P., & Rosati, A. G. (2020). Shifting sociality during primate ageing. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *375*(1811), 20190620. https://doi.org/10.1098/rstb.2019.0620

Mayr, E. (1993). Proximate and ultimate causations. *Biology and Philosophy*, *8*(1).

Meier, S. M., Mattheisen, M., Mors, O., Mortensen, P. B., Laursen, T. M., & Penninx, B. W. (2016). Increased mortality among people with anxiety disorders: Total population study. *British Journal of Psychiatry*, *209*(3), 216–221. https://doi.org/10.1192/bjp.bp.115.171975

Mendes, W. B. (2010). Weakened links between mind and body in older age: The case for maturational dualism in the experience of emotion. *Emotion Review*, *2*(3), 240–244. https://doi.org/10.1177/1754073910364149

Miloyan, B., Bulley, A., Bandeen-Roche, K., Eaton, W. W., & Gonçalves-Bradley, D. C. (2016). Anxiety disorders and all-cause mortality: Systematic review and meta-analysis. *Social Psychiatry and Psychiatric Epidemiology*, *51*(11), 1467–1475. https://doi.org/10.1007/s00127-016-1284-6

Petrican, R., Moscovitch, M., & Grady, C. (2014). Proficiency in positive vs. Negative emotion identification and subjective well-being among long-term married elderly couples. *Frontiers in Psychology*, *5*, 338.

Phillips, K. A., Bales, K. L., Capitanio, J. P., Conley, A., Czoty, P. W., t Hart, B. A., Hopkins, W. D., Hu, S.-L., Miller, L. A., Nader, M. A., Nathanielsz, P. W., Rogers, J., Shively, C. A., Voytko, M. L., ’t Hart, B. A., Hopkins, W. D., Hu, S.-L., Miller, L. A., Nader, M. A., … Voytko, M. L. (2014). Why primate models matter. *American Journal of Primatology*, *76*(9), 801–827. https://doi.org/10.1002/ajp.22281

Plant, T. M., Ramaswamy, S., Simorangkir, D., & Marshall, G. R. (2005). Postnatal and pubertal development of the rhesus monkey (Macaca mulatta) testis. *Annals of the New York Academy of Sciences*, *1061*(1), 149–162.

Pratt, L. A., Druss, B. G., Manderscheid, R. W., & Walker, E. R. (2016). Excess mortality due to depression and anxiety in the United States: Results from a nationally representative survey. *General Hospital Psychiatry*, *39*, 39–45.

Preuss, T. M., & Wise, S. P. (2022). Evolution of prefrontal cortex. *Neuropsychopharmacology*, *47*(1), 3–19. https://doi.org/10.1038/s41386-021-01076-5

Russell, J. A. (2003). Core affect and the psychological construction of emotion. *Psychol Rev*, *110*(1), 145–172.

Schachter, S., Fd, A., & Singer, J. E. (1962). *COGNITIVE, SOCIAL, AND PHYSIOLOGICAL DETERMINANTS OF EMOTIONAL STATE*. *69*(5), 21.

Schulz, R., Beach, S. R., Ives, D. G., Martire, L. M., Ariyo, A. A., & Kop, W. J. (2000). Association between depression and mortality in older adults: The Cardiovascular Health Study. *Archives of Internal Medicine*, *160*(12), 1761–1768.

Steptoe, A., Shankar, A., Demakakos, P., & Wardle, J. (2013). Social isolation, loneliness, and all-cause mortality in older men and women. *Proceedings of the National Academy of Sciences*, *110*(15), 5797–5801. https://doi.org/10.1073/pnas.1219686110

Thomas, M. L., Kaufmann, C. N., Palmer, B. W., Depp, C. A., Martin, A. S., Glorioso, D. K., Thompson, W. K., & Jeste, D. V. (2016). Paradoxical trend for improvement in mental health with aging: A community-based study of 1,546 adults aged 21-100 years. *The Journal of Clinical Psychiatry*, *77*(8), 0–0.

Tinbergen, N. (1963). On aims and methods of ethology. *Zeitschrift Für Tierpsychologie*, *20*(4), 410–433.

United Nations, Department of Economic and Social Affairs, & Population Division. (2020). *World population ageing, 2019 highlights.*

Upright, N. A., & Baxter, M. G. (2021). Prefrontal cortex and cognitive aging in macaque monkeys. *American Journal of Primatology*. https://doi.org/10.1002/ajp.23250

Chapter 1

See no evil: Attentional bias towards threat is diminished in aged rhesus monkeys (*Macaca mulatta*)

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Abstract

Prior evidence demonstrates that relative to younger adults, older human adults exhibit attentional biases towards positive and/or away from negative socioaffective stimuli (i.e., the age-related *positivity effect*). Whether or not the effect is phylogenetically conserved is currently unknown and its biopsychosocial origins are debated. To address this gap, we evaluated how visual processing of socioaffective stimuli differs in aged, compared to middle-aged, rhesus monkeys (*Macaca mulatta*) using eye-tracking in two experimental designs that are directly comparable to those historically used for evaluating attentional biases in humans. Results of our study demonstrate that while younger rhesus possess robust attentional biases towards threating pictures of conspecifics faces, aged animals evidence no such bias. Critically, these biases emerged only when threatening faces were paired with neutral and not ostensibly 'positive' faces, suggesting social context modifies the effect. Results of our study suggest evolutionarily shared mechanisms drive age-related decline in visual biases towards negative stimuli in aging across primate species.

Keywords: affective aging, nonhuman primates, positivity effect, visual attention, emotion

See no evil: Attentional bias towards threat is diminished in aged rhesus monkeys (*Macaca mulatta*)

Mounting evidence demonstrates that older adults' emotional lives fare relatively well despite the vicissitudes of aging. On average, older adults report improvement (that is, reduced negativity and/or increased positivity) in momentary affective experiences as they age (Carstensen et al., 2011; Gross et al., 1997; Mroczek, 2001; Scheibe et al., 2013), are thought to possess more effective emotion regulation strategies compared to younger adults (Eldesouky & English, 2018; Gross et al., 1997; but see Isaacowitz, 2021), and exhibit information processing biases (e.g., in memory and attention) towards positive and/or away from negative affective information (for a review see Carstensen & DeLiema, 2018; for a meta-analysis see Reed et al., 2014). Understanding the biopsychosocial factors that drive these age-related improvements in wellbeing is critical because affective disorders like depression carry potentially deadly consequences for older adults (Fiske et al., 2009; Wei et al., 2021). In this report, we adopt a comparative approach by studying nonhuman primates to evaluate the possibility that there are evolutionarily conserved psychological features of aging that can be used to infer phylogenetically shared mechanisms that promote wellbeing later in life.

A hallmark feature of human socioaffective aging is a phenomenon referred to as the age-related *positivity effect*—an age-related information processing bias towards positive, and/or away from negative, affective information (for a review see Carstensen & DeLiema, 2018; for a meta-analysis see Reed et al., 2014).[1] For example, compared to younger adults, older adults tend to recall proportionately more positive relative to negative information (Charles et al., 2003; Gerhardsson et al., 2019; Joubert et al., 2018; Q.

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[1] Importantly, the age-related positivity effect does *not* refer to any age-related biases in affective experience. While there is some evidence of improvement in affective experiences with age (Carstensen et al., 2011; Mroczek, 2001; Sheibe et al., 2013), the positivity effect is solely concerned with information processing (e.g., memory and attention) biases related to valenced stimuli.

Kennedy et al., 2004; Mammarella et al., 2016), use more positive language (Kyröläinen et al., 2021), and attend more to positively and less to negatively valenced visual stimuli (Isaacowitz et al., 2006a, 2006b; Lee & Knight, 2009; Mather & Carstensen, 2003, 2005; Nikitin & Freund, 2011; Orgeta, 2011; Talbot et al., 2018; Tomaszczyk & Fernandes, 2014; Wang et al., 2020). Such selective processing of valenced stimuli is hypothesized as one mechanism through which older adults regulate their affective states (Isaacowitz et al., 2008; D. R. Johnson, 2009; Noh et al., 2011; Urry & Gross, 2010); as such, understanding the biopsychosocial mechanisms that facilitate the positivity effect is paramount to promoting wellbeing in aging populations.

One way in which we may understand mechanisms driving the age-related positivity effect is through the study of nonhuman primates, who possess central (e.g., Preuss & Wise, 2021) and autonomic (e.g., Bliss-Moreau, Machado, et al., 2013) nervous systems that are largely homologous with humans in both structure and function. As nonhuman primates' neurophysiology undergoes changes that are similar to those observed in aging humans (Alexander et al., 2008; Shively et al., 2020; Stonebarger et al., 2021; Upright & Baxter, 2021), we may expect nonhuman primates to display age-related changes to affective processing that are comparable to those observed in humans. If they do not undergo such age-related changes in affective processing, then it suggests that the mechanisms of the age-related positivity effect may be human specific and not solely dependent on aging neurobiological systems that are evolutionarily conserved.

There is a paucity of research on how affective processing in nonhuman primates is impacted in aging even though there is great promise from such investigations. In one recent study in free-ranging rhesus macaques (*Macaca mulatta*), older monkeys possessed an attentional bias *towards* photographs of conspecifics making facial displays associated with threatening (Rosati et al., 2018)—the opposite pattern observed in aged humans. In a second study of Barbary macaques (*Macaca sylvanus*), there were no age-related differences in looking time towards photographs of close social partners (positive condition) compared to non-close social partners (neutral condition) (Almeling et al., 2016).

In contrast to the sparsity of studies on age-related changes to nonhuman primates psychological processing of affective stimuli, there is a literature that reveals substantial variation in primates' social behavior across their lifespans (for a review see Machanda & Rosati, 2020). Compared to younger monkeys, older rhesus (*Macaca mulatta*) (Corr, 2003), Japanese (*Macaca fuscata*) (Hauser & Tyrrell, 1984; Nakamichi, 1984), stump-tail (*Macaca arctoides*) (Hauser & Tyrrell, 1984), and Barbary (*Macaca sylvanus*) (Almeling et al., 2016, 2017) macaques spend less time in close proximity with other animals and tend to groom fewer social partners, but are themselves groomed at equivalent rates. These behaviors mirror developmental shifts in aged humans demonstrating people become more socially selective with age (Carstensen & Fredrickson, 1998; English & Carstensen, 2014; Fung & Carstensen, 2006; Lansford et al., 1998). For example, older people's social networks are typically smaller in size compared to younger people's (for a review see Wrzus et al., 2013) and this appears due to active culling of social connections leaving only those that are meaningful (English & Carstensen, 2014; Luong et al., 2011). This feature of human's social network reconfiguration is concomitant with processing biases towards positive and away from negatively valenced stimuli, leading some authors to conclude that the psychological features driving the positivity effect and the network pruning are due to shared mechanisms (English & Carstensen, 2014).

Given the current dearth of studies on socioaffective aging in nonhuman primates that afford direct comparison to studies done in humans, we evaluated age-related differences in monkeys' attention to socioaffective visual stimuli using a highly translatable experimental design. Eleven (N = 6 aged) rhesus monkeys (*Macaca mulatta*) completed two laboratory-based tasks that are commonly used for assessing attentional biases towards affective information in humans: the dot-probe and competing attention tasks (e.g., see Isaacowitz et al., 2006a, 2006b). Based on previous literature (Orgeta, 2011; Tomaszczyk & Fernandes, 2014), we hypothesized that initial orienting responses towards affective facial stimuli would be preserved in aging but that older rhesus would evidence biases towards positive and/or away from negatively valenced facial stimuli in the competing attention task (Isaacowitz et al., 2006a, 2006b). Results of our experiments help to inform the psychological mechanisms that drive the age-related positivity effect in humans.

Materials & Methods

This study was carried out at the California National Primate Research Center (CNPRC) following the recommendations in the Guide for the Care and Use of Laboratory Monkeys by the National Institutes of Health. All experimental procedures were approved by the University of California, Davis Institutional Animal Care and Use Committee under protocol 21881.

Subjects

Subjects were N=5 middle-aged (3 females, median age: 10.6 years, range: 9.4 – 14) and N=6 older adult rhesus macaques (*Macaca mulatta*) (3 females, median age: 20.5 years, range: 17.3 – 23.3) that were born and reared at the CNPRC. Monkeys were socially housed with a compatible partner, each having access to standard adult macaque laboratory caging (66 cm wide × 61 cm long × 81 cm high). Monkeys were paired either for a minimum of 6 hours per day, 5-days a week, or 24 hours per day in either full access (allowing both monkeys access to both enclosures during the pairing time) or through a metal grate (allowing tactile access, but preventing full contact). Five of the monkeys were housed in same-sex pairs.

The housing room was maintained on a 12-hour light and dark cycle, with lights turned on at 0600 hrs and off at 1800 hrs. Monkeys were fed monkey chow (Lab Diet #5047, PMI Nutrition International INC, Brentwood, MO) twice daily, provided with fresh fruit and vegetables twice per week, and had access to water *ad libitum*. As standard practice at the CNPRC, monkeys received daily enrichment (e.g., a rice/oat/pea mixture on their forage boards once per day, a rubber Kong toy/metal ball, fresh coconuts once per month, and periodic delivery of fruit and vegetables in puzzle balls or puzzle tubes).

Candidate monkeys underwent physical examinations prior to enrollment in the study. Monkeys with cardiac abnormalities (e.g., lateral ventricular hypertrophy), problems with vision that would interfere with eye-tracking, or other health problems that would interfere with eye-tracking data collection were not enrolled.

Training

Monkeys were first trained to enter a plexiglas primate chair from a metal transport box and to lift their heads into a yoked position using methods previously described (Bliss-Moreau, Machado, et al., 2013a; Bliss-Moreau, Theil, et al., 2013). All eye-tracker training and testing occurred while monkeys sat in the primate chair to minimize movement and ensure quality eye-tracking data collection.

Monkeys were trained to interact with the eye-tracker in two phases: in the first phase, monkeys learned to fixate for 500 ms on a white circle (radius of 2 visual degrees) displayed on the center of a Tobii Pro TX300 infrared eye tracker (Tobii, Stockholm, Sweden) for a small juice reward (0.1 mL). The juice reward was followed by a 2-6s variable inter-trial interval (ITI). After reliably making central fixations, monkeys entered the second phase of testing in which the central fixation was no longer rewarded, however after making the central fixation a white circle appeared randomly on the left- or right-hand side of the screen (radius of 2 visual degrees, 10-degrees away from the center of the screen). If the animal fixated on this circle (hereafter referred to as the “probe”) within 20 seconds, they were rewarded and the trial was terminated. If the animal did not fixate on the probe within 20 seconds, the trial was terminated and the animal was not rewarded. Monkeys were considered trained once they completed 48 trials of Phase 2 within one hour over three consecutive days of training.

Experimental protocol

Testing occurred Monday through Friday between 0800 and 1800 hours over fifteen days of testing. Monkeys were transported individually from their home enclosure to the testing room where they were transferred into the primate chair and placed 65 cm from the eye-tracker. The eye-tracker was then calibrated using Tobii Studio's (Tobii, Stockholm, Sweden) five-point calibration designed for infants by having monkeys make fixations at video stimuli presented in each of the four corners of the screen as well as in the center. Lighting in the test room was turned off and a white noise generator (60 dB) masked auditory distractions for the duration of the experiment. A divider placed in the room ensured the experimenter was out of view from the monkey.

Stimuli

One hundred and seventy-eight facial stimuli from twenty monkeys unfamiliar to the test subjects were used as stimuli. The stimuli consisted of two facial behaviors (lip-smack or open-mouth threat) or a neutral face (no behavior) directed at the camera and were selected from an established photo library (Gothard et al., 2004). In rhesus monkeys, a "lip-smack" behavior is typically an affiliative/submissive social signal that consists of pursed lips, ears slightly pinned back, and a relaxed brow. The lip-smack is the only facial behavior made by monkeys thought to typically carry positive affective valence (for a review see Bliss-Moreau & Moadab, 2017). An open-mouth threat face consists of a widely opened mouth (with or without the bottom teeth displayed), slightly furrowed brow, and intense eyes and is generally a signal of aggression dominance (Bliss-Moreau & Moadab, 2017). Images were preprocessed by first manually removing the background—leaving only the face and ears—then converting the images to black and white. The edges of the faces were smoothed and any large blemishes were removed. Both the dot-probe and competing attention tasks described below used the same set of stimuli.

Eye-Tracking Data Collection and Processing

Eye-tracking data were sampled continuously at 300 Hz using a Tobii Pro TX300 infrared eye tracker (Tobii, Stockholm, Sweden) and integrated with the display of stimuli using the Tobii Pro SDK for Python (Tobii, Stockholm, Sweden). On each day, a standard five-point calibration was conducted using the Tobii

Pro Software prior to testing to ensure accuracy of eye position data. Gaze location coordinates were used to compute time-to-fixate on the probe (dot-probe task) and looking time (competing attention task) on each trial.

Dot-Probe Task

Monkeys completed a visual version of the dot-probe task (MacLeod et al., 1986) to test for age-related differences in orienting response towards the facial stimuli. On each trial, monkeys were required to make a 500 ms central fixation on the screen, immediately after which two faces (approximately 7° x 7°) simultaneously flashed for 200 ms on the left- and right-hand side of the screen (**Figure 1.1**). The faces depicted the same animal generating different facial behaviors (i.e., a lip-smack, neutral face, or open-mouth threat). Immediately following the stimuli, the "probe" appeared pseudo-randomly under one of the faces. Subjects were then required to fixate on the probe within 20 seconds to receive a juice reward, followed by a 2-6 s ITI. Each animal completed 210 trials over five days of testing (42 trials each day), with 14 trials of lip-smack vs. neutral, 14 lip-smack vs. threat, and 14 neutral vs. threat presented in a randomized order on each day. Facial stimuli and probe locations were counterbalanced such that each appeared equally on the left- and right-hand side of the screen. Stimuli were presented and gaze location recorded using PsychoPy (Peirce et al., 2019).

Competing Attention Task

The competing attention task proceeded nearly identically to the dot-probe task, insofar as monkeys made a central fixation (500 ms) after which two faces were displayed on each trial with the only difference being that the facial stimuli were displayed for 5000 ms. Animals then fixated on the probe (200 ms fixation) for receipt of a juice reward followed by a 2000-6000 ms variable ITI. Presenting stimuli for this extended time frame (5000 ms) allowed for voluntary control of attention towards the visual stimuli.

Monkeys completed 420 trials over ten days of testing (42 trials each day), with 14 trials of lip-smack vs. neutral, 14 lip-smack vs. threat, and 14 neutral vs. threat presented in a randomized order on each day.

Statistical methods

All analyses were conducted in R version 4.0.3. Mixed effects Cox proportional hazards models using the *coxme* package (Therneau, 2020) and mixed effects logistic regression models using the *lme4* package (Bates et al., 2015) were used to model, at a trial level, the time-to-fixate on the probe (Dot-Probe) and the proportion of time looking at a target stimuli relative to total looking time at both stimuli (Competing Attention), respectively. The utilization of proportional hazards modeling (a modeling technique within the family of survival analysis) was required due to the censoring of the dependent variable in the dot-probe task—that is, on some trials, monkeys did not fixate on the probe within the allotted time frame and therefore the time-to-fixate was not observed. Survival analysis methods account for this censoring process and allow for unbiased estimation of parameters of interest in the presence of censoring. Bayesian mixed effects bivariate log-normal hurdle models were used to jointly model looking times at each of the faces during the competing attention task. Mixed effects log-normal models were used for the looking time data because these data are typically known to follow log-normal distributions (Csibra et al., 2016). Hurdle models decompose a dependent variable (in this case, looking time) into zero and non-zero values. One model is used to predict whether or not the dependent variable was zero (i.e., crossing over the "hurdle"), whereas another model is used to model the value of the response conditional on the dependent variable being non-zero.

Separate models were fit for each of the three conditions: lip-smack vs. neutral, threat vs. neutral, and lip-smack vs. threat. Primary age-related hypotheses were tested by including monkeys' age as a continuous covariate in the model with interaction terms where appropriate. Random intercepts were given for subjects to account for any within-subject correlation of responses. Null hypothesis significance testing was conducted at the $\alpha = 0.05$ level and 95% confidence intervals (CI), or their Bayesian counterparts, are presented where appropriate.

Transparency and Openness

Data, analysis, and research code are available upon reasonable request and will be uploaded to OSF (https://osf.io/qn32t/) once all papers from this set of experiments have been completed. The study design and analysis plan were not pre-registered. The initial target sample size was N = 12 monkeys and that estimate was based on availability of aged monkeys to participate in the project and realistic estimates of time and cost. Ultimately, because of delays related to the COVID-19 pandemic, only N = 11 animals were able to complete the study.

Dot-Probe Task

Separate mixed effects Cox proportional hazards models were used to test for age-related differences in the time-to-fixate on the probe, treating trials nested within monkeys. Specifically, an interaction term between animal age (continuously coded) and the facial behavior under which the probe appeared was used to test for age-related differences in the time-to-fixate as a function of the facial behavior under which the probe appeared. All models adjusted for animal sex, stimulus animal sex, and probe location (left or right side of the screen). One animal was unable to be trained to perform this experiment (the animal would not fixate on the probe for a reward) and thus did not partake in this experiment, resulting in N = 10 subjects (N = 6 aged, N = 4 middle-aged).

Across all monkeys and trial types, the median time-to-fixate on the probe was 1.23 seconds (95% CI: [1.2, 1.3]) and monkeys' median time-to-fixate on the probe ranged from 0.8 s to 3.0 s. On average, the facial behavior under which the probe appeared did not significantly influence the time-to-fixate in any of the three conditions (lip-smack vs. neutral: HR = 0.97, 95% CI: [0.84, 1.12], z = -0.41, p = 0.68; threat vs. neutral: HR = 1.07, 95% CI: [0.92, 1.24], z = 0.92, p = 0.36; lip-smack vs. threat: HR = 1.01, 95% CI: [0.87, 1.18], $z = 0.18$, $p = 0.86$). Further, there was no significant evidence for age-related differences in the degree to which facial behaviors influenced fixation times in any of the three experimental conditions (see **Table 1.1**). Probe location was, however, a significant predictor of time-to-fixation in lip-smack vs. neutral and lip-smack vs. threat trials, with monkeys fixating faster when the probe was located on the right hand side of the screen (lip-smack vs. neutral: $HR = 1.29$, 95% CI: [1.11, 1.49], $z = 3.29$, $p = 0.001$; lip-smack vs. threat: $HR = 1.19$, 95% CI: [1.02, 1.38], $z = 2.21$, $p = 0.027$), highlighting the importance of counterbalancing the location of stimuli in dot-probe tasks in nonhuman primates.

Competing Attention Task

Separate mixed effects logistic regression models for each of the three experimental conditions (lip-smack vs. neutral, threat vs. neutral, and lip-smack vs. threat) were fit to investigate age-related differences in biases in the proportion of time spent looking at affective faces. We computed an index that provides information about how attention was biased towards/away from particular stimuli—the time looking at the target image divided by the total looking time at both images on each trial. Values of 0.5 thus correspond to no bias because looking time would be the same for both stimuli; values close to one indicate biases in favor of looking towards a given facial behavior; values close to zero reflect biases in favor of the non-target image. Only trials during which monkeys looked at least one of the stimuli were analyzed. All models adjusted for animal sex, stimulus animal sex, and age (continuously coded and mean centered for interpretability of the intercept). Results of the models are presented in **Table 1.2** and **Figure 1.2**.

Across all monkeys, there was no average bias in visual attention towards lip-smack compared to neutral faces ($p = 0.36$) or lip-smack compared to threat faces ($p = 0.58$). There was however a significant bias towards threat compared to neutral faces, with an odds of 1.4 in favor of looking at threat compared to neutral facial stimuli ($Odds = 1.4$, 95% CI [1.15, 1.72], $p = 0.001$). Whereas there was no significant evidence that age was associated with a bias in visual attention towards lip-smack compared to neutral ($OR = 1.01$, 95% CI [0.99, 1.03], $z = 0.87$, $p = 0.38$) or lip-smack compared to threat ($OR = 1.00$, 95% CI [0.98, 1.03], *z* = 0.43, *p* = 0.67) faces, there was a significant association between age and bias in visual attention towards threat compared to neutral faces such that the odds of looking at threat decline by a factor of 0.97 for each year increase in age (*OR* = 0.97, 95% CI [0.95, 0.99], *z* = -2.25, *p* = 0.024), resulting in no looking time bias in older monkeys (**Figure 1.2b**). Neither monkey sex nor sex of the monkey making the facial behavior were significant predictors of bias in visual attention in any of the models (**Table 1.2**).

While the models above assessed the relative amount of time animals spent looking at each stimulus when they looked at one or both stimuli per trial, we performed a complimentary set of analyses on *absolute* looking time in order to assess overall visual engagement with the stimuli including all trials with no exclusion criteria. This analysis was performed using a hurdle model, which decomposes looking time into two independent processes: 1) a logistic regression model that predicts whether or not the animal spent *any* time looking at a stimulus and 2) a model of how long the animal looked at stimuli conditional on them spending a non-zero amount of time looking at a stimulus (i.e., jumping over the ‘hurdle’). On lip-smack vs neutral trials, animals had a 40% (95% Bayesian CI [26%, 55%]) chance of looking at the lip-smack and a 37% (95% Bayesian CI [24%, 51%]) chance of looking at neutral stimuli. Further, age was not associated with the odds of looking at lip-smack (*OR* = 1.02, 95% Bayesian CI [0.93, 1.13]) or neutral faces (*OR* = 1.04, 95% Bayesian CI [0.96, 1.44]). On threat vs neutral trials, animals had a 37% (95% Bayesian CI [22%, 55%]) chance of looking at the lip-smack and a 46% (95% Bayesian CI [32%, 61%]) chance of looking at neutral stimuli. Again, age was not associated with the odds of looking at lip-smack (*OR* = 1.06, 95% Bayesian CI [0.95, 1.19]) or neutral faces (*OR* = 1.01, 95% Bayesian CI [0.92, 1.12]). Lastly, on lip-smack vs threat trials, animals had a 38% (95% Bayesian CI [24%, 54%]) chance of looking at the lip-smack and a 36% (95% Bayesian CI [21%, 53%]) chance of looking at threat stimuli and age was not associated with the odds of looking at lip-smack (*OR* = 1.03, 95% Bayesian CI [0.93, 1.14]) or neutral faces (*OR* = 1.03, 95% Bayesian CI [0.92, 1.16]).

On lip-smack vs. neutral trials, overall looking time did not differ between stimuli (b = 0.18, 95% Bayesian CI [-0.29, 0.63]), and age was modestly associated with looking time towards lip-smack, with older animals attending less to lip-smack faces (b = -0.05, 95% Bayesian CI [-0.09, 0.00]) and neutral faces (b = -0.04, 95% Bayesian CI [-0.10, 0.01]). On threat vs. neutral trials, overall looking time did not differ between stimuli (b = 0.29, 95% Bayesian CI [-0.2, 0.79]), and age was modestly associated with looking time towards threat, with older animals attending less to threatening stimuli (b = -0.06, 95% Bayesian CI [-0.11, 0.00]) and neutral faces (b = -0.06, 95% Bayesian CI [-0.12, 0.00]). Lastly, on lip-smack vs. threat trials, overall looking time did not differ between stimuli (b = -0.03, 95% Bayesian CI [-0.52, 0.45]), and age was again modestly and negatively associated with looking times, with older animals attending less to both lip-smack (b = -0.06, 95% Bayesian CI [-0.12, 0.00]) and threat faces (b = -0.05, 95% Bayesian CI [-0.10, 0.01]).

Discussion

The goal of this study was to test the hypothesis that, like humans, rhesus monkeys display an age-related bias in visual attention towards positive, or away from negative, affective stimuli (i.e., the age-related *positivity effect*) (for a review see Carstensen & DeLiema, 2018; for a meta-analysis see Reed et al., 2014). Critically, unlike previous work in nonhuman primates (Rosati et al., 2018; Rosati & Santos, 2017), our experiments used precise eye-tracking technology that allows for direct comparison to research performed in humans (e.g., Isaacowitz et al., 2006a, 2006b; Mather & Carstensen, 2003). Our results demonstrate a nuanced age-related difference in visual attention towards faces of conspecifics engaging in different facial behaviors. Despite no age- or facial behavior-related differences in the dot-probe task, the competing attention task revealed a robust bias in looking time towards open-mouth threat compared to neutral faces that was present in middle-aged but absent in aged monkeys. No such biases were apparent in looking time in lip-smack vs neutral or lip-smack vs threat conditions. These results suggest that rhesus monkeys display age-related differences in attentional biases towards threat analogous to the human positivity effect. No such looking time biases were present in the lip-smack vs. threat or lip-smack vs. neutral conditions of the competing attention task. While age did not impact the odds that monkeys looked at facial stimuli, older animals spent less time overall surveying facial stimuli but when animals *were* looking at stimuli, younger animals evidenced a bias towards attending towards threatening faces whereas older animals evidenced no such bias.

Though the positivity effect has been documented using the dot-probe task in humans (Lee & Knight, 2009; Mather & Carstensen, 2003; Orgeta, 2011; Talbot et al., 2018; Tomaszczyk & Fernandes, 2014), the effect only emerges under certain experimental configurations making it altogether not particularly surprising that we did not find effects in this sample. For example, Orgeta (2011) found no evidence of the effect when stimuli were presented for 17 ms or 500 ms but did when stimuli were presented for 1000 ms. The observation that the positivity effect typically emerges at longer timescales (> 500 ms) has led several authors to conclude that this is a feature rather than a limitation of the dot-probe paradigm. That is, because the effect is only observed at longer time scales, it may be driven by regulatory mechanisms and not due to biases in the initial threat detection (Isaacowitz et al., 2009; Lee & Knight, 2009; Mather & Knight, 2006; Orgeta, 2011; however see Kennedy et al., 2020)—and thus better indexed in tasks that give the option for longer looking times, as in our competing attention task. It is for this reason that we used a shorter presentation time (200 ms) in our dot-probe paradigm. We hypothesized that there would be no age-related differences as a function of probe location (i.e., in the location of a threat or lip-smack) but that all monkeys would fixate on the probe more quickly when under a threat or lip-smack, serving as evidence for preserved salience detection in aging. Our results initially appear to corroborate this hypothesis; however, the dot-probe task itself failed to induce biases in reaction times rendering our null results equivocal.

There are several potential reasons why the facial behavior stimuli failed to significantly influence reaction times in the dot-probe task. First, low reliability of the dot-probe task (Amir et al., 2016; Chapman et al., 2019; Kappenman et al., 2014; Reutter et al., 2017; Schmukle, 2005; Staugaard, 2009; Strauss et al., 2005; Waechter et al., 2014; Waechter & Stolz, 2015; White et al., 2016) potentially lowered statistical power (Matheson, 2019) to detect differences in reaction times as a function of stimulus animal facial behaviors. Relatedly, our limited sample size of eleven animals likely reduced the statistical power of our study as the effect sizes found in the human literature are relatively small[2]. It is also possible that our animals did not fixate on the probe quickly enough for the effect to reveal itself. Our data, however, suggest this is not the case; our monkeys fixated on the probe between 0.8 and 3.1 s on average, which is within the time ranges in which humans typically respond while performing dot-probe tasks. A last potential reason is that the dot-probe paradigm is not effective for assessing attentional biases in monkeys—this too does not appear to be the case as several groups have successfully utilized the paradigm in nonhuman primates (Cassidy et al., 2021; King et al., 2012; Kret et al., 2016; Parr et al., 2013; for a review see van Rooijen et al., 2017). It is possible, however, that our stimuli were not potent enough to induce the required capture of attention in order to detect differences in reaction times. A future study using more salient stimuli, in a larger sample, with a greater number of trials is warranted.

In contrast to the dot-probe task, results from our competing attention paradigm, which has been shown to be more reliable than the dot-probe task in humans (Waechter et al., 2014)[3], revealed a robust bias in looking time towards threat vs. neutral faces in middle-aged animals that was absent in aged animals. While the human literature typically demonstrates looking time biases both towards positive *and* away from negatively valenced facial expressions (for a review see Reed et al., 2014), our findings only provide evidence for the latter in monkeys (and only when negative faces are paired with a neutral face). This may suggest important species differences in age-related changes in affective processing; however, it is

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[2] For example, most dot-probe effect sizes in Reed et al. (2014) have Cohens’ *d* < 0.5

[3] Waechter and colleagues (2014) showed that displaying faces on a screen for 5000 ms, exactly as we did, had higher reliability for detecting individual differences in peoples’ attention towards threatening faces compared to the dot-probe paradigm.

important to note that neither younger nor older animals in our study showed any visual attention bias towards (or away from) the lip-smack facial behavior compared to the neutral behavior. This may be because, in contrast to the open-mouth threat facial configuration that is largely unambiguous for rhesus monkeys inasmuch as it invariably carries negative valence, lip-smack behaviors are more subtle, dynamic (including movement of the lips) and are used in a wider range of social contexts (sometimes signaling affiliation and sometimes as a subordinate display) (Maestripieri, 1997; Maestripieri & Wallen, 1997). For this reason, the lip-smack behavior may not be necessarily "positive", as is typically assumed for human smiles (Niedenthal, 2007; but see Barrett et al., 2019), thus we caution comparing our results directly to results using smiling faces in the human literature.

Our finding of age-related decline in attention to threat is consistent with the human literature and some of the nonhuman primate literature but contradicts at least one previously published finding in nonhuman primates. Consistent with our findings of no age-related differences in attention between lip-smack and neutral faces, a study in Barbary macaques (*Macaca sylvanus*) found no age differences in looking time towards photographs of close social partners (positive condition) compared to non-close social partners (neutral condition) (Almeling et al., 2016). In contrast to our effects, Rosati and colleagues (2018) observed that older monkeys (*Macaca mulatta*) evidenced an age-related bias in looking *towards* open-mouth threat faces over neutral faces compared to younger monkeys—the exact opposite effect that we observed. Critically, each of these studies presented stimuli in succession and thus compared overall looking times and not simultaneously, as is typically done when assessing looking time biases in the human literature and as we did here. Perhaps more importantly, these experiments were conducted outdoors in field-like settings in which the subjects examined were willing to approach the experimenters. This difference in design may have led to the differences in observed findings through several mechanisms. First, animals tested in field settings may have led to selection bias as propensity to approach the experimenters was likely associated with animals' rank, age, and temperament. Further, looking time in these experiments was indexed using video cameras and scored by hand and not an eye tracker, which may have also influenced the pattern of results. Lastly, as our animals are housed indoors in less rich social conditions than those of animals living in large social groups which may lead to differences in social processing. Further studies evaluating how social context modifies visual looking patterns may help to illuminate these differences in results. That said, using methods comparable to those employed in humans, our report identified robust evidence of the positivity effect in nonhuman primates, which calls into question one of the major hypotheses regarding the psychological underpinnings of the positivity effect in humans.

Socioemotional selectivity theory (SST) proposes that this age-related shift in visual processing of affective information is driven by an individual's perception of "time horizons" (Carstensen et al., 1999; English & Carstensen, 2016). When an individual's inferred time horizon is distant—as is the case for healthy adolescents and young-to-middle-aged adults—people preferentially engage in behaviors that may benefit them in the distant future, even if there is some negative affective cost to those behaviors in the present. When time horizons shrink—as people age or when they are diagnosed with terminal illnesses (Mather & Carstensen, 2003)—people become more focused on the present and prioritize immediate affective goals. Within this theoretical framework, the positivity effect is purported to emerge due to goal-directed cognitive control of attentional resources towards positive and/or away from negative information, driven by knowledge that one's life is coming to a close (Carstensen & DeLiema, 2018). The claim that biases in visual attention specifically occur as a result of shifting time horizons has mixed results, with limited evidence either for (Cypryańska et al., 2014) or against (Barber et al., 2020; Demeyer & De Raedt, 2013, 2014) the propensity for shifting time perspectives to modify visual attention. Regardless, given that rhesus monkeys presumably do not perceive such time horizons, our data suggest that inferences about time-horizons are not *required* for the positivity effect to emerge.

Evolutionary reasoning may help to inform why visual attention towards threatening stimuli wanes in aged primates. First, engaging with threat comes with a physiological tax that aged bodies cannot afford.

That is, both older humans (Piazza et al., 2013) and non-human primates (Shively et al., 2020) are less metabolically efficient in recovering from affective stressors, resulting in increased allostatic load and subsequent negative health consequences. One way to circumvent such metabolically taxing states is through developing behavioral strategies to avoid these situations in the first place. Such strategies are invoked in aging human adults, as reviewed above, and are also observed in some aspects of non-human primates' social behavior, including age-related increases in social selectivity and decreases in received aggression (Almeling et al., 2016, 2017; Rosati et al., 2020). A plausible line of reasoning follows that decline in threat vigilance promotes survival of aged animals that belong to species with protracted lifespans through more efficient physiological regulation. This theory could be tested by evaluating socioaffective predictors of physiological expenditure in comparative studies across several species.

Regarding neural mechanisms that underlie such changes to socioaffective behavior, several lines of research point to age-related decline in the structure and function of the insula and anterior cingulate cortex (ACC) as potential mediators of the positivity effect. First, both the insula and the cingulate play critical roles in attentional processing of affective (and homeostatically relevant, generally) stimuli (for reviews see Kleckner et al., 2017; Menon & Uddin, 2010; Seeley, 2019; Uddin, 2014). Additionally, decline in cingulo-insular function mediates age-related deficits in attention and memory in humans (Andreano et al., 2017; He et al., 2014; La Corte et al., 2016; Lee et al., 2020; Touroutoglou et al., 2018; Ueno et al., 2020). Given that rhesus monkeys' cingulo-insular networks are largely homologous to humans (Touroutoglou et al., 2016), it stands to reason that age-related changes to the function of these two regions may underlie the shared behavioral features of socioaffective aging between monkeys and humans shown in this report. Causal evidence from nonhuman primates supports this hypothesis of the cingulate in young nonhuman primates supports this hypothesis—much like the aged animals in this report, young monkeys with selective ibotenic acid lesions to the cingulate initially show robust behavioral responses to threat that wanes over time (Bliss-Moreau et al., 2021). Establishing affective homologies in aging between monkeys and humans opens up the possibility of causal manipulations to uncover mechanisms that potentially cause deleterious effects of aging in humans. Understanding such mechanisms will help to promote healthy aging in both humans and animals.

References

Alexander, G. E., Chen, K., Aschenbrenner, M., Merkley, T. L., Santerre-Lemmon, L. E., Shamy, J. L., Skaggs, W. E., Buonocore, M. H., Rapp, P. R., & Barnes, C. A. (2008). Age-Related Regional Network of Magnetic Resonance Imaging Gray Matter in the Rhesus Macaque. *Journal of Neuroscience*, *28*(11), 2710–2718. https://doi.org/10.1523/JNEUROSCI.1852-07.2008

Almeling, L., Hammerschmidt, K., Sennhenn-Reulen, H., Freund, A. M., & Fischer, J. (2016). Motivational shifts in aging monkeys and the origins of social selectivity. *Curr Biol*, *26*(13), 1744–1749. https://doi.org/10.1016/j.cub.2016.04.066

Almeling, L., Sennhenn-Reulen, H., Hammerschmidt, K., Freund, A. M., & Fischer, J. (2017). Social interactions and activity patterns of old Barbary macaques: Further insights into the foundations of social selectivity. *American Journal of Primatology*, *79*(11), e22711. https://doi.org/10.1002/ajp.22711

Amir, I., Zvielli, A., & Bernstein, A. (2016). (De) coupling of our eyes and our mind’s eye: A dynamic process perspective on attentional bias. *Emotion*, *16*(7), 978.

Andreano, J. M., Touroutoglou, A., Dickerson, B. C., & Barrett, L. F. (2017). Resting connectivity between salience nodes predicts recognition memory. *Social Cognitive and Affective Neuroscience*, *12*(6), 948–955. https://doi.org/10.1093/scan/nsx026

Barber, S. J., Lopez, N., Cadambi, K., & Alferez, S. (2020). The limited roles of cognitive capabilities and future time perspective in contributing to positivity effects. *Cognition*, *200*, 104267. https://doi.org/10.1016/j.cognition.2020.104267

Barrett, L. F., Adolphs, R., Marsella, S., Martinez, A. M., & Pollak, S. D. (2019). Emotional Expressions Reconsidered: Challenges to Inferring Emotion From Human Facial Movements. *Psychological Science in the Public Interest*, *20*(1), 1–68. https://doi.org/10.1177/1529100619832930

Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using lme4. *Journal of Statistical Software*, *67*(1), 1–48. https://doi.org/10.18637/jss.v067.i01

Bliss-Moreau, E., Machado, C. J., & Amaral, D. G. (2013). Macaque cardiac physiology is sensitive to the valence of passively viewed sensory stimuli. *PLoS One*, *8*(8), e71170. https://doi.org/10.1371/journal.pone.0071170

Bliss-Moreau, E., & Moadab, G. (2017). The faces monkeys make. *The Science of Facial Expression. New York, NY: Oxford*.

Bliss-Moreau, E., Santistevan, A. C., Bennet, J., Moadab, G., & Amaral, D. G. (2021). Anterior cingulate cortex ablation disrupts affective vigor and vigilance. *Journal of Neuroscience*.

Bliss-Moreau, E., Theil, J. H., & Moadab, G. (2013). Efficient Cooperative Restraint Training With Rhesus Macaques. *Journal of Applied Animal Welfare Science*, *16*(2). https://doi.org/10.1080/10888705.2013.768897

Carstensen, L. L., & Fredrickson, B. L. (1998). *Influence of HIV Status and Age on Cognitive Representations of Others*. 19.

Carstensen, L. L., Isaacowitz, D. M., & Charles, S. T. (1999). Taking Time Seriously: A Theory of Socioemotional Selectivity. *American Psychologist*, 17.

Carstensen, L. L., Turan, B., Scheibe, S., Ram, N., Ersner-Hershfield, H., Samanez-Larkin, G. R., Brooks, K. P., & Nesselroade, J. R. (2011). Emotional experience improves with age: Evidence based on over 10 years of experience sampling. *Psychology and Aging*, *26*(1), 21.

Cassidy, L. C., Bethell, E. J., Brockhausen, R. R., Boretius, S., Treue, S., & Pfefferle, D. (2021). The dot-probe attention bias task as a method to assess psychological wellbeing after anesthesia: A study with adult female long-tailed macaques (Macaca fascicularis). *European Surgical Research*. https://doi.org/10.1159/000521440

Chapman, A., Devue, C., & Grimshaw, G. M. (2019). Fleeting reliability in the dot-probe task. *Psychological Research*, *83*(2), 308–320. https://doi.org/10.1007/s00426-017-0947-6

Charles, S. T., Mather, M., & Carstensen, L. L. (2003). Aging and emotional memory: The forgettable nature of negative images for older adults. *Journal of Experimental Psychology: General*, *132*(2), 310–324. https://doi.org/10.1037/0096-3445.132.2.310

Corr, J. (2003). Social behavior in aged rhesus macaques. *Collegium Antropologicum*, *27*(1), 87–94.

Csibra, G., Hernik, M., Mascaro, O., Tatone, D., & Lengyel, M. (2016). Statistical treatment of looking-time data. *Developmental Psychology*, *52*(4), 521–536. https://doi.org/10.1037/dev0000083

Cypryańska, M., Krejtz, I., Jaskó\lowska, A., Kulawik, A., Żukowska, A., De Zavala, A. G., Niewiarowski, J., & Nezlek, J. B. (2014). An experimental study of the influence of limited time horizon on positivity effects among young adults using eye-tracking. *Psychological Reports*, *115*(3), 813–827.

Demeyer, I., & De Raedt, R. (2013). Attentional bias for emotional information in older adults: The role of emotion and future time perspective. *PloS One*, *8*(6), e65429.

Demeyer, I., & De Raedt, R. (2014). The effect of future time perspective manipulation on affect and attentional bias. *Cognitive Therapy and Research*, *38*(3), 302–312.

Eldesouky, L., & English, T. (2018). Another year older, another year wiser? Emotion regulation strategy selection and flexibility across adulthood. *Psychology and Aging*, *33*(4), 572–585. https://doi.org/10.1037/pag0000251

English, T., & Carstensen, L. L. (2014). Selective narrowing of social networks across adulthood is associated with improved emotional experience in daily life. *International Journal of Behavioral Development*, *38*(2), 195–202. https://doi.org/10.1177/0165025413515404

English, T., & Carstensen, L. L. (2016). Socioemotional Selectivity Theory. In N. A. Pachana (Ed.), *Encyclopedia of Geropsychology* (pp. 1–6). Springer Singapore. https://doi.org/10.1007/978-981-287-080-3_110-1

Fiske, A., Wetherell, J. L., & Gatz, M. (2009). Depression in Older Adults. *Annual Review of Clinical Psychology*, *5*(1), 363–389. https://doi.org/10.1146/annurev.clinpsy.032408.153621

Fung, H. H., & Carstensen, L. L. (2006). Goals Change When Life's Fragility is Primed: Lessons Learned From Older Adults, the September 11 Attacks and Sars. *Social Cognition*, *24*(3), 248–278. https://doi.org/10.1521/soco.2006.24.3.248

Gerhardsson, A., Fischer, H., Lekander, M., Kecklund, G., Axelsson, J., Åkerstedt, T., & Schwarz, J. (2019). *Positivity Effect and Working Memory Performance Remains Intact in Older Adults After Sleep Deprivation* [Preprint]. Open Science Framework. https://doi.org/10.31219/osf.io/nkaqr

Gothard, K. M., Erickson, C. A., & Amaral, D. G. (2004). How do rhesus monkeys (Macaca mulatta) scan faces in a visual paired comparison task? *Anim Cogn*, *7*(1), 25–36. https://doi.org/10.1007/s10071-003-0179-6

Gross, J. J., Carstensen, L. L., Pasupathi, M., Tsai, J., Götestam Skorpen, C., & Hsu, A. Y. C. (1997). Emotion and aging: Experience, expression, and control. *Psychology and Aging*, *12*(4), 590–599.

Hauser, M. D., & Tyrrell, G. (1984). Old age and its behavioral manifestations: A study on two species of macaque. *Folia Primatologica*, *43*(1), 24–35.

He, X., Qin, W., Liu, Y., Zhang, X., Duan, Y., Song, J., Li, K., Jiang, T., & Yu, C. (2014). Abnormal salience network in normal aging and in amnestic mild cognitive impairment and Alzheimer's disease. *Human Brain Mapping*, *35*(7), 3446–3464.

Isaacowitz, D. M., Allard, E. S., Murphy, N. A., & Schlangel, M. (2009). The Time Course of Age-Related Preferences Toward Positive and Negative Stimuli. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *64B*(2), 188–192. https://doi.org/10.1093/geronb/gbn036

Isaacowitz, D. M., Toner, K., Goren, D., & Wilson, H. R. (2008). Looking while unhappy: Mood-congruent gaze in young adults, positive gaze in older adults. *Psychological Science*, *19*(9), 848–853.

Isaacowitz, D. M., Wadlinger, H. A., Goren, D., & Wilson, H. R. (2006a). *Is There an Age-Related Positivity Effect in Visual Attention? A Comparison of Two Methodologies*. https://doi.org/10.1037/1528-3542.6.3.511

Isaacowitz, D. M., Wadlinger, H. A., Goren, D., & Wilson, H. R. (2006b). Selective preference in visual fixation away from negative images in old age? An eye-tracking study. *Psychol Aging*, *21*(1), 40–48. https://doi.org/10.1037/0882-7974.21.1.40

Johnson, D. R. (2009). Goal-directed attentional deployment to emotional faces and individual differences in emotional regulation. *Journal of Research in Personality*, *43*(1), 8–13.

Joubert, C., Davidson, P. S. R., & Chainay, H. (2018). When Do Older Adults Show a Positivity Effect in Emotional Memory? *Experimental Aging Research*, *44*(5), 455–468. https://doi.org/10.1080/0361073X.2018.1521498

Kappenman, E. S., Farrens, J. L., Luck, S. J., & Proudfit, G. H. (2014). Behavioral and ERP measures of attentional bias to threat in the dot-probe task: Poor reliability and lack of correlation with anxiety. *Frontiers in Psychology*, *5*. https://doi.org/10.3389/fpsyg.2014.01368

Kennedy, B. L., Huang, R., & Mather, M. (2020). Age differences in emotion-induced blindness: Positivity effects in early attention. *Emotion*, *20*(7), 1266–1278. https://doi.org/10.1037/emo0000643

Kennedy, Q., Mather, M., & Carstensen, L. L. (2004). The Role of Motivation in the Age-Related Positivity Effect in Autobiographical Memory. *Psychological Science*, *15*(3), 208–214. https://doi.org/10.1111/j.0956-7976.2004.01503011.x

King, H. M., Kurdziel, L. B., Meyer, J. S., & Lacreuse, A. (2012). Effects of testosterone on attention and memory for emotional stimuli in male rhesus monkeys. *Psychoneuroendocrinology*, *37*(3), 396–409. https://doi.org/10.1016/j.psyneuen.2011.07.010

Kleckner, I. R., Zhang, J., Touroutoglou, A., Chanes, L., Xia, C., Simmons, W. K., Quigley, K. S., Dickerson, B. C., & Feldman Barrett, L. (2017). Evidence for a large-scale brain system supporting allostasis and interoception in humans. *Nature Human Behaviour*, *1*(5), 0069. https://doi.org/10.1038/s41562-017-0069

Kret, M. E., Jaasma, L., Bionda, T., & Wijnen, J. G. (2016). Bonobos (*Pan paniscus*) show an attentional bias toward conspecifics' emotions. *Proceedings of the National Academy of Sciences*, *113*(14), 3761–3766. https://doi.org/10.1073/pnas.1522060113

Kyröläinen, A.-J., Keuleers, E., Mandera, P., Brysbaert, M., & Kuperman, V. (2021). Affect across adulthood: Evidence from English, Dutch, and Spanish. *Journal of Experimental Psychology: General*, *150*(4), 792.

La Corte, V., Sperduti, M., Malherbe, C., Vialatte, F., Lion, S., Gallarda, T., Oppenheim, C., & Piolino, P. (2016). Cognitive Decline and Reorganization of Functional Connectivity in Healthy Aging: The Pivotal Role of the Salience Network in the Prediction of Age and Cognitive Performances. *Frontiers in Aging Neuroscience*, *8*. https://doi.org/10.3389/fnagi.2016.00204

Lansford, J. E., Sherman, A. M., & Antonucci, T. C. (1998). Satisfaction with social networks: An examination of socioemotional selectivity theory across cohorts. *Psychol Aging*, *13*(4), 544–552.

Lee, L. O., & Knight, B. G. (2009). Attentional bias for threat in older adults: Moderation of the positivity bias by trait anxiety and stimulus modality. *Psychology and Aging*, *24*(3), 741–747. https://doi.org/10.1037/a0016409

Lee, T.-H., Kim, S. H., Katz, B., & Mather, M. (2020). The Decline in Intrinsic Connectivity Between the Salience Network and Locus Coeruleus in Older Adults: Implications for Distractibility. *Frontiers in Aging Neuroscience*, *12*, 2. https://doi.org/10.3389/fnagi.2020.00002

Luong, G., Charles, S. T., & Fingerman, K. L. (2011). Better with age: Social relationships across adulthood. *Journal of Social and Personal Relationships*, *28*(1), 9–23.

Machanda, Z. P., & Rosati, A. G. (2020). Shifting sociality during primate ageing. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *375*(1811), 20190620. https://doi.org/10.1098/rstb.2019.0620

MacLeod, C., Mathews, A., & Tata, P. (1986). Attentional Bias in Emotional Disorders. *Journal of Abnormal Psychology*, *95*(1), 15–20. https://doi.org/10.1037/0021-843X.95.1.15

Maestripieri, D. (1997). Gestural communication in macaques: Usage and meaning of nonvocal signals. *Evolution of Communication*, *1*(2), 193–222.

Maestripieri, D., & Wallen, K. (1997). Affiliative and submissive communication in rhesus macaques. *Primates*, *38*(2), 127–138.

Mammarella, N., Di Domenico, A., Palumbo, R., & Fairfield, B. (2016). When green is positive and red is negative: Aging and the influence of color on emotional memories. *Psychology and Aging*, *31*(8), 914–926. https://doi.org/10.1037/pag0000122

Mather, M., & Carstensen, L. L. (2003). Aging and attentional biases for emotional faces. *Psychological Science*, *14*(5), 409–415.

Mather, M., & Carstensen, L. L. (2005). Aging and motivated cognition: The positivity effect in attention and memory. *Trends Cogn Sci*, *9*(10), 496–502. https://doi.org/10.1016/j.tics.2005.08.005

Mather, M., & Knight, M. R. (2006). Angry Faces Get Noticed Quickly: Threat Detection is not Impaired Among Older Adults. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *61*(1), P54–P57. https://doi.org/10.1093/geronb/61.1.P54

Matheson, G. J. (2019). We need to talk about reliability: Making better use of test-retest studies for study design and interpretation. *PeerJ*, *7*, e6918. https://doi.org/10.7717/peerj.6918

Menon, V., & Uddin, L. Q. (2010). Saliency, switching, attention and control: A network model of insula function. *Brain Structure and Function*, *214*(5–6), 655–667.

Mroczek, D. K. (2001). Age and emotion in adulthood. *Current Directions in Psychological Science*, *10*(3), 87–90.

Nakamichi, M. (1984). Behavioral characteristics of old female Japanese monkeys in a free-ranging group. *Primates*, *25*(2), 192–203.

Niedenthal, P. M. (2007). Embodying Emotion. *Science*, *316*(5827), 1002–1005. https://doi.org/10.1126/science.1136930

Nikitin, J., & Freund, A. M. (2011). Age and motivation predict gaze behavior for facial expressions. *Psychol Aging*, *26*(3), 695–700. https://doi.org/10.1037/a0023281

Noh, S. R., Lohani, M., & Isaacowitz, D. M. (2011). Deliberate real-time mood regulation in adulthood: The importance of age, fixation and attentional functioning. *Cognition & Emotion*, *25*(6), 998–1013. https://doi.org/10.1080/02699931.2010.541668

Orgeta, V. (2011). Avoiding threat in late adulthood: Testing two life span theories of emotion. *Experimental Aging Research*, *37*(4), 449–472.

Parr, L. A., Modi, M., Siebert, E., & Young, L. J. (2013). Intranasal oxytocin selectively attenuates rhesus monkeys' attention to negative facial expressions. *Psychoneuroendocrinology*, *38*(9), 1748–1756.

Peirce, J., Gray, J. R., Simpson, S., MacAskill, M., Höchenberger, R., Sogo, H., Kastman, E., & Lindeløv, J. K. (2019). PsychoPy2: Experiments in behavior made easy. *Behavior Research Methods*, *51*(1), 195–203.

Piazza, J. R., Charles, S. T., Stawski, R. S., & Almeida, D. M. (2013). Age and the association between negative affective states and diurnal cortisol. *Psychology and Aging*, *28*(1), 47.

Preuss, T. M., & Wise, S. P. (2021). Evolution of Prefrontal Cortex. *Neuropsychopharmacology*, 1–17. https://doi.org/10.1038/s41386-021-01076-5

Reed, A. E., Chan, L., & Mikels, J. A. (2014). Meta-analysis of the age-related positivity effect: Age differences in preferences for positive over negative information. *Psychology and Aging*, *29*(1), 1–15. https://doi.org/10.1037/a0035194

Reutter, M., Hewig, J., Wieser, M. J., & Osinsky, R. (2017). The N2pc component reliably captures attentional bias in social anxiety: N2pc and attentional bias in social anxiety. *Psychophysiology*, *54*(4), 519–527. https://doi.org/10.1111/psyp.12809

Rosati, A. G., Arre, A. M., Platt, M. L., Santos, L. R., Amici, F., & Widdig, A. (2018). Developmental shifts in social cognition: Socio-emotional biases across the lifespan in rhesus monkeys. *Behavioral Ecology and Sociobiology*, *72*, 163. https://doi.org/10.1007/s00265-018-2573-8

Rosati, A. G., Hagberg, L., Enigk, D. K., Otali, E., Emery Thompson, M., Muller, M. N., Wrangham, R. W., & Machanda, Z. P. (2020). Social selectivity in aging wild chimpanzees. *Science*, *370*(6515), 473–476. https://doi.org/10.1126/science.aaz9129

Rosati, A. G., & Santos, L. R. (2017). Tolerant Barbary macaques maintain juvenile levels of social attention in old age, but despotic rhesus macaques do not. *Animal Behaviour*, *130*, 199–207.

Scheibe, S., English, T., Tsai, J. L., & Carstensen, L. L. (2013). Striving to feel good: Ideal affect, actual affect, and their correspondence across adulthood. *Psychology and Aging*, *28*(1), 160–171. https://doi.org/10.1037/a0030561

Schmukle, S. C. (2005). Unreliability of the dot probe task. *European Journal of Personality*, *19*(7), 595–605.

Seeley, W. W. (2019). The salience network: A neural system for perceiving and responding to homeostatic demands. *Journal of Neuroscience*, *39*(50), 9878–9882.

Shively, C. A., Appt, S. E., Chen, H., Day, S. M., Frye, B. M., Shaltout, H. A., Silverstein-Metzler, M. G., Snyder-Mackler, N., Uberseder, B., Vitolins, M. Z., & Register, T. C. (2020). Mediterranean diet, stress resilience, and aging in nonhuman primates. *Neurobiology of Stress*, *13*, 100254. https://doi.org/10.1016/j.ynstr.2020.100254

Staugaard, S. R. (2009). Reliability of two versions of the dot-probe task using photographic faces. *Psychology Science Quarterly*, *51*(3), 339–350.

Stonebarger, G. A., Bimonte-Nelson, H. A., & Urbanski, H. F. (2021). The Rhesus Macaque as a Translational Model for Neurodegeneration and Alzheimer's Disease. *Frontiers in Aging Neuroscience*, *13*, 581. https://doi.org/10.3389/fnagi.2021.734173

Strauss, G. P., Allen, D. N., Jorgensen, M. L., & Cramer, S. L. (2005). Test-retest reliability of standard and emotional stroop tasks: An investigation of color-word and picture-word versions. *Assessment*, *12*(3), 330–337.

Talbot, C. E., Ksander, J. C., & Gutchess, A. (2018). Aging Impairs Disengagement From Negative Words in a Dot Probe Task. *Frontiers in Psychology*, *9*, 2361. https://doi.org/10.3389/fpsyg.2018.02361

Therneau, T. M. (2020). *coxme: Mixed Effects Cox Models*. https://CRAN.R-project.org/package=coxme

Tomaszczyk, J. C., & Fernandes, M. A. (2014). Age-related differences in attentional bias for emotional faces. *Aging, Neuropsychology, and Cognition*, *21*(5), 544–559.

Touroutoglou, A., Bliss-Moreau, E., Zhang, J., Mantini, D., Vanduffel, W., Dickerson, B. C., & Barrett, L. F. (2016). A ventral salience network in the macaque brain. *NeuroImage*. https://doi.org/10.1016/j.neuroimage.2016.02.029

Touroutoglou, A., Zhang, J., Andreano, J. M., Dickerson, B. C., & Barrett, L. F. (2018). Dissociable effects of aging on salience subnetwork connectivity mediate age-related changes in executive function and affect. *Frontiers in Aging Neuroscience*, *10*, 410. https://doi.org/10.3389/fnagi.2018.00410

Uddin, L. Q. (2014). Salience processing and insular cortical function and dysfunction. In *Nat Rev Neurosci*. http://www.nature.com/nrn/journal/vaop/ncurrent/full/nrn3857.html

Ueno, D., Matsuoka, T., Kato, Y., Ayani, N., Maeda, S., Takeda, M., & Narumoto, J. (2020). Individual differences in interoceptive accuracy are correlated with salience network connectivity in older adults. *Frontiers in Aging Neuroscience*, *12*, 592002. https://doi.org/10.3389/fnagi.2020.592002

Upright, N. A., & Baxter, M. G. (2021). Prefrontal cortex and cognitive aging in macaque monkeys. *American Journal of Primatology*. https://doi.org/10.1002/ajp.23250

Urry, H. L., & Gross, J. J. (2010). Emotion Regulation in Older Age. *Current Directions in Psychological Science*, *19*(6), 352–357. https://doi.org/10.1177/0963721410388395

van Rooijen, R., Ploeger, A., & Kret, M. E. (2017). The dot-probe task to measure emotional attention: A suitable measure in comparative studies? *Psychonomic Bulletin & Review*, *24*(6), 1686–1717. https://doi.org/10.3758/s13423-016-1224-1

Waechter, S., Nelson, A. L., Wright, C., Hyatt, A., & Oakman, J. (2014). Measuring attentional bias to threat: Reliability of dot probe and eye movement indices. *Cognitive Therapy and Research*, *38*(3), 313–333.

Waechter, S., & Stolz, J. A. (2015). Trait anxiety, state anxiety, and attentional bias to threat: Assessing the psychometric properties of response time measures. *Cognitive Therapy and Research*, *39*(4), 441–458.

Wang, J., Xie, F., He, L., Meadmore, K. L., Paterson, K. B., & Benson, V. (2020). Eye movements reveal a similar positivity effect in Chinese and UK older adults. *Quarterly Journal of Experimental Psychology*, *73*(11), 1921–1929. https://doi.org/10.1177/1747021820935861

Wei, J., Lu, Y., Li, K., Goodman, M., & Xu, H. (2021). The Associations of Late-life Depression with All-cause and Cardiovascular Mortality: The NHANES 2005-2014. *Journal of Affective Disorders*, S0165032721014233. https://doi.org/10.1016/j.jad.2021.12.104

White, L. K., Britton, J. C., Sequeira, S., Ronkin, E. G., Chen, G., Bar-Haim, Y., Shechner, T., Ernst, M., Fox, N. A., Leibenluft, E., & others. (2016). Behavioral and neural stability of attention bias to threat in healthy adolescents. *Neuroimage*, *136*, 84–93.

Wrzus, C., Hänel, M., Wagner, J., & Neyer, F. J. (2013). Social network changes and life events across the life span: A meta-analysis. *Psychological Bulletin*, *139*(1), 53.

Figures

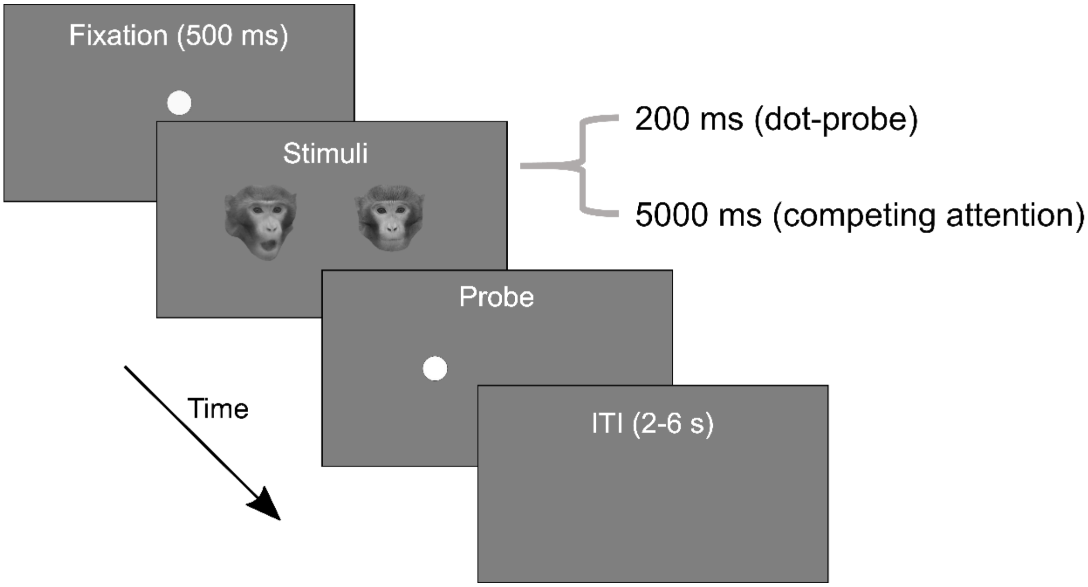

Figure 1.1 Design of the dot-probe and competing attention tasks. Monkeys were required to make a 500 ms central fixation on the screen, immediately after which two faces (approximately 7° x 7°) simultaneously flashed for 200 ms (dot-probe) or 5000 ms (competing attention) on the left- and right-hand side of the screen. The faces depicted the same animal but differed in affective content (i.e., displayed either a lip-smack, neutral expression, or open-mouth threat). Immediately following facial presentation, the "probe" appeared pseudo-randomly under one of the faces. Subjects were then required to fixate on the probe within 20 seconds to receive a juice reward. Images not shown to scale.

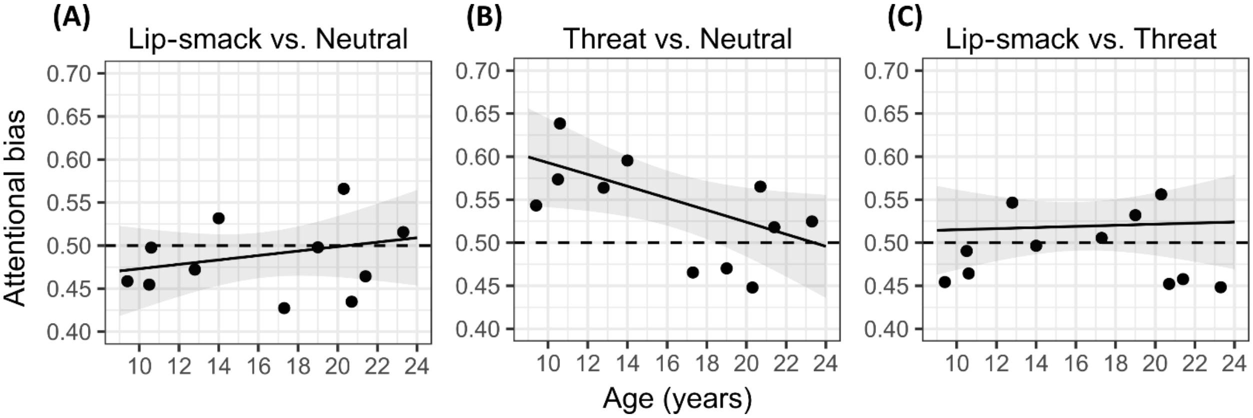

Figure 1.2 Age-related differences in the competing attention task when monkeys looked at least one stimulus. There was no association between age and bias in looking time towards (A) lip-smack vs. neutral (p = 0.38) or (C) lip-smack vs. threat (p = 0.67); however, (B) a looking time bias towards threat vs. neutral faces in middle-aged monkeys was absent in older monkeys (p = 0.024). Data points depict average bias in looking time for each animal in each condition, with attentional bias = 0.5 corresponding to equal time looking at each of the faces (no bias). Shaded regions depict 95% bootstrapped confidence intervals with 10,000 bootstrapped replications.

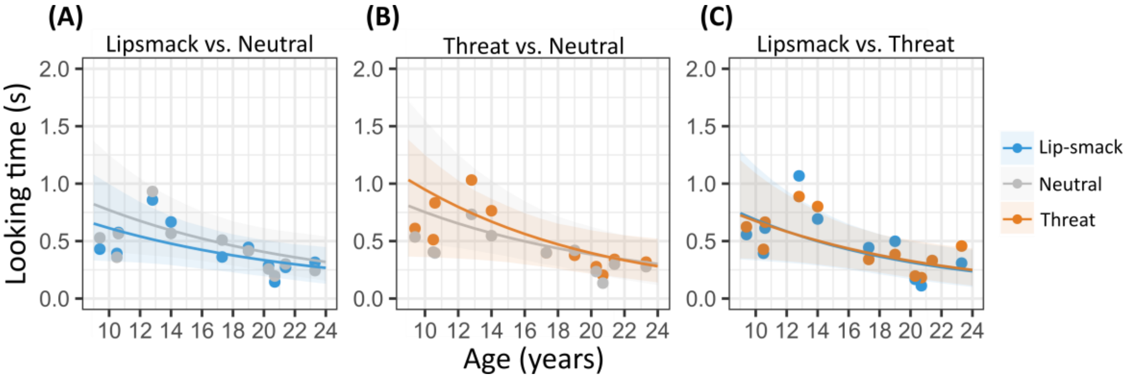

Figure 3. Looking times in competing attention task for all trials (regardless of whether monkeys looked at the stimuli). Age was negatively correlated with looking times towards faces in (A) lip-smack vs. neutral (B) threat vs. neutral and (C) lip-smack vs threat trials. Regions depict 95% confidence intervals.

Table 1.1 Dot-probe models. Mixed effects Cox proportional hazards model results of the time-to-detect the probe on lip-smack vs. neutral (Model 1), threat vs. neutral (Model 2) and lip-smack vs threat (Model 3) trials. Significant parameters ($p < 0.05$) are shown in bold. τ_{00} = random intercept variance, # of events = number of trials on which animals fixated on the probe within 20 seconds, # of trials = total number of trials analyzed.

	Model 1 Lip-smack vs. Neutral			Model 2 Threat vs. Neutral			Model 3 Lip-smack vs. Threat		
Predictors	*HR [95% CI]*	*z*	*p*	*HR [95% CI]*	*z*	*p*	*HR [95% CI]*	*z*	*p*
Facial behavior	0.97 [0.84 – 1.12]	-0.41	0.681	1.07 [0.92 – 1.24]	0.92	0.355	1.01 [0.87 – 1.18]	0.18	0.859
Age [mean centered years]	1.01 [0.96 – 1.06]	0.28	0.776	1.01 [0.95 – 1.07]	0.27	0.79	1.03 [0.98 – 1.09]	1.18	0.237
Sex [M]	0.83 [0.52 – 1.34]	-0.74	0.456	0.78 [0.47 – 1.30]	-0.96	0.335	0.85 [0.52 – 1.40]	-0.63	0.53
Stimulus animal sex [M]	1.02 [0.88 – 1.19]	0.28	0.781	1.00 [0.86 – 1.16]	-0.06	0.953	0.97 [0.83 – 1.13]	-0.38	0.702
Probe location [Right]	1.29 [1.11 – 1.49]	3.29	0.001	1.08 [0.93 – 1.25]	1.02	0.307	1.19 [1.02 – 1.38]	2.21	0.027
Age * Facial behavior	1.01 [0.98 – 1.04]	0.73	0.467	1.00 [0.97 – 1.04]	0.2	0.843	0.99 [0.96 – 1.02]	-0.72	0.473
Random Effects									
τ_{00}	0.35_{Animal}			0.38_{Animal}			0.37_{Animal}		
# of events / # of trials	707 / 784			715 / 784			685 / 784		

Table 1.2 Competing attention models. Generalized linear mixed effects model results of the proportion of time spent looking at lip-smack (Model 1), threat (Model 2) and lip-smack (Model 3) faces. Significant parameters ($p < 0.05$) are shown in bold. σ^2 = residual variance, τ_{00} = random intercept variance, # of trials = total number of trials analyzed.

	Model 1 Lip-smack vs. Neutral			Model 2 Threat vs. Neutral			Model 3 Lip-smack vs. Threat		
Predictors	*Exp(Estimate) [95% CI]*	*z*	*p*	*Exp(Estimate) [95% CI]*	*z*	*p*	*Exp(Estimate) [95% CI]*	*z*	*p*
(Intercept)	1.09 [0.90 – 1.31]	0.91	0.36	1.40 [1.15 – 1.72]	3.30	0.001	1.05 [0.88 – 1.26]	0.55	0.58
Age [mean centered years]	1.01 [0.99 – 1.03]	0.87	0.38	0.97 [0.95 – 0.99]	-2.25	0.024	1.00 [0.98 – 1.03]	0.43	0.67
Sex [M]	0.92 [0.73 – 1.15]	-0.72	0.47	0.86 [0.67 – 1.09]	-1.23	0.22	0.89 [0.71 – 1.12]	-0.99	0.32
Stimulus animal sex [M]	0.82 [0.66 – 1.02]	-1.75	0.08	0.87 [0.70 – 1.09]	-1.17	0.24	1.17 [0.94 – 1.46]	1.37	0.17
Random Effects									
σ^2	3.29			3.29			3.29		
τ_{00}	0.00 $_{\text{Animal}}$			0.01 $_{\text{Animal}}$			0.00 $_{\text{Animal}}$		
# of trials	1328			1329			1333		

Chapter 2

Cardiac psychophysiological tuning to socioaffective content is disrupted in aged rhesus monkeys (*Macaca mulatta*)

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Abstract

Aging ushers in numerous disruptions to autonomic nervous system (ANS) function. Although the effects of aging on ANS function at rest are well characterized, there is surprising variation in reports of age-related differences in ANS reactivity to psychosocial stressors, with some reports decreases and other reports of increases in reactivity with age. The sources of variation in age-related differences are largely unknown. Nonhuman primate models of socioaffective aging may help to uncover sources of these sources of variation as nonhuman primates share key features of human ANS structure and function and researchers have precise control over the environments in which they age. In this report, we assess how response patterns to dynamic socioaffective stimuli in the parasympathetic and sympathetic branches of rhesus monkeys (*Macaca mulatta*) ANS differ in aged compared to middle-aged monkeys. We find that respiratory sinus arrhythmia, a cardiac indicator of activity in the parasympathetic branch of the ANS, exhibits age-related disruptions in responding while monkeys view videos of conspecifics.

Keywords: Nonhuman primates, respiratory sinus arrhythmia, pre-ejection period, emotion, aging, affect, autonomic nervous system, cardiovascular system

Chapter 2

Cardiac psychophysiological tuning to socioaffective content is disrupted in aged rhesus monkeys (*Macaca Mulatta*)

Aging is associated with disruptions to the function of all physiological systems and the autonomic nervous system (ANS) is no exception. The fact that ANS activity is part of the foundation from which affective, emotional, and social processes emerge (Barrett & Bliss-Moreau, 2009) suggests that such disruptions may carry significant consequences for processing socioaffective signals (e.g. see Charles, 2010; Mendes, 2010). That said, numerous socioeconomic confounds exist between health, aging, and socioaffective processing in humans making studies of age-related changes to ANS function difficult to interpret (e.g., people from higher socioeconomic backgrounds may have better health, wellbeing, and thus live longer, muddying the causal association between aging, ANS function, and wellbeing). Comparative studies in animal models may help remedy this problem because experimenters have precise control over the environments in which animals age and can illuminate features of senescence that are evolutionarily conserved. Given that rhesus monkeys *(Macaca mulatta*) share key features of central and autonomic nervous system (ANS) structure (Kawashima et al., 2005) and function (e.g., Bliss-Moreau et al., 2013), psychophysiological investigations in this species may prove especially useful in understanding how aging of the ANS and socioaffective processing are related. That said, there is a dearth of research evaluating age-related differences in autonomic nervous system function during psychological processing in rhesus monkeys. In this report, we assess how aged, compared to middle-aged, rhesus monkeys' cardiac psychophysiology responds while viewing a rich set of dynamic video stimuli to test the hypothesis that aging disrupts how monkeys' ANS responds to socioaffective stimuli.

Both the sympathetic (SNS) and parasympathetic (PNS) branches of the ANS undergo numerous changes to function as animals age. This is especially important because these two branches work synergistically to regulate systemic physiology and therefore changes to their function may have serious consequences for health and wellbeing. For example, in humans, resting sympathetic tone (that is, SNS activity absent any socioaffective/environmental stimuli) increases with age (for a review Hotta & Uchida, 2010), resulting in elevated levels of circulating noradrenergics (Seals & Esler, 2000), which contributes to increases in the incidence of obesity (Seals & Bell, 2004) and hypertension (Esler et al., 2001; Krum et al., 2009). Simultaneously, cardiovascular sensitivity to sympathetic input declines with age (Lakatta, 1993), attenuating changes in cardiac output normally associated with sympathetic activation (Ferrari et al., 2003; Hotta & Uchida, 2010; Stratton et al., 2003). In addition to decline in responsivity to SNS activation, the cardiovascular system becomes less responsive to cholinergic parasympathetic nervous system inputs (Baker et al., 2018; Poller et al., 1997). Further, these age-related changes to physiological function are not unique to humans as nonhuman primates evidence similar age-related increases in sympathetic activity (Shively et al., 2020), decline in parasympathetic modulation of cardiac function (Shively et al., 2007b, 2020), and experience similar adverse cardiovascular outcomes as a result of these changes to autonomic function (Shively & Clarkson, 1994). In summary, age-related changes to the ANS diminish both the dynamic range of cardiac function and the efficiency with which the body recovers from physiological challenges and this is a shared feature of senesce across primate phylogeny.

The processing of socioaffective stimuli drives changes in autonomic nervous system activity, therefore understanding how aging impacts ANS responsivity towards socioaffective stimuli is of particular importance. That said, in humans, there is a relative dearth of such investigations and results from the studies that do exist are mixed and depend largely on both the physiological measures being used and the contextual demands of the tasks (Uchino et al, 2010). Specifically, many of the physiological measures that have been used in humans reflect a blend of SNS and PNS activity (e.g., heart rate, blood pressure, etc.), which precludes the ability to make inferences regarding neural systems driving changes in autonomic function. According to a meta-analysis of 31 studies, age is associated with a decrease in heart rate reactivity, but *increased* systolic blood pressure (SBP) reactivity to evocative stimuli (Uchino et al., 2010). That said, age-related differences in SBP reactivity were shown to be attenuated in extremely evocative tasks (Uchino et al., 2010), suggesting that some aspects of older adults physiological reactivity is similar to younger adults when under extreme duress. Studies using cardiac pre-ejection period (PEP) or galvanic skin response (GSR), relatively specific measures of SNS activity (Berntson, Quigley, et al., 2016), yield no consensus regarding how SNS reactivity changes in age (Gurel et al., 2019; Mikkelsen et al., 2019; Smith et al., 2009; Steptoe et al., 2005; Uchino et al., 1999, 2001, 2005) and studies of respiratory sinus arrhythmia (RSA, a measure of relatively specific parasympathetic influence on the heart) are similarly inconclusive (Kuraoka et al., 2018; Mikkelsen et al., 2019; Smith et al., 2009; Uchino et al., 1999, 2005). Together, current research in humans paints an unclear picture of the impact of aging on SNS and PNS reactivity.

Understanding age-related differences in the responsivity of the SNS and PNS to socioaffective stimuli holds great importance for informing theories of socioaffective aging. According to the strength and vulnerability integration (SAVI) model (Charles, 2010), emotional wellbeing later in life is determined by a delicate balance between age-related strengths in socioaffective processing (e.g., older adults are thought to have improved emotion regulation strategies, however see Isaacowitz, 2022) and physiological vulnerabilities. That is, according to this model older adults typically report improved wellbeing because they employ strategies that have been learned over their lifetimes to avoid negative or vulnerable settings; however, if they are unable to avoid these settings, they actually fare off worse than younger adults. Maturational dualism (Mendes, 2010) is a complimentary model and hypothesizes that the ability to sense physiological signals arising from the internal milieu (interoception) is compromised in aging and that this decline in interoceptive ability drives age-related changes in social behavior. As far back as James (1884), scholars in affective science have hypothesized that emotions arise in part from physiological signals arising from the body (e.g., Barrett, 2017; Damasio et al., 1996; Russell, 2003; Schachter et al., 1962). According to Mendes (2010), if the ability to sense these signals is compromised with age, or if the nature of these interoceptive signals change, so too will our affective experiences and social behaviors. Understanding the psychosocial contexts in which the SNS and PNS activity are compromised (or preserved) in aging will help inform driving forces behind older adults' socioaffective behavior—be it due to vulnerabilities, changes in interoception, or both.

Studies performed in nonhuman primates may prove especially useful in uncovering how aging of the ANS contributes to changes in socioaffective experience and behavior because experimenters have precise control and measurement of the environments in which monkeys live and can manipulate animals' biology as they age. That said, the studies of affective psychophysiology in aging nonhuman primates has generally been performed in field (or field-like) settings, in which autonomic function has only been measured at coarse timescales (e.g., urinary cortisol measurements at the timescale of hours/days). These lines of work revealed that aged nonhuman primates possess elevated SNS responsivity to socioaffective stressors—as measured primarily by quantifying glucocorticoids—and take longer to return their ANS to baseline following perturbation (Emery Thompson et al., 2020; Goncharova et al., 2019; Goncharova & Oganyan, 2018; Shively et al., 2020), consistent with what is observed in aging people (for a review Ferrari et al., 2003; and a meta-analysis Otte et al., 2005). Critically, existing work primarily captures variation in SNS/PNS responding to affective stimuli that are negative but to our knowledge no one has carried out a study of fleeting negative and positive affective states akin to the mood induction work in aged humans. Given that rhesus monkeys' ANS responds in a similar matter to humans while watching potent socioaffective stimuli (Bliss-Moreau et al., 2013), this model serves as an excellent species for undertaking such investigations. To address this gap in the literature, we investigate how aged, compared to middle-aged, rhesus monkeys' cardiac psychophysiology responds while viewing a rich set of videos varying in socioaffective content that are ethologically relevant to monkeys.

Materials & Methods

This study was carried out at the California National Primate Research Center (CNPRC) following the recommendations in the Guide for the Care and Use of Laboratory Animals by the National Institutes of Health. All experimental procedures were approved by the University of California, Davis Institutional Animal Care and Use Committee under protocol 21881.

Subjects

Subjects were N=5 middle-aged (3 females, median age: 10.6 years, range: 9.4 – 14) and N=5 aged adult rhesus macaques (*Macaca mulatta*) (2 females, median age: 20.7 years, range: 17.3 – 23.3) that were born and reared at the CNPRC. Monkeys were housed in standard adult macaque laboratory caging (66 cm wide × 61 cm long × 81 cm high) and were socially housed with a compatible social partner. Monkeys were paired either for a minimum of 6 hours per day, 5-days a week, or 24 hours per day in either full access (allowing both monkeys access to both enclosures during the pairing time) or through a metal grate (allowing tactile access but preventing full contact). Five of the monkeys were housed in same-sex pairs.

The housing room was maintained on a 12-hour light and dark cycle, with lights turned on at 0600 hrs and off at 1800 hrs. Monkeys were fed monkey chow (Lab Diet #5047, PMI Nutrition International INC, Brentwood, MO) twice daily, provided with fresh fruit and vegetables twice per week, and had access to water ad libitum. As standard practice at the CNPRC, monkeys received daily enrichment (e.g., a rice/oat/pea mixture on their forage boards once per day, a rubber Kong toy/metal ball, fresh coconuts once per month, and periodic delivery of fruit and vegetables in puzzle balls or puzzle tubes). Candidate monkeys underwent physical examinations prior to being enrolled in the study. Monkeys with cardiac abnormalities (e.g., lateral ventricular hypertrophy), problems with vision that would interfere with eye-tracking, or other health problems that would interfere with the experiment were not enrolled.

Experimental protocol

Testing occurred Monday through Friday between 0800 and 1800 hours over two weeks (ten days) of testing, with a two-day break on the weekend. Animals had been previously acclimated to this testing environment and trained to interact with the eye-tracker for a juice reward for the purposes of another eye-tracking experiment that preceded this study (Santistevan et al., under review). Animals were box transported individually from their home enclosure to the testing room, where they were transferred to a custom nonhuman primate chair, had their arms and legs lightly restrained with soft leather straps, and had disposable spot Ag/AgCl+ electrodes (Covidien, Dublin, Ireland) placed on their chest and back to record electrocardiogram (*ECG,* modified Lead 2 configuration) and impedance cardiogram (ICG). Monkeys' chests and backs were shaved and cleaned with 70% ethanol solution, and then allowed to air dry, prior to attaching the electrodes. Once electrodes were attached, a stretchy neoprene with Velcro closures knee-brace was wrapped around the monkeys' torso to keep the electrodes in place for the duration of the experiment. Cardiac physiology data was recorded at 1000 Hz with MindWare hardware and software (MindWare Technologies, Gahanna, OH). Cardiac impedance was measured by passing a small current (0.4 mA) between the outer electrodes and measuring, via the inner electrodes, basal impedance resulting from changes in blood volume and distribution (Zo) and its first derivative (dZ/dt). After clean ECG and ICG signals were verified using BioLab software (MindWare Technologies, Gahanna, OH), animals were placed 65 cm away from a Tobii Pro TX300 infrared eye tracker (Tobii, Stockholm, Sweden). Gaze data were continuously sampled at 300 Hz. A standard five-point calibration was conducted each day to ensure accuracy of gaze location data. Calibration stimuli were videos of rhesus monkeys and were displayed on the eye tracker's integrated display (58.4 cm diagonal; 1920 x 1080 pixel resolution). Animals were acclimated to this process for three consecutive days prior to beginning the study, during which we followed the protocol above and gave animals treats for 20 minutes while recording ECG and ICG.

Video stimuli

Video stimuli consisted of 400 videos (200 social, 200 nonsocial) from an established video library created in our group (Bliss-Moreau, Machado, et al., 2013a; Machado et al., 2011) plus additional videos added to the collection for subsequent experiments to balance the number of positively and negatively videos relative to their arousal. The social stimuli were videos recorded of rhesus monkeys at the CNPRC engaging in naturalistic behaviors ranging in affective content. These behaviors included aggression between animals (n = 49 videos), single monkeys displaying aggression directed towards the camera (n = 20), single monkeys displaying submissive/affiliative behaviors directed towards the camera (n = 14), single monkeys displaying neutral behavior directed towards the camera (n = 15), foraging (n = 19), grooming (n = 29), mounting (n = 16), and play (n = 24), and nonspecific social content (e.g., monkeys walking around the field enclosure, n = 14). Nonsocial stimuli consisted of footage from nature documentaries that did not feature human or non-human primates engaging in any behaviors. Each of the videos were rated on five dimensions by at least three different raters. The overall ratings evidence excellent intraclass correlation (ICC): valence (ICC = 0.89), arousal (ICC = 0.90), presence of dominance information/signals (ICC = 0.87), presence of submission information/signals (ICC = 0.90), number of interactions (ICC = 0.94), closeness of animals (ICC = 0.92), and novelty/familiarity of content (ICC = 0.96) and thus ratings were averaged and then used as regressors in the models indicated below. See the Supplementary **Table S2.1** for descriptive statistics of the socioaffective ratings across video categories.

Passive Viewing Task

Each testing day started with a 5-minute-long acclimation period (*Baseline*) followed by the presentation of 40 stimulus videos (such that animals viewed a total of 400 unique videos across the 10 days of the experiment). Two-hundred of the videos included footage of conspecifics engaging in naturalistic behaviors (*Social Videos*: e.g., grooming, aggression, etc.) and the other 200 videos included footage from nature documentaries which served as non-social controls (*Nonsocial videos*). None of the videos included footage of humans, non-macaque nonhuman primates, snakes, or predators of macaques. Videos were from our established video library used in previous experiments from our laboratory (Bliss-Moreau, Machado, et al., 2013a; Machado et al., 2011) Video presentation order was counterbalanced across trials and days such that social, nonsocial, and affective content of videos were uniformly distributed across trials and test days.

After the five-minute baseline, animals were required to fixate on a dark grey square (2° x 2°) for 500 ms to receive a small juice reward (0.1 mL). After delivery of the juice reward, a 30-second-long video played. A 30s long inter-trial interval in which only a grey screen was displayed on the monitor allowed animals to return to baseline, after which the experiment proceeded. Cardiac psychophysiological (ECG/ICG), eye-tracking measures (number of fixations and fixation durations) and pupillometry were measured at both baseline and during the presentation of the video stimuli to evaluate psychophysiological reactivity towards the stimuli and to assess attention towards the stimuli.

Psychophysiological Data Processing

Physiological data were subjected to standardized scoring procedures using commercially available software (MindWare HRV Analysis v3.1.5, MindWare IMP Analysis v3.1.6; MindWare Technologies, Gahanna, OH). RSA was computed from the ECG with the Zo as the respiration signal using HRV 3.1.5 software according to accepted scoring parameters. The ECG signal for each 30 s epoch was visually inspected to ensure proper placement of the R-points and artifacts were removed or corrected. The data were de-trended, tapered, and underwent Fourier transformation. Respiratory sinus arrhythmia (RSA) was computed as the natural log integral of the high frequency power of R-R intervals (0.24 to 1.04 Hz). The high frequency band was set to 0.24 to 1.04 based on previous established protocols from our group (Bliss-Moreau et al., 2013). Some subjects evidenced a large portion of their trials with an RSA estimated to be numerically 0. As a result, we additionally utilized the root mean squared of successive RR interval differences (RMSSD), another common measure of heart rate variability, to validate results from RSA analyses (Supplementary Table S2.2). We note that results did not differ qualitatively regardless of using RSA or RMSSD (which correlated ~0.92), therefore we report only the results using RSA.

Cardiac PEP was computed using IMP software as the time difference between the ECG’s Q-point (initiation of left ventricle contraction) and the dZ/dt's B point (opening of the aortic valve). The cleaned ECG data (from processing the RSA) was inputted into the IMP software and ECG and impedance data were combined across 30-sec epochs. Q and B points were manually identified from the average ECG waveform (Q) and average impedance waveform (B). We note that the automated scoring procedures in the IMP software do not work for monkey data. Data segments in which there were severe motion artifacts were removed from the analysis/not scored.

Eye-Tracking Data Processing

The total number of fixations and the total fixation duration were computed using the Tobii Pro Lab software (Tobii, Stockholm, Sweden). Eye-tracking samples were collected at 300 Hz. Fixations were computed using Tobii's I-VT (velocity threshold) fixation filter which makes fixation classifications based on the velocity of directional shits in the eye. The following parameters were used for defining a fixation: gap-fill in: 75 ms, velocity threshold 30 visual degrees/s, velocity window length of 30 ms, maximum time between fixations: 75 ms, maximum angle between fixations: 0.5 degrees, with fixations shorter than 60 ms discarded.

Statistical methods

All analyses were conducted in R version 4.0.3. Generalized linear mixed effects models, estimated in a frequentist framework using the *lme4* package (Bates et al., 2015) or in a Bayesian framework using *brms* (Bürkner, 2017, 2018), were used to model heart rate variability (RSA), pre-ejection period (PEP), and the number of fixations made towards the stimuli. Bayesian estimation was used in cases where frequentist models experienced problems with convergence. Interactions between age and affective properties (specifically, valence, arousal, and dominance building upon Bliss-Moreau et al., 2013) were used to test for age-related differences in psychophysiological reactivity towards the stimuli. Random intercepts were given for both subjects and stimuli, treating stimuli as crossed random effects, to account for both within-subject correlation of repeated measurements and stimulus-related variation. We note that treating stimuli as crossed random effects explicitly accounts for between-stimulus variability and thus ensures the nominal type I error rate (Barr et al., 2013; Judd et al., 2012). Null hypothesis significance testing was conducted at the $\alpha = 0.05$ level and 95% confidence intervals (CI) are presented where appropriate. Degrees of freedom for mixed models were estimated using the Satterthwaite method implemented in the *lmerTest* R package (Kuznetsova et al., 2017). We note that the Sattherwaite method allows for non-integer values of the degrees of freedom. In cases of Bayesian estimation, median posterior density estimates are provided along with 95% highest posterior density (HPD) intervals.

Results

ANS responsivity to socioaffective content

To assess parasympathetic reactivity in response to the dynamic video stimuli, we fit a linear mixed effects model regressing respiratory sinus arrhythmia (RSA) on properties of the video stimuli (valence, arousal, and dominance ratings) while also adjusting for animal age, sex, test day, and trial number. Building upon our previous work (Bliss-Moreau et al., 2013), we included a three-way interaction between valence, arousal, and dominance ratings given that dominance information was known to alter rhesus monkeys' psychophysiological tuning towards these stimuli. Although arousal was not included in the interaction our previous report, we included the dimension in this analysis based on the hypothesis that the influence of arousal may be specifically affected by aging processes.

Valence, arousal, and dominance ratings of videos jointly determined parasympathetic activity, as indexed by RSA (Valence x Arousal x Dominance: $b = 0.13$, 95% CI [0.04, 0.23], $t(362.53) = 2.69$, $p = 0.007$) (**Table 2.1**, Model 1)—therefore we do not interpret main effects due to the presence of an interaction. Specifically, in videos with low levels of dominance information, valence positively correlated with parasympathetic activity and the magnitude of this correlation was largely unaffected by arousal ratings of the videos. The content of these videos largely consisted of grooming, foraging, play, and mounting, and did not contain any behaviors associated with dominance (such as displacements or threats). In contrast, in videos with higher levels of dominance information, valence ratings *negatively* correlated with parasympathetic activity and the magnitude of this negative slope decreased with increasing arousal ratings. Videos that were low in arousal but low in valence were foraging videos featuring some displacements, and videos that were low in arousal and high in valence and dominance were grooming videos that featured some displacements.

We fit the same model above using cardiac pre-ejection period (PEP) as the dependent variable to evaluate how socioaffective content altered monkeys' sympathetic nervous system activity. We found no significant evidence that there was a three-way interaction between socioaffective content and sympathetic arousal, as measured by PEP (Valence x Arousal x Dominance: *b* = 0.07, 95% CI [-0.40, 0.55], *t*(3099.04) = 0.29, *p* = 0.77) (**Table 2.2**, Model 1). This is not entirely unexpected as our previous report only demonstrated that PEP correlated with stimulus video valence (Bliss-Moreau et al., 2013)—therefore in an attempt to replicate these findings, we fit a more restrictive model only including valence, arousal, and dominance but with no interaction terms. Results of this simplified model demonstrated no significant association between any of valence (*b* = 0.019, 95% CI [-0.22, 0.25], *t*(3103.01) = 0.16, *p* = 0.89), arousal (*b* = 0.00, 95% CI [-0.27, 0.27], *t*(3103.01) = 0.44, *p* = 0.99), or dominance (*b* = 0.10, 95% CI [-0.34, 0.54], *t*(3103.01) = 0.44, *p* = 0.99) information and cardiac PEP.

Lastly, we additionally modeled how heart rate itself responded to the socioaffective stimuli. Like PEP, we found no significant interaction between socioaffective content and monkeys' heart rate (Valence x Arousal x Dominance: *b* = -0.21, 95% CI [-1.43, 1.00], *t*(3821.00) = -0.34, *p* = 0.73) (**Table 2.3**, Model 1). A restricted model that did not include this interaction term revealed no significant association between valence (*b* = -0.16, 95% CI [-0.76, 0.44], *t*(3825.00) = -0.53, *p* = 0.60), arousal (*b* = 0.36, 95% CI [-0.33, 1.05], *t*(3825.00) = 1.02, *p* = 0.31), or dominance (*b* = -0.77, 95% CI [-1.90, 0.36], *t*(3825.00) = -1.33, *p* = 0.18) with heart rate.

Age-related differences in ANS responsivity to socioaffective content

In order to test our primary hypothesis that aging blunted psychophysiological tuning in response to socioaffective stimuli, we included (mean centered) age as a further term in the interaction identified above (**Table 2.1**, Model 2). Consistent with our hypothesis, age modified how valence, arousal, and dominance information jointly determined parasympathetic activity (Age [mean centered] X Valence X Arousal X Dominance: b = -0.02, 95% CI [-0.04, -0.01], t(3429.27) = -2.18, p = 0.03). Specifically, age was found to blunt the association between video content (Valence X Arousal X Dominance interaction) and parasympathetic activity, such that younger animals evidenced a strong association between RSA and valence when video arousal was low and dominance information was high and this association was diminished in aged animals (**Figure 2.1**). Notably, younger animals evidenced a significant positive association between valence and RSA while viewing stimuli low in dominance (e.g., foraging, grooming, play, and mounting), whereas older animals RSA did not respond to such videos.

For completeness, we fit the same model as above on PEP and on heart rate. There was no significant interaction between age and the socioaffective content in terms of predicting PEP (Age [mean centered] X Valence X Arousal X Dominance: b = 0.00, 95% CI [-0.09, 0.09], t(3092.03) = 0.02, p = 0.99) (**Table 2.2**, Model 2) or heart rate (Age [mean centered] X Valence X Arousal X Dominance: b = 0.15, 95% CI [-0.09, 0.40], t(3814.00) = 1.22, p = 0.22) (**Table 2.3**, Model 2).

Associations between visual attention and socioaffective content

In order to assess differences in visual attention towards the stimuli, we fit a hierarchical zero-inflated negative binomial model regressing the number of fixations that animals made towards the video on properties of the stimuli while also adjusting for animal age, sex, test day, and trial number. Due to convergence problems with estimating this model in a frequentist framework, we utilized Bayesian estimation using the *brms* package (Bürkner, 2017, 2018). Independent variables were entered in the same form as Model 2 above (i.e., subject sex, test day, trial number, and a four-way interaction between age, valence, arousal, and dominance, with random intercepts for stimulus and animal). A four-way interaction between valence, arousal, dominance, and age was again identified (Age [mean centered] X Valence X Arousal X Dominance: *b* = -0.01, 95% HPD [-0.03, 0.00]), such that younger animals' visual attention as indexed by the number of fixations on the videos was modified by content, whereas older animals' attention was affected by stimulus content to a lesser degree (**Figure 2.2**). Specifically, younger animals' visual attention declined with increasing valence of videos when those videos were low in arousal and high in dominance information (*b* = -0.34, 95% HPD [-0.55, -0.11]); older animals evidenced no such Valence X Arousal X Dominance interaction and were equally attentive to negatively and positively valenced videos low in arousal and high in dominance (*b* = -0.028, 95% HPD [-0.21, 0.17]). Middle-aged and aged animals evidenced similar patterning in visual attention towards all other types of stimuli (see **Figure 2.2**).

We similarly fit a Bayesian hierarchical log-normal hurdle model on the average fixation durations on each trial. Log-normal models were used because these fixation duration data are fit well by log-normal distributions (Csibra et al., 2016). Hurdle models decompose a dependent variable (in this case, average fixation duration) into zero and non-zero values. One model is used to predict whether or not the dependent variable was zero (i.e., crossing over the "hurdle"), whereas another model is used to model the value of the response conditional on the dependent variable being non-zero.

Unlike the absolute number of fixations, the average duration of fixations was not found to be influenced jointly by age and the socioaffective content of the video stimuli (Age [mean centered] X Valence X Arousal X Dominance: *b* = 0.01, 95% HPD [-0.01, 0.03]). Further, although we did not identify an interaction between valence, arousal, and dominance information (Valence X Arousal X Dominance: *b* = -0.02, 95% HPD [-0.10, 0.06]), there were marginal effects such that animals made longer fixations on videos high in valence (*b* = 0.16, 95% HPD [0.10, 0.22]) and in dominance information (*b* = 0.87, 95% HPD [0.68, 1.07]), but shorter fixations while watching videos higher in arousal (*b* = -0.15, 95% HPD [-0.23, -0.08]).

Lastly, age was moderately associated with fixation duration such that older animals made slightly shorter fixations to all stimuli compared to their younger counterparts (*b* = -0.08, 95% HPD [-0.18, 0.00]).

Psychophysiological reactivity and age effects persist after controlling for visual attention

While the models above demonstrate robust effects of stimulus video content on parasympathetic activity (RSA) that are modified by the age of the animal, it is possible that the differences in visual attention towards the stimuli documented above confounded the association between psychophysiological reactivity towards the videos and affective content. To evaluate this possibility, we adjusted for the number of fixations made on the videos as they were presented. Number of fixations were significantly associated with parasympathetic activity, such that the more fixations the animal made the lower their RSA was (*b* = -0.01, 95% CI [-0.01, -0.009], *t*(3671.70) = -5.55, *p* < 0.001). Critically, adjusting for visual attention did not alter the psychophysiological results above (Valence X Arousal X Dominance: *b* = 0.14, 95% CI [0.04, 0.23], *t*(359.51) = 2.72, *p* = 0.007; Age [mean centered] X Valence X Arousal X Dominance: *b* = -0.02, 95% CI [-0.04, -0.01], *t*(3423.53) = -2.26, *p* = 0.024). Thus, the age-related differences in psychophysiological reactivity towards the stimuli are robust to any differences in visual attention towards the stimuli.

Lastly, we additionally fit the same model as above however using PEP and heart rate as our dependent variables. Monkeys' cardiac PEP was negatively correlated with the number of fixations (*b* = -0.04, 95% CI [-0.06, -0.03], *t*(3091.60) = -5.09, *p* < 0.001) and adjusting for fixations did not meaningfully change any of the aforementioned null associations between PEP and socioaffective ratings of videos (**Table 2.2**, Model 3). Similarly, monkeys' heart rate was positively correlated with the number of fixations (*b* = 0.13, 95% CI [0.08, 0.18], *t*(3813.35) = 5.64, *p* < 0.001) and adjusting for fixations did not meaningfully change any of the aforementioned null associations between heart rate and socioaffective ratings of videos (**Table 2.2**, Model 3).

Discussion

Results from this investigation demonstrate that monkeys' parasympathetic control of cardiac activity, as indexed by respiratory sinus arrhythmia (RSA), is tuned to the affective content of dynamic visual stimuli. Specifically, RSA was sensitive to the combined effects of valence, arousal, and dominance information, such that monkeys' RSA increased with valence while watching videos low in dominance information, irrespective of level of arousal. The association between valence and RSA was reversed while monkeys watched videos high in dominance information and low in arousal, such that with increasing valence RSA decreased. We found no significant association between sympathetic arousal (PEP) and the valence, arousal, or dominance (or their interaction) of video stimuli. Lastly, relative to younger animals, aged animals' RSA was relatively unaffected by the socioaffective content of the videos—even after adjusting for the potential confound of visual attention towards the stimuli.

The finding that RSA was a complex function of socioaffective content above and beyond the individual influence of valence, arousal, or dominance is explicitly anticipated by some theoretical frameworks, such as polyvagal theory (Porges, 1995, 1998, 2021), and supported by past research in our group (Bliss-Moreau et al., 2013). According to polyvagal theory, PNS activity originating in the nucleus ambiguus of the brainstem (ventral vagal pathway) is predominantly responsible for respiratory-linked high frequency heart rate variability (of which RSA is one index) in mammals and promotes social engagement. In this model, activity originating in the dorsal motor nucleus (dorsal vagal pathway) primarily acts to offset sympathetic activity (a reactive homeostatic process). Importantly, by our view, increases in PNS in service of social engagement need not be prosocial—especially for rhesus monkeys, which are a despotic species and handle much of their social communication through minor levels of aggression (Thierry, 2007). In this context, parasympathetic activity originating along the ventral vagal pathway serves to widen the dynamic range of cardiac output (Berntson, Cacioppo, et al., 2016) effectively preparing the body for the *possibility* of engaging further metabolic resources (i.e., engaging in allostasis). Indeed, threat-anticipatory freezing behavior in mammals is largely mediated through increases in vagal activity and is coupled with increases in heart rate variability (for a review see Roelofs, 2017). Together, this set of changes to behavior and physiology can be conceptualized as facilitating information gathering and preparing for action. To that end, our data are entirely consistent with view that vagal activity may promote social engagement (either pro-socially or agonistically) as the middle-aged animals' RSA increased while attending to videos that were rated as negative and that contain dominance features (we note the majority of these videos were videos that contained only moderate levels of aggression that were not camera-directed) in addition to while watching ostensibly positive videos (monkeys playing and mounting).

The fact that most psychophysiological investigations of RSA to date in nonhuman primates evaluated animals in response to highly arousing negative stimuli in which monkeys are most likely in 'flight' states, such as under threat of capture (Bowers et al., 1998), or in states in which monkeys have no control of the outcome, such as risk of being shocked or startled (e.g., Fletcher et al., 2012). Results from these studies generally reveal RSA withdrawal, potentially leading to the erroneous conclusion that RSA withdrawal always indicates that the animal is in a negatively valenced state; however, these contexts preclude the ability for observing positive RSA responses even in response to putatively negatively valenced stimuli. This highlights the benefit of studies such as the current investigation and our previous report (Bliss-Moreau et al., 2013) that assess the same animals in a variety of social contexts spanning the entire affective plane.

Although RSA correlated with the socioaffective content of videos in the young monkeys of our study, this was not the case for our aged animals—even though older monkeys were just as engaged with the video stimuli compared to their younger counterparts (as indexed by the number of fixations made to the stimuli). Age-related diminishment in RSA activation may be one mechanism through which aging leads to several changes in socioaffective behavior in humans and nonhuman primates, such as decline in overall sociality (humans: Cornwell et al., 2008; McPherson et al., 2006, nonhuman primates Rosati et al., 2021) and preferential psychological processing of positive over negative affective information (Carstensen &

DeLiema, 2018; Santistevan et al., under review, however see Rosati et al., 2017). That is, if it is the case that the vagal activity is involved in mediating social approach, the fact that the vagal system is disrupted in aging lends credence to the hypothesis that age-related changes to vagal function and social behavior are causally linked. Specifically, we hypothesize that because a wide dynamic range of cardiac output is necessary for navigating uncertain social interactions, the ontogeny of behavioral mechanisms to avoid these situations in individuals with diminished autonomic flexibility (such as aged individuals) is required for these organisms to maximize their fitness and was thus selected for evolutionarily. Indeed, our finding of age-related reduction in reduced autonomic flexibility view is in line with views made by the strengths and vulnerabilities (SAVI) model (Charles, 2010) and our data provide evolutionary support to this model.

Although our study does not directly speak to the interoceptive hypothesis born of maturational dualism (Mendes, 2010)—that is, whether or not age-related decline in the ability to sense signals (e.g., heart rate) from the body cause changes in social behavior—future work directly manipulating vagal activity in aging nonhuman primates in various social environments can test this hypothesis. Recent work from our group has demonstrated that rhesus monkeys' visual attention is sensitive to interoceptive signals (Charbonneau et al., 2022), opening the possibility that age-related decline in interoceptive ability in monkeys may too influence social behavior. This line of research is especially important given recent interest in vagal nerve stimulation as a treatment for patients with psychiatric disorders (Aaronson et al., 2017) or for promoting wellbeing in aged humans (B. Bretherton et al., 2019). To date, there is inconclusive evidence regarding the efficacy of these treatments (Wolf et al., 2021), highlighting the need for animals models (particularly nonhuman primate models) to uncover when, where, and in whom vagal stimulation proves beneficial.

Like all studies, ours is not without its limitations. Most notably, as reviewed in the introduction, the socioenvironmental context in which aged humans are situated while performing laboratory tasks plays a crucial role in determining their degree and patterning of autonomic reactivity. This forces us to examine the social context of our own subjects to situate our findings within the larger literature. Even though all the monkeys in our research were paired with a social partner, they were housed indoors in relatively restricted environments compared to their natural habitat and social groups (features of which are replicated in captivity in our large outdoor groups, in which all animals in this study were born and reared). This relatively impoverished socioenvironmental setting is known to alter monkeys' behavior (Hennessy et al., 2014a) and we have recently demonstrated that variance in indoor housing social environments also impacts behavioral affective reactivity (Charbonneau et al., 2021) and monkeys' survival (Santistevan et al., in prep). As a result, it is possible that our aging effects are best conceptualized with the restricted environmental nature in mind—further work that evaluates similar aging trajectories for group-housed animals is critical for developing normative theory. It's also worth noting that to carry out the present experiments, monkeys were removed from their home cages and transported to the laboratory—which has the possibility of being a negative mood induction in and of itself. Thus, our study represents autonomic responsivity to socioaffective videos in a particular set of conditions which could have differentially impacted older compared to younger animals. The blunting of older animals PNS tuning to the video content could result from their reaction to being moved into the novel environment; that is, their physiology RSA was so deviated from baseline and that could have overshadowed any potential for identifying small changes to physiology in response to the videos (i.e., floor effect). Similar floor effects might be responsible for our overall null finding regarding PEP measures, though we note we were able to detect PEP effects in our previous work (Bliss-Moreau et al., 2013). That said, by the time the animals participated in this experiment they already had approximately two months of experience in the experimental setting from a previous set of experiments (Santistevan et al., under review) and were well habituated to the experimental procedures. Future work using ANS measures via telemetry of aged animals in more naturalistic social environments may help to address these limitations.

Conclusion

Results of our study provide novel evidence that monkeys' parasympathetic tuning towards socioaffective stimuli is disrupted in aging and provide evolutionary support for the strengths and vulnerabilities model (SAVI). Given the important role that the parasympathetic nervous system plays in both managing metabolic resources and facilitating organisms' ability to engage in social processing, age-related decline in parasympathetic function may underlie the breadth of changes observed in both human and nonhuman primates' socioaffective behavior in aging. Future work evaluating decline in parasympathetic function as a mediator of changes to social behavior in aging and causal work manipulating parasympathetic function in nonhuman primates will help to identify mechanisms in which we can promote healthy aging in humans.

References

Aaronson, S. T., Sears, P., Ruvuna, F., Bunker, M., Conway, C. R., Dougherty, D. D., Reimherr, F. W., Schwartz, T. L., & Zajecka, J. M. (2017). A 5-Year Observational Study of Patients With Treatment-Resistant Depression Treated With Vagus Nerve Stimulation or Treatment as Usual: Comparison of Response, Remission, and Suicidality. *American Journal of Psychiatry*, *174*(7), 640–648. https://doi.org/10.1176/appi.ajp.2017.16010034

Baker, S. E., Limberg, J. K., Dillon, G. A., Curry, T. B., Joyner, M. J., & Nicholson, W. T. (2018). Aging Alters the Relative Contributions of the Sympathetic and Parasympathetic Nervous System to Blood Pressure Control in Women. *Hypertension*, *72*(5), 1236–1242. https://doi.org/10.1161/HYPERTENSIONAHA.118.11550

Barr, D. J., Levy, R., Scheepers, C., & Tily, H. J. (2013). Random effects structure for confirmatory hypothesis testing: Keep it maximal. *Journal of Memory and Language*, *68*(3), 255–278. https://doi.org/10.1016/j.jml.2012.11.001

Barrett, L. F. (2017). The theory of constructed emotion: An active inference account of interoception and categorization. *Social Cognitive and Affective Neuroscience*, *12*(1), 1–23. https://doi.org/10.1093/scan/nsw154

Barrett, L. F., & Bliss-Moreau, E. (2009). Affect as a psychological primitive. *Advances in Experimental Social Psychology*, *41*(08), 167–218. https://doi.org/10.1016/S0065-2601(08)00404-8

Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using lme4. *Journal of Statistical Software*, *67*(1), 1–48. https://doi.org/10.18637/jss.v067.i01

Berntson, G. G., Cacioppo, J. T., & Bosch, J. A. (2016). From Homeostasis to Allodynamic Regulation. In J. T. Cacioppo, L. G. Tassinary, & G. G. Berntson (Eds.), *Handbook of Psychophysiology* (4th ed., pp. 401–426). Cambridge University Press. https://doi.org/10.1017/9781107415782.018

Berntson, G. G., Quigley, K. S., Norman, G. J., & Lozano, D. L. (2016). Cardiovascular Psychophysiology. In J. T. Cacioppo, L. G. Tassinary, & G. G. Berntson (Eds.), *Handbook of Psychophysiology* (4th ed., pp. 183–216). Cambridge University Press. https://doi.org/10.1017/9781107415782.009

Bliss-Moreau, E., Machado, C. J., & Amaral, D. G. (2013). Macaque cardiac physiology is sensitive to the valence of passively viewed sensory stimuli. *PLoS One*, *8*(8), e71170. https://doi.org/10.1371/journal.pone.0071170

Bretherton, B., Atkinson, L., Murray, A., Clancy, J., Deuchars, S., & Deuchars, J. (2019). Effects of transcutaneous vagus nerve stimulation in individuals aged 55 years or above: Potential benefits of daily stimulation. *Aging*, *11*(14), 4836–4857. https://doi.org/10.18632/aging.102074

Bürkner, P.-C. (2017). brms: An R Package for Bayesian Multilevel Models Using Stan. *Journal of Statistical Software*, *80*(1), 1–28. https://doi.org/10.18637/jss.v080.i01

Bürkner, P.-C. (2018). Advanced Bayesian Multilevel Modeling with the R Package brms. *The R Journal*, *10*(1), 395–411. https://doi.org/10.32614/RJ-2018-017

Charbonneau, J. A., Amaral, D. G., & Bliss-Moreau, E. (2021). *Social housing status impacts rhesus monkeys' affective responding in classic threat processing tasks* [Preprint]. Animal Behavior and Cognition. https://doi.org/10.1101/2021.05.16.444352

Charbonneau, J. A., Maister, L., Tsakiris, M., & Bliss-Moreau, E. (2022). Rhesus monkeys have an interoceptive sense of their beating hearts. *Proceedings of the National Academy of Sciences*. In press.

Charles, S. T. (2010). Strength and vulnerability integration: A model of emotional well-being across adulthood. *Psychological Bulletin*, *136*(6), 1068–1091. https://doi.org/10.1037/a0021232

Cornwell, B., Laumann, E. O., & Schumm, L. P. (2008). The social connectedness of older adults: A national profile. *American Sociological Review*, *73*(2), 185–203.

Damasio, A. R., Everitt, B. J., & Bishop, D. (1996). The Somatic Marker Hypothesis and the Possible Functions of the Prefrontal Cortex. *Philosophical Transactions: Biological Sciences*, *351*(1346,), 1413–1420.

Emery Thompson, M., Fox, S. A., Berghänel, A., Sabbi, K. H., Phillips-Garcia, S., Enigk, D. K., Otali, E., Machanda, Z. P., Wrangham, R. W., & Muller, M. N. (2020). Wild chimpanzees exhibit humanlike aging of glucocorticoid regulation. *Proceedings of the National Academy of Sciences*, *117*(15), 8424–8430. https://doi.org/10.1073/pnas.1920593117

Esler, M., Rumantir, M., Kaye, D., Jennings, G., Hastings, J., Socratous, F., & Lambert, G. (2001). Sympathetic nerve biology in essential hypertension. *Clinical and Experimental Pharmacology and Physiology*, *28*(12), 986–989.

Ferrari, A. U., Radaelli, A., & Centola, M. (2003). Invited review: Aging and the cardiovascular system. *J Appl Physiol*, *95*(6), 2591–2597. https://doi.org/10.1152/japplphysiol.00601.2003

Goncharova, N. D., Chigarova, O., Rudenko, N., & Oganyan, T. (2019). Glucocorticoid Negative Feedback in Regulation of the Hypothalamic-Pituitary-Adrenal Axis in Rhesus Monkeys With Various Types of Adaptive Behavior: Individual and Age-Related Differences. *Frontiers in Endocrinology*, *10*, 24. https://doi.org/10.3389/fendo.2019.00024

Goncharova, N. D., & Oganyan, T. E. (2018). Age-related differences in stress responsiveness of the hypothalamic-pituitary-adrenal axis of nonhuman primates with various types of adaptive behavior. *General and Comparative Endocrinology*, *258*, 163–172. https://doi.org/10.1016/j.ygcen.2017.08.007

Gurel, N. Z., Carek, A. M., Inan, O. T., Levantsevych, O., Abdelhadi, N., Hammadah, M., O'Neal, W. T., Kelli, H., Wilmot, K., Ward, L., Rhodes, S., Pearce, B. D., Mehta, P. K., Kutner, M., Garcia, E., Quyyumi, A., Vaccarino, V., Raggi, P., Bremner, J. D., & Shah, A. J. (2019). Comparison of autonomic stress reactivity in young healthy versus aging subjects with heart disease. *PLOS ONE*, *14*(5), e0216278. https://doi.org/10.1371/journal.pone.0216278

Hennessy, M. B., McCowan, B., Jiang, J., & Capitanio, J. P. (2014). Depressive-like behavioral response of adult male rhesus monkeys during routine animal husbandry procedure. *Frontiers in Behavioral Neuroscience*, *8*, 309.

Hotta, H., & Uchida, S. (2010). Aging of the autonomic nervous system and possible improvements in autonomic activity using somatic afferent stimulation: Aging of the autonomic nervous system. *Geriatrics & Gerontology International*, *10*, S127–S136. https://doi.org/10.1111/j.1447-0594.2010.00592.x

James, W. (1884). What is an Emotion? *Mind*, *9*(34), 188–205.

Judd, C. M., Westfall, J., & Kenny, D. A. (2012). Treating stimuli as a random factor in social psychology: A new and comprehensive solution to a pervasive but largely ignored problem. *Journal of Personality and Social Psychology*, *103*(1), 54–69. https://doi.org/10.1037/a0028347

Kawashima, T., Sato, K., Akita, K., & Sasaki, H. (2005). Comparative anatomical study of the autonomic cardiac nervous system in macaque monkeys. *Journal of Morphology*, *266*(1), 112–124. https://doi.org/10.1002/jmor.10371

Krum, H., Schlaich, M., Whitbourn, R., Sobotka, P. A., Sadowski, J., Bartus, K., Kapelak, B., Walton, A., Sievert, H., Thambar, S., & others. (2009). Catheter-based renal sympathetic denervation for resistant hypertension: A multicentre safety and proof-of-principle cohort study. *The Lancet*, *373*(9671), 1275–1281.

Kuraoka, H., Kurosaka, C., Wada, C., & Miyake, S. (2018). Effect of Age on Heart Rate Responses and Subjective Mental Workload During Mental Tasks. *Congress of the International Ergonomics Association*, 316–321.

Kuznetsova, A., Brockhoff, P. B., & Christensen, R. H. B. (2017). lmerTest Package: Tests in Linear Mixed Effects Models. *Journal of Statistical Software*, *82*(13), 1–26. https://doi.org/10.18637/jss.v082.i13

Lakatta, E. (1993). Deficient neuroendocrine regulation of the cardiovascular system with advancing age in healthy humans. *Circulation*, *87*(2), 631–636.

Machado, C. J., Bliss-Moreau, E., Platt, M. L., & Amaral, D. G. (2011). Social and Nonsocial Content Differentially Modulates Visual Attention and Autonomic Arousal in Rhesus Macaques. In *PLoS One* (Vol. 6). http://dx.plos.org/10.1371/journal.pone.0026598.g003 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3202553/pdf/pone.0026598.pdf

McPherson, M., Smith-Lovin, L., & Brashears, M. E. (2006). Social isolation in America: Changes in core discussion networks over two decades. *American Sociological Review*, *71*(3), 353–375.

Mendes, W. B. (2010). Weakened links between mind and body in older age: The case for maturational dualism in the experience of emotion. *Emotion Review*, *2*(3), 240–244. https://doi.org/10.1177/1754073910364149

Mikkelsen, M. B., O'Toole, M. S., Lyby, M. S., Wallot, S., & Mehlsen, M. (2019). Emotional reactivity and interoceptive sensitivity: Exploring the role of age. *Psychonomic Bulletin & Review*. https://doi.org/10.3758/s13423-019-01603-y

Otte, C., Hart, S., Neylan, T. C., Marmar, C. R., Yaffe, K., & Mohr, D. C. (2005). A meta-analysis of cortisol response to challenge in human aging: Importance of gender. *Psychoneuroendocrinology*, *30*(1), 80–91.

Poller, U., Nedelka, G., Radke, J., Pönicke, K., & Brodde, O.-E. (1997). Age-dependent changes in cardiac muscarinic receptor function in healthy volunteers. *Journal of the American College of Cardiology*, *29*(1), 187–193.

Roelofs, K. (2017). Freeze for action: Neurobiological mechanisms in animal and human freezing. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *372*(1718), 20160206. https://doi.org/10.1098/rstb.2016.0206

Russell, J. A. (2003). Core affect and the psychological construction of emotion. *Psychol Rev*, *110*(1), 145–172.

Santistevan, A. C., Fiske, O., Moadab, G., Isaacowitz, D. M., & Bliss-Moreau, E. (2022). *See no evil: Attentional bias towards threat is diminished in aged monkeys*.

Santistevan, A. C., Kinnally, E. L., Capitanio, J. P., & Bliss-Moreau, E. (2022). *From womb-to-tomb: Infant monkeys' BioBehavioral profile predicts mortality across two decades of follow-up*.

Schachter, S., Fd, A., & Singer, J. E. (1962). *COGNITIVE, SOCIAL, AND PHYSIOLOGICAL DETERMINANTS OF EMOTIONAL STATE*. *69*(5), 21.

Seals, D. R., & Bell, C. (2004). Chronic sympathetic activation: Consequence and cause of age-associated obesity? *Diabetes*, *53*(2), 276–284.

Seals, D. R., & Esler, M. D. (2000). Human ageing and the sympathoadrenal system. *The Journal of Physiology*, *528*(3), 407–417.

Shively, C. A., Appt, S. E., Chen, H., Day, S. M., Frye, B. M., Shaltout, H. A., Silverstein-Metzler, M. G., Snyder-Mackler, N., Uberseder, B., Vitolins, M. Z., & Register, T. C. (2020). Mediterranean diet, stress resilience, and aging in nonhuman primates. *Neurobiology of Stress*, *13*, 100254. https://doi.org/10.1016/j.ynstr.2020.100254

Smith, T. W., Uchino, B. N., Berg, C. A., Florsheim, P., Pearce, G., Hawkins, M., Henry, N. J. M., Beveridge, R. M., Skinner, M. A., Ko, K. J., & Olsen-Cerny, C. (2009). Conflict and collaboration in middle-aged and older couples: II. Cardiovascular reactivity during marital interaction. *Psychology and Aging*, *24*(2), 274–286. https://doi.org/10.1037/a0016067

Steptoe, A., Kunz-Ebrecht, S. R., Wright, C., & Feldman, P. J. (2005). Socioeconomic position and cardiovascular and neuroendocrine responses following cognitive challenge in old age. *Biological Psychology*, *69*(2), 149–166. https://doi.org/10.1016/j.biopsycho.2004.07.008

Stratton, J. R., Levy, W. C., Caldwell, J. H., Jacobson, A., May, J., Matsuoka, D., & Madden, K. (2003). Effects of aging on cardiovascular responses to parasympathetic withdrawal. *Journal of the American College of Cardiology*, *41*(11), 2077–2083. https://doi.org/10.1016/S0735-1097(03)00418-2

Thierry, B. (2007). Unity in diversity: Lessons from macaque societies. *Evolutionary Anthropology: Issues, News, and Reviews: Issues, News, and Reviews*, *16*(6), 224–238.

Uchino, B. N., Birmingham, W., & Berg, C. A. (2010). Are Older Adults Less or More Physiologically Reactive? A Meta-Analysis of Age-Related Differences in Cardiovascular Reactivity to Laboratory Tasks. *The Journals of Gerontology: Series B*, *65B*(2), 154–162. https://doi.org/10.1093/geronb/gbp127

Uchino, B. N., Holt-Lunstad, J., Bloor, L. E., & Campo, R. A. (2005). Aging and Cardiovascular Reactivity to Stress: Longitudinal Evidence for Changes in Stress Reactivity. *Psychology and Aging*, *20*(1), 134–143. https://doi.org/10.1037/0882-7974.20.1.134

Uchino, B. N., Holt-Lunstad, J., Uno, D., & Flinders, J. B. (2001). Heterogeneity in the Social Networks of Young and Older Adults: Prediction of Mental Health and Cardiovascular Reactivity During Acute Stress. *Journal of Behavioral Medicine*, 22.

Uchino, B. N., Uno, D., Holt-Lunstad, J., & Flinders, J. B. (1999). Age-related differences in cardiovascular reactivity during acute psychological stress in men and women. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *54*(6), P339–P346.

Wolf, V., Kühnel, A., Teckentrup, V., Koenig, J., & Kroemer, N. B. (2021). Does transcutaneous auricular vagus nerve stimulation affect vagally mediated heart rate variability? A living and interactive Bayesian meta-analysis. *Psychophysiology*, *58*(11). https://doi.org/10.1111/psyp.13933

Table 2.1 Linear mixed effects models of respiratory sinus arrhythmia (RSA) reactivity towards video stimuli. Models additionally adjusted for animal sex, trial number, and day of testing and treated trials as nested within animals and stimuli (crossed random effects). Significant ($p < 0.05$) predictors are in bold.

	Model 1			Model 2			Model 3		
Predictors	*Estimates [95% CI]*	*t*	*p*	*Estimates [95% CI]*	*t*	*p*	*Estimates [95% CI]*	*t*	*p*
(Intercept)	2.83 [1.13 – 4.53]	3.26	0.014	2.83 [1.12 – 4.53]	3.25	0.014	2.96 [1.25 – 4.67]	3.40	0.011
Valence	0.05 [-0.04 – 0.14]	1.12	0.265	0.05 [-0.04 – 0.14]	1.07	0.285	0.03 [-0.06 – 0.12]	0.73	0.464
Arousal	-0.01 [-0.10 – 0.08]	-0.24	0.808	-0.01 [-0.10 – 0.08]	-0.25	0.800	-0.01 [-0.11 – 0.08]	-0.24	0.808
Dominance	-0.42 [-0.72 – -0.11]	-2.68	0.008	-0.42 [-0.72 – -0.11]	-2.67	0.008	-0.49 [-0.80 – -0.18]	-3.12	0.002
Age [mean centered]	-0.09 [-0.34 – 0.15]	-0.75	0.479	-0.09 [-0.34 – 0.15]	-0.74	0.483	-0.09 [-0.34 – 0.15]	-0.72	0.494
Valence * Arousal * Dominance	0.13 [0.04 – 0.23]	2.69	0.007	0.13 [0.03 – 0.23]	2.66	0.008	0.14 [0.04 – 0.23]	2.72	0.007
Valence * Arousal * Dominance * Age [mean centered]				-0.02 [-0.04 – -0.01]	-2.18	0.036	-0.02 [-0.04 – -0.01]	-2.26	0.037
# of Fixations							-0.01 [-0.01 – -0.01]	-5.55	<0.001
Random Effects									
σ^2	1.39			1.39			1.37		
τ_{00}	0.02_{stimuli}			0.02_{stimuli}			0.02_{stimuli}		
	3.74_{animal}			3.73_{animal}			3.76_{animal}		
Intraclass correlation (ICC)	0.73			0.73			0.73		
Observations	3828			3828			3828		
Marginal R^2 / Conditional R^2	0.043 / 0.742			0.043 / 0.742			0.045 / 0.746		

Table 2.2 Linear mixed effects models of pre-ejection period (PEP) reactivity towards video stimuli. Models additionally adjusted for animal sex, trial number, and day of testing and treated trials as nested within animals. Random effects for stimuli were not included in this model as their variance was estimated to be zero. Significant (*p* <0.05) predictors are in bold.

	Model 1			Model 2			Model 3		
Predictors	*Estimates [95% CI]*	*t*	*p*	*Estimates [95% CI]*	*t*	*p*	*Estimates [95% CI]*	*t*	*p*
(Intercept)	48.08 [41.3 – 54.9]	13.9	<0.001	48.09 [41.31 – 54.87]	13.9	<0.001	48.67 [41.88 – 55.46]	14.1	<0.001
Valence	0.04 [-0.39 – 0.47]	0.18	0.859	0.04 [-0.39 – 0.47]	0.18	0.857	-0.03 [-0.46 – 0.40]	-0.15	0.879
Arousal	0.05 [-0.40 – 0.51]	0.24	0.813	0.05 [-0.40 – 0.51]	0.23	0.819	0.06 [-0.40 – 0.51]	0.25	0.804
Dominance	-0.26 [-1.76 – 1.24]	-0.34	0.733	-0.26 [-1.77 – 1.24]	-0.34	0.732	-0.67 [-2.18 – 0.83]	-0.87	0.383
Age [mean centered]	-0.01 [-0.98 – 0.96]	-0.01	0.990	0.00 [-0.97 – 0.97]	0.01	0.995	0.01 [-0.96 – 0.99]	0.03	0.979
Valence * Arousal * Dominance	0.07 [-0.40 – 0.55]	0.29	0.769	0.07 [-0.40 – 0.55]	0.30	0.763	0.10 [-0.38 – 0.57]	0.41	0.685
Valence * Arousal * Dominance * Age [mean centered]				0.00 [-0.09 – 0.09]	0.02	0.985	0.00 [-0.10 – 0.09]	-0.06	0.954
# of Fixations							-0.04 [-0.06 – -0.03]	-5.09	<0.001
Random Effects									
σ^2	30.09			30.13			28.29		
τ_{00}	58.85 $_{\text{animal}}$			58.90 $_{\text{animal}}$			59.10 $_{\text{animal}}$		
Intraclass correlation (ICC)	0.66			0.66			0.66		
Observations	3118			3118			3828		
Marginal R^2 / Conditional R^2	0.068 / 0.685			0.069 / 0.685			0.071 / 0.688		

Table 2.3 Linear mixed effects model of heart rate (HR) reactivity towards video stimuli. Models additionally adjusted for animal sex, trial number, and day of testing. Random effects for stimuli were not included in this model as their variance was estimated to be zero. Significant ($p < 0.05$) predictors are in bold.

	Model 1			Model 2			Model 3		
Predictors	*Estimates [95% CI]*	*t*	*p*	*Estimates [95% CI]*	*t*	*p*	*Estimates [95% CI]*	*t*	*p*
(Intercept)	181.35 [150.15 – 212.54]	13.7	<0.001	181.37 [150.18 –212.57]	13.7	<0.001	179.66 [148.34 – 210.98]	13.6	<0.001
Valence	-1.04 [-2.14 – 0.05]	-1.87	0.06	-1.03 [2.12 – 0.07]	-1.84	0.065	-0.83 [-1.92 – 0.26]	-1.49	0.138
Arousal	0.04 [-1.11 – 1.20]	0.07	0.941	0.05 [-1.11 – 1.21]	0.08	0.936	0.04 [-1.11 – 1.20]	0.07	0.941
Dominance	0.40 [-3.41 – 4.22]	0.21	0.837	0.4 [-3.42 – 4.21]	0.2	0.786	1.42 [-2.39 – 5.24]	0.73	0.464
Age [mean centered]	0.59 [-3.89 – 5.07]	0.31	0.764	0.53 [-3.95 – 5.02]	0.28	0.786	0.51 [3.99 – 5.01]	0.27	0.80
Valence * Arousal * Dominance	-0.21 [-1.43 – 1.00]	-0.34	0.733	-0.21 [-1.42 – 1.01]	-0.33	0.739	-0.26 [-1.48 – 0.95]	-0.43	0.669
Valence * Arousal * Dominance * Age [mean centered]				0.15 [-0.09 – 0.40]	1.22	0.224	0.16 [-0.08 – 0.41]	1.3	0.195
# of Fixations							0.13 [0.08 – 0.18]	5.64	<0.001
Random Effects									
σ^2	244.16			243.92			241.97		
τ_{00}	864.43_{animal}			864.34_{animal}			871.25_{animal}		
Intraclass correlation (ICC)	0.78			0.78			0.78		
Observations	3840			3840			3840		
Marginal R^2 / Conditional R^2	0.091 / 0.800			0.091 / 0.800			0.093 / 0.803		

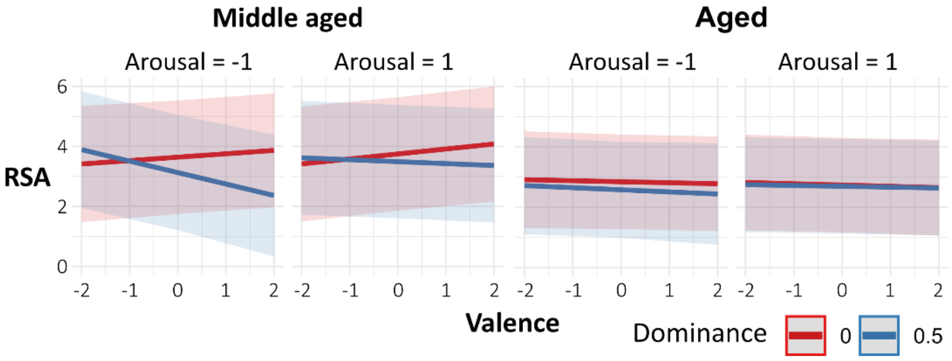

Figure 2.2 Fitted respiratory sinus arrhythmia (RSA) response to dynamic video stimuli. Lines are the estimated marginal means from the mixed effects model 3 in Table 3.1. Shaded regions depict 95% confidence intervals for the marginal mean (marginalized across participants).

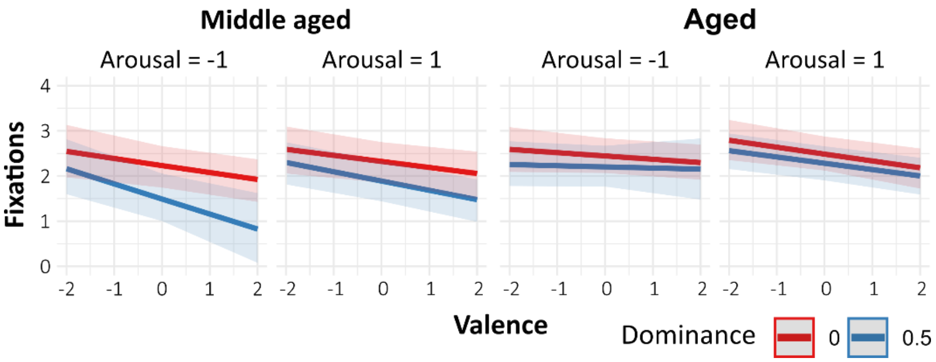

Figure 3.2 Association between the number of fixations and socioaffective content of video stimuli. Lines are the estimated marginal means from the Bayesian mixed effects model described in the text. Shaded regions depict 95% Bayesian confidence intervals for the marginal mean (marginalized across participants).

Supplementary Information

Table S2.1 Average (sd) socioaffective ratings of stimuli grouped by video content.

Video content	Valence	Arousal	Dominance
Aggression (n = 49)	-1.6 (0.6)	1.7 (0.5)	1.8 (0.5)
Aggressive Camera Directed (n = 20)	-2.3 (0.3)	2.0 (0.2)	1.9 (0.3)
Foraging (n = 19)	0.4 (0.2)	-0.5 (0.3)	0.1 (0.1)
Grooming (n = 29)	1.9 (0.3)	-1.5 (0.3)	0.0 (0.1)
Mounting (n = 16)	1.6 (0.3)	1.3 (0.4)	0.6 (0.3)
Neutral Camera Directed (n = 15)	-0.1 (0.2)	0.2 (0.3)	0.1 (0.2)
Nonsocial videos (n = 200)	-0.0 (0.1)	0.2 (0.4)	0.0 (0.1)
Nonspecific Social (n = 14)	0.0 (0.3)	-0.3 (0.7)	0.2 (0.3)
Play (n = 24)	1.7 (0.3)	1.7 (0.4)	0.6 (0.2)
Submissive Camera Directed (n = 14)	-0.4 (0.4)	2.3 (0.3)	0.7 (0.3)

Table S2.2 **Linear mixed effects model of log(RMSSD) reactivity towards video stimuli.** Models additionally adjusted for animal sex, trial number, and day of testing. Random effects for stimuli were not included in this model as their variance was estimated to be zero. Significant (p <0.05) predictors are in bold.

	Model 1				Model 2				Model 3				
Predictors	*Estimates [95% CI]*	*Statistic*	*p*	*df*	*Estimates [95% CI]*	*Statistic*	*p*	*df*	*Estimates [95% CI]*	*CI*	*Statistic*	*p*	*df*
(Intercept)	2.85 [0.47 – 5.22]	2.83	0.025	7.01	2.83 [0.45 – 5.20]	2.81	0.026	7.03	2.86 [0.48 – 5.25]		2.84	0.025	7.03
Valence	-0.01 [-0.05 – 0.04]	-0.27	0.791	371.33	0.17 [0.02 – 0.33]	2.16	0.031	3799.61	0.17 [0.01 – 0.32]		2.07	0.038	3799.3
Arousal	-0.03 [-0.08 – 0.02]	-1.28	0.202	362.96	0.1 [-0.07 – 0.27]	1.18	0.236	3800.82	0.1 [-0.07 – 0.26]		1.18	0.238	3800.35
Dominance	-0.21 [-0.38 – -0.04]	-2.49	0.013	361.4	-0.59 [-1.14 – -0.04]	-2.11	0.035	3800.67	-0.64 [-1.19 – -0.09]		-2.3	0.022	3800.31
Age	-0.06 [-0.20 – 0.08]	-1.07	0.32	7	-0.06 [-0.20 – 0.08]	-1.05	0.327	7.02	-0.06 [-0.20 – 0.08]		-1.04	0.334	7.02
(valence * arousal) * dominance	0.07 [0.01 – 0.12]	2.47	0.014	359.49	0.23 [0.06 – 0.41]	2.6	0.009	3800.71	0.24 [0.06 – 0.41]		2.67	0.008	3800.26
(valence * arousal * dominance) * age					-0.01 [-0.02 – 0.00]	-1.95	0.051	3428.76	-0.01 [-0.02 – -0.00]		-2.01	0.045	3425.98
# of Fixations									0 [-0.01 – -0.00]		-3.83	<0.001	3637.38

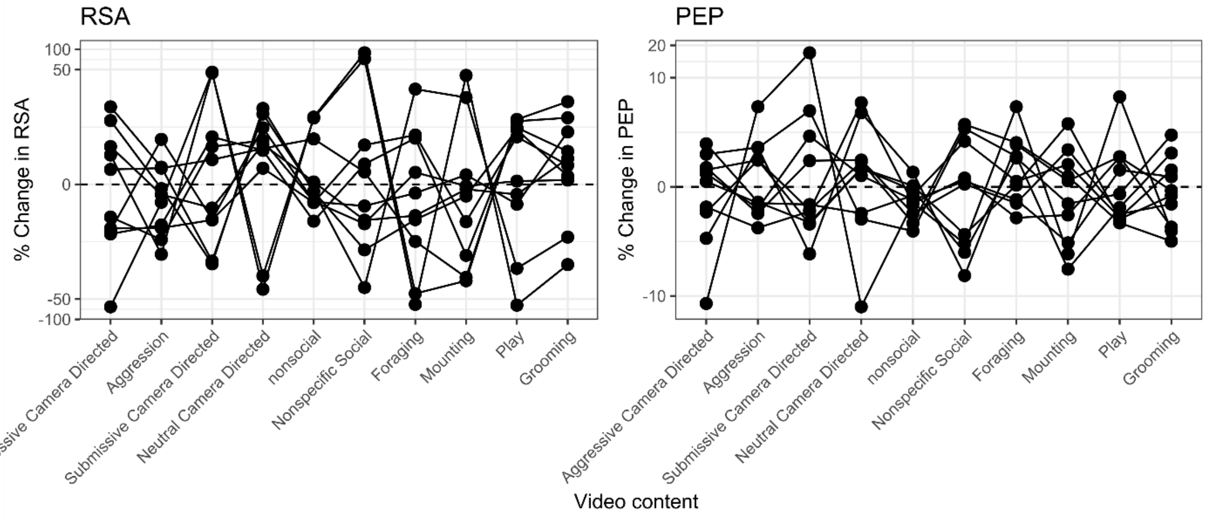

Figure S2.1 Percent change (relative to each animal's average) in respiratory sinus arrhythmia (RSA) and pre-ejection period (PEP) across stimulus type. Points represent within-monkey average values and lines connect data points between the same animal.

Chapter 3

From womb-to-tomb: Infant monkeys' social environment and BioBehavioral profiles predict mortality rates across two decades of follow-up

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Abstract

Identifying early life predictors of mortality is critical for developing treatments and interventions that promote wellbeing. Given that infants' psychological functioning and social environments are known to impact adult socioemotional outcomes throughout development, variation in these two psychosocial features may inform risks and resilience towards mortality across the lifespan. However, the impacts that infant social environment and behavior have on mortality rates is largely unknown due to the difficulty of conducting lifespan studies in humans. We overcome this difficulty by leveraging data from an ongoing longitudinal study on the development of a large population (N = 4,939) of rhesus monkeys (*Macaca mulatta*) (Capitanio, 2021)—a species with shorter lifespans compared to people but that share key features of human neurobiology, physiology, and development—to evaluate how individual differences in rearing environment, behavioral, and physiological (BioBehavioral) reactivity to a psychosocial stressful manipulation predict mortality rates across 20 years of follow-up. Mortality rates were positively correlated with measures of how reactive animals were to being relocated to the testing environment (indexed by both behavior and cortisol response) and negatively correlated with measures of physical activity in the presence of a novel human. Critically, the social environment in which infants were raised was the single most important predictor of mortality and modified the association between infant social environment, behaviors, and mortality. We identify critical windows during development in which BioBehavioral measures are most predictive of survival and, using the genetic relatedness between monkeys, estimate heritability of mortality rates.

Keywords: Nonhuman primates, mortality, infants, stress, behavioral inhibition, cortisol, affect, emotion

From womb-to-tomb: Infant monkeys' social environment and BioBehavioral profiles predict mortality rates across two decades of follow-up

Aspects of our adult psyches can be gleaned from our temperaments within the first years of our lives and—in theory—inform our risks and resilience towards life's challenges. Survival is the ultimate measure of resilience, which raises the question: what features of infants' behaviors and the environments in which they are raised best predict mortality? The evidence needed to answer this question requires large-scale longitudinal studies that, by definition, take a lifetime to perform and therefore pose a significant challenge to undertake in humans. That said, mortality rates are exceptionally important, not only because they speak generally to the health of communities (Miladinov, 2020; Preston, 2007) but also because they are used to inform public policy. For example, mortality rates drive decisions ranging from seat belt laws (Center for Disease Control, 2011; Cohen & Einav, 2003) to the implementation of home visit programs that reduce infant and maternal mortality (Finello et al., 2016; Home Visiting Accountability Act of 2012; Pediatrics, 2009; Slade et al., 2005). Given the importance of mortality rates as a litmus test for community health and a metric that drives policy, identifying early psychological indicators of survival—and the critical developmental windows in which their effects emerge—is necessary for informing public policies that promote the wellbeing of the most vulnerable populations in our global community.

Studies in humans demonstrate that infant temperament is correlated with numerous psychological and behavioral outcomes into adulthood, with some evidence for a link between infant behavioral profiles and mortality rates. For example, socially withdrawn infants (Tang et al., 2020) and children (Asendorpf et al., 2008; Caspi, 1996; Caspi et al., 2003) are at elevated risk for developing depression, anxiety, and impaired social functioning as adults—all of which contribute to early mortality (Holt-Lunstad et al., 2010; Meng et al., 2020; Miloyan et al., 2016). To that end, evidence from one ambitious 70-year-long study (Power & Elliott, 2006) demonstrates that teachers' subjective reports of externalizing (e.g., aggression/impulsivity) and internalizing (e.g., anxious/avoidant) behaviors in children aged 7-11 predict mortality rates as people age (Jokela et al., 2009). However, the work assessing early life behavioral predictors of mortality in humans is often limited by relying on subjective survey responses in place of standardized behavioral assessments, primarily using estimates of behavioral and psychological features in childhood rather than infancy, and take decades before conclusions can be drawn. Early interventions are critical for course correction during adverse socioaffective development (Bayer et al., 2010; N. A. Fox et al., 2011; Kagitcibasi et al., 2001; McCoy et al., 2018; Nelson III et al., 2007) therefore obtaining which features of infants psychological lives impact mortality most—and when—will inform public policy.

Research in rhesus monkeys (*Macaca mulatta*) may prove especially useful for overcoming the difficult challenge inherent to human lifespan research. Rhesus monkeys have shorter lifespans compared to people (with a median lifespan in the wild of approximately 15 years (Hoffman et al., 2010) and up to 25 in captivity (Colman et al., 2009)) but share key features of human neurobiology, physiology, and development (for reviews Kolk & Rakic, 2022; Laubach et al., 2018; Phillips et al., 2014; Preuss & Wise, 2022). Rhesus monkeys mature at a rate that is 3-4 times faster than humans, reaching “adulthood” and sexual maturity around 3.5-5 years of age (Plant et al., 2005) and old age around 18 years of age (Fooden, 2000) which functionally means that a lifespan study can be carried out in a single researcher’s career.

Although research investigating how infant rhesus temperament impacts survival is sparse, there is a rich history of studying the psychological impacts that features of the early social environment have on lifelong behavioral and health outcomes. One particularly impactful example is Harry Harlow’s classic work in which monkeys were raised in various conditions of social isolation (Harlow, 1958; Harlow et al., 1965; Harlow & Zimmermann, 1959) and their affective and social behavior were tracked across development. These studies revealed that forming socioaffective bonds with a caregiver in infancy is requisite for normative socioaffective development with lasting behavioral effects into adulthood (Mitchell et al., 1966; Ruppenthal et al., 1976).

Indeed, these studies served as foundational evidence supporting one of the most influential psychological theories of the 20th century—Bowlby & Ainsworth's attachment theory (Ainsworth, 1967; Ainsworth & Bowlby, 1991; Bowlby, 1969, 1973, 1980; I. Bretherton, 1992)—which, in Bowlby's words "regards the propensity to make intimate emotional bonds to particular individuals as a basic component of human nature" (Bowlby, 1988, p. 120) and that socioemotional bonds are not secondary to other "basic" needs such as food, water, and shelter (Bowlby, 1988). The contributions that work in nonhuman primates made to this theoretical development (for reviews see van der Horst et al., 2008; van Rosmalen et al., 2020) highlights their utility for understanding aspects of the human condition. Although social deprivation serves as an extreme example of the role our social environment plays in normative development, investigations like the ones carried out by Harlow and colleagues (Capitanio et al., 1986; Harlow, 1958; Harlow et al., 1965; Harlow & Zimmermann, 1959; Mitchell et al., 1966; Ruppenthal et al., 1976; Suomi & Harlow, 1972) sowed the seeds for subsequent inquiries into how more subtle variation in socioaffective processing in infancy contributes to behavioral and health outcomes from womb-to-tomb.

Over the past two decades, an ongoing study at the California National Primate Research Center (CNPRC) has evaluated how biological, behavioral, and socioenvironmental factors in infancy foreshadow behavioral and health outcomes across monkeys' lives (Capitanio, 2021). Since 2001, approximately 5,000 infant monkeys (3-4 months of age; ~ 12-14 months of age in human years) have undergone a BioBehavioral Assessment (BBA) consisting of an extensive 25-hour-long evaluation that includes (but is not limited to) measurements of behavioral responsiveness when physically alone (but in a room with other infants), behavioral reactivity to an acute social stressor, and measurements of hypothalamic-pituitary-adrenal axis activity and reactivity (i.e., plasma cortisol response at four time points) (Capitanio, 2021). This research program has produced a wealth of insights including identifying behavioral, genetic, and epigenetic indicators of social functioning in early adolescence (A. S. Fox et al., 2021; Kinnally et al., 2010; Weinstein & Capitanio, 2008) and risks for developing self-injurious (Gottlieb et al., 2013) and depressive-like behaviors in adulthood (Hennessy et al., 2014b). The BBA program has additionally identified environmental, behavioral, and physiological predictors of negative health outcomes including asthma (Capitanio et al., 2011; Chun et al., 2013), chronic gastroenteritis (Gottlieb et al., 2018), and suboptimal cardiac regulation (Bliss-Moreau et al., 2017) but has not yet been harnessed for testing important hypotheses specifically regarding mortality—as in this report.

Given the established literature documenting the relationship between mortality and psychological factors such as depression (Pratt et al., 2016, 2016; Wei et al., 2021), anxiety (Meier et al., 2016; Miloyan et al., 2016; Pratt et al., 2016), and limited social connections (Holt-Lunstad et al., 2010; Steptoe et al., 2013; Yu et al., 2020), we focused the current study on how variation in social and affective processing and social environment impacted mortality, making a unique contribution because of our large sample of infants who were subsequently tracked over time. We begin by separately evaluating the associations of each of our BioBehavioral Assessment measures that related to socioaffective processing with mortality (adjusting for confounders such as sex and age at assessment). We then include all measures into a single multivariable model that incorporates relatedness between animals allowing us to evaluate which measures are most predictive of mortality after adjusting for the other predictors' effects, while simultaneously estimating heritability of mortality rates. Lastly, we assess how features of monkeys' social environment—and changes thereto—influence mortality rates and how monkeys' BioBehavioral measures in infancy modify how these social stressors impact mortality rates. Our large sample of nearly five-thousand monkeys combined with unique colony records that detail monkeys' social environment and physical health allows for precise estimation of time-varying effects uncovering critical development windows in which aspects of infant responsiveness to stressors contribute most to mortality.

Infant monkeys' BioBehavioral profiles predict mortality rates across two decades of follow-up

We performed survival analysis using Cox proportional hazards regression models to assess the relationship between infant monkeys' BioBehavioral profiles and mortality rates in a sample of 4,939 rhesus monkeys (2,695 female). Such models estimate hazards ratios (*HR*) which indicate how higher/lower expected mortality rates are as a function of a given predictor (with HR > 1 indicating higher mortality rates and HR < 1 indicating lower mortality rates). Given that the CNPRC is a research institute and breeding facility, some animal's lives end due to experiments rather than natural causes. As a result, treating deaths from animals who were a part of experiments with terminal endpoints would lead to biased estimates of how early life behavioral responsiveness—and adversity trough life—are associated with mortality. To address this issue, four raters were trained to review each animal's records to determine if and when animals should be considered *censored* (i.e., we only include portions of animals' lives during which they were not enrolled on projects that interfered with their life expectancy). All analyses discussed below took this censoring process into account. See the Methods for details regarding the censoring procedure.

Monkeys that were born and reared at the California National Primate Research Center (CNPRC) between the years of 2001 and 2019 and that underwent the BioBehavioral Assessment were included in the analysis. Subjects were reared in either large social groups (~60-180 members) in 0.2 hectare (hA) outdoor encloses (*field corral*: N = 3,853), outdoors in smaller social groups in approximately 400 square foot enclosures (~7-22 members) (*corn crib*: N = 398), indoors in standard primate caging with their mothers (and, at most, an additional mother-infant pair) (*indoor mother reared*: N = 371), or reared by humans in a nursery with another infant (*nursery reared*: N = 317). This variation in rearing experiences affords us the ability to test hypotheses about how early social environments influence mortality, and how these experiences modify the relationship between infant socioaffective responsiveness and mortality. While testing these hypotheses, we define *normal rearing* as being raised in field corrals or in corn cribs because these environments more closely reflect natural social environments in which monkeys are raised. We define *adverse rearing* as being either mother- or nursery reared.

Aspects of affective reactivity and physiological reactivity were all found to modestly correlate with mortality (unadjusted hazard ratios shown in **Figure 3.1a**) and some of these measures influenced mortality only during critical developmental windows (**Figure 3.1b**).

Adverse rearing conditions are associated with nearly 50% increase in monkeys' mortality rates

Monkeys raised in adverse rearing conditions had significantly higher mortality rates compared to monkeys raised in normal rearing environments (HR = 1.44, 95% CI: [1.26, 1.66], $P = 2.4 \times 10^{-7}$) (**Figure 3.1a**). However, the association between adverse rearing condition and mortality rates was not constant over monkeys' lifespans ($P = 3.0 \times 10^{-3}$). Specifically, monkeys that were raised in adverse rearing conditions had elevated mortality rates reaching a peak in late adolescence/early adulthood (2-5 years old) but rearing condition did not significantly influence mortality rates once animals reached later adulthood (> 6 years) (**Figure 3.1b**). Adolescence therefore appears to be a particularly sensitive developmental period in which early life adverse experiences contribute specifically to excess mortality in nonhuman primates.

Infant monkeys' behavioral responsiveness predicts mortality rates across their entire lifespan

As part of the BBA program, we performed focal observations after the animals were relocated to the holding cages on the first day of testing (Day 1) and again approximately 22 hrs later (Day 2) in order to evaluate monkeys' behavioral responsivity to the acute stressor of being relocated into a novel environment. These focal observations were used to compute "Activity" and "Affective Reactivity" scores (hereafter referred to as "holding cage Activity" and "holding cage Affective Reactivity") derived from factor analysis as previously described (Golub et al., 2009). Holding cage Activity scores correspond to exploratory behavior and the proportion of time in locomotion. Holding cage Affective Reactivity scores were derived from rates of cooing, barking, and whether or not the animal scratched (all of which are thought to be related to anxiety-like states monkeys; Coleman & Pierre, 2014).[4]

Day 1 holding cage Activity (*HR* = 1.06, 95% CI: [1.01, 1.12], *P* = 0.028) and Day 1 holding cage Affective Reactivity (*HR* = 1.06, 95% CI: [1.01, 1.12], *P* = 0.021) were both positively and significantly associated with increased mortality rates across the entire lifespan such that infants with higher holding cage activity and affective reactivity died earlier—though we note the effect sizes are modest (**Figure 3.1a**). We additionally computed difference scores between Day 2 and Day 1 measures for each of holding cage Activity and holding cage Affective Reactivity to evaluate how adaptability to the stress of relocating to a novel environment was predictive of survival. Difference scores greater than 1 indicate that animals were more active/reactive on the second day of testing compared to the first and less inhibited and more exploratory/calm on their second day of testing. Neither the difference score for holding cage Activity (*HR* = 0.96, 95% CI: [0.91, 1.01], *P* = 0.09) nor holding cage Affective Reactivity (*HR* = 0.96, 95% CI: [0.92, 1.01], *P* = 0.09) (**Figure 3.1a**) reached statistical significance. These results indicate that we have insufficient evidence to say whether or not infant monkeys' behavioral adaptation to the novel environment across the two days of testing holds predictive ability for mortality.

Infant monkeys that are more active and reactive in the presence of a novel threatening human have increased mortality rates across development

To assess how the animals responded to an ostensibly threating stimulus, monkeys underwent a variant of the "human intruder" task (Gottlieb & Capitanio, 2013) as part of BBA. Originally developed by

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[4] The BBA program refers to this score as "emotionality" but here we opt to use "affective reactivity" as it is theoretically consistent with modern views on emotion theory (see Bliss-Moreau 2017, 2020) which do not assume that behaviors map to discrete emotions and recognize that the evidence that nonhuman animals have discrete human-like emotions is limited at best. Nevertheless, affect – global states characterized by some degree of valence/hedonics and some degree of arousal/activation and hypothesized to be evolutionary old and present across phylogeny, and behavioral reactivity of the sort indexed in BBA is thought to represent activity in the affect system.

(Kalin & Shelton, 1989), human intruder is a standard task used in nonhuman primate research in which a novel human ("intruder") stands in progressively more threatening positions towards the animal. This procedure produces robust affective responses in which consistent individual variation is observed in nonhuman primates. A previous factor analysis of the behaviors generated by infant monkeys while tested on this task during the BBA demonstrated a four-factor structure consisting of the following subscales: Activity, Affective Reactivity[5], Aggression, and Displacement (Gottlieb & Capitanio, 2013) and animals that underwent BBA were given scores on each of these four factors. For more details see the Methods.

Monkeys' human intruder Activity (*HR* = 1.06, 95% CI: [1.01, 1.12], *P* = 0.024) and human intruder Affective Reactivity (*HR* = 1.05, 95% CI: [1.00, 1.10], *P* = 0.034) were both positively and significantly associated with increased mortality rates, meaning that infants that were more active and with higher affective reactivity in the presence of a novel human intruder had shorter life expectancy. Human intruder Aggression (*HR* = 1.01, 95% CI: [0.96, 1.06], *P* = 0.80) and displacement (*HR* = 1.01, 95% CI: [0.96, 1.07], *P* = 0.61) behaviors were unrelated to survival (**Figure 3.1a**). In summary, consistent with the relationship between home cage behavior and mortality, monkeys that were more behaviorally reactive (indexed by both physical activity and affective reactivity) to a moderate momentary social stressor show elevated risks for mortality across their entire lives but their aggression and displacement behaviors held no such predictive ability.

Cortisol response in infancy is positively associated with mortality rates—but only during a critical window in early development

We sampled plasma cortisol measurements at four time points during the BBA assessment in order to evaluate hypothalamic-pituitary-adrenal (HPA) activity and reactivity. The first sample was taken

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[5] We again note we change nomenclature from "Emotionality" in the original reference to "Affective Reactivity".

approximately two hours following relocation to the holding cage and after the focal observations described above. The second was taken approximately five hours after the first (and after several behavioral assessments had been performed). Adjusting for the platform on which cortisol was assayed, plasma cortisol at the first (*HR* = 1.14, 95% CI: [1.08, 1.20], *P* = 8.73 x 10^{-7}) and the second time points (*HR* = 1.10, 95% CI: [1.05, 1.16], *P* = 2.0 x 10^{-4}) were positively associated with mortality, indicating that infants with more robust glucocorticoid responses died at younger ages. The difference between the cortisol measurement at the second and first time points was not significant (*HR* = 0.96, 95% CI: [0.89, 1.03], *P* = 0.22), indicating that animals' change in physiological responding throughout the day did not predict mortality (**Figure 3.1a**).

Although there was not a significant linear departure from the proportional hazards assumption for either of these cortisol measurements (*Ps* > 0.05), visual inspection revealed that the first two cortisol measures were most predictive of mortality from 3-4 months of age and their predictive ability declined until approximately 2.5 years of age after which cortisol carried no significant influence on mortality rates (**Figure 3.1b**). This indicates that higher physiological reactivity (as measured via plasma cortisol) in infancy is a risk factor for mortality in infancy.

The final two cortisol samples represent physiological probes of the hypothalamic-pituitary-adrenal (HPA) axis. Sample 3 involved a performance on the dexamethasone (DEX) suppression test, which serves as a measure of negative feedback sensitivity in the HPA axis function. Dexamethasone is a synthetic glucocorticoid that should normally lead to lower levels of circulating cortisol in the blood via negative feedback mechanisms—therefore a reduction in circulating cortisol levels following dexamethasone administration indicate normal HPA function. The fourth sample reflects stimulation of the HPA axis by Adrenocorticotropic hormone (ACTH), was administered at the last time point and which probes the evaluated the rebound of the adrenal cortex from the earlier dexamethasone blockade—abnormally low cortisol response to ACTH administration suggests HPA dysfunction. Neither cortisol levels following DEX

(HR = 1.04, 95% CI: [0.98, 1.10], *P* = 0.18) nor ACTH (HR = 1.01, 95% CI: [0.95, 1.07], *P* = 0.74) were significantly associated with mortality rates, indicating physiological responsivity to glucocorticoid suppression/challenge did not hold predictive ability for mortality rates. That said, the difference between responsivity on ACTH challenge and DEX suppression was positively associated with mortality (HR = 1.13, 95% CI: [1.01, 1.27], *P* = 0.03). This indicates that HPA physiological hypersensitivity in infancy is a risk factor for increased mortality rates specifically among infancy.

Multivariable modeling reveals early life social environment modifies the association between BioBehavioral measures and mortality

Next, we fit a single multivariable model incorporating all of the BioBehavioral measures to estimate adjusted effects and to test the hypothesis that rearing condition (normal vs adverse) modified the relationship between BioBehavioral measures and mortality rates. Results from the multivariable model (**Figure 3.2a**) revealed that even after adjusting for all other BioBehavioral measures, the single most important predictor of mortality was monkeys' rearing condition, such that animals raised under adverse conditions had significantly higher mortality rates than those raised in normal social conditions (*HR* = 1.40, 95% CI: [1.08, 1.80], *P* = 0.01). A significant association between the first cortisol measurement and mortality (*HR* = 1.28, 95% CI: [1.13, 1.43], *P* = 1.0 x 10^{-4}) was also identified, however none of the other cortisol measurements held predictive ability once adjusting for all other BioBehavioral measures.

Further, we identified an interaction between rearing condition and Day 1 holding cage Affective Reactivity (*P* = 0.0070) and an interaction between rearing condition and human intruder Activity (*P* = 0.01) (**Figure 3.2b**). Investigating these interactions revealed that, adjusting for all other BioBehavioral factors being considered, monkeys raised in normal social environments evidenced a positive association between holding cage Day 1 Affective Reactivity and mortality (*HR* = 1.10, 95% CI: [1.03, 1.17], *P* = 0.003) and no such association existed for monkeys reared in adverse environments (*HR* = 0.85, 95% CI: [0.71, 1.01], *P* = 0.07). This means that as holding cage Day 1 Affective Reactivity increased, so too did mortality rates—but only for infants raised under normal rearing conditions. Monkeys raised under adverse rearing conditions had higher mortality rates overall, but holding cage Affective Reactivity did not hold predictive power above and beyond the fact that they were raised under adverse rearing conditions (potentially due to a floor effect).

Further, adjusting for all other factors, there was a *negative* association between activity during the human intruder task and mortality in animals that were raised in normal social environments (*HR* = 0.89, 95% CI: [0.81, 0.98], *P* = 0.02) and no such association in monkeys raised under adversity (*HR* = 1.09, 95% CI: [0.97, 1.23], *P* = 0.16). This indicates that monkeys that were less exploratory during the human intruder task had shorter lifespans—but this was only true for monkeys raised in normal rearing conditions.

Heritable risks for mortality account for substantial variation in life expectancy

The multivariable model fit above also took advantage of the fact that we have knowledge of each monkey's pedigree at the CNPRC reaching back up to 12 generations to the 1960's, allowing us to incorporate relatedness information into this analysis to estimate heritability of risk factors for mortality. Briefly, pedigrees were used to construct a kinship matrix (Φ) in which entries ϕ_{ij} represent the estimated probability that two random alleles drawn with replacement from subjects *i* and *j* are identical by descent (IBD). This matrix was then used to inform the covariance structure of the random effects in a mixed effects Cox regression models. This allows us not only to adjust for the fact that animals are related to one another at our center, thus accounting for non-independence between monkeys in our sample, but to also estimate potential genetic contributions to early mortality. When fitting these models, a so-called *frailty term* (monkey-specific random intercept, which is a monkey-specific log hazard ratio) is estimated for each animal. Frailty terms are estimates of excess mortality risk (or excess longevity) for that monkey that has been estimated through its relationship with the other monkeys in the analysis.

There was significant variation in the frailty terms estimated by incorporating pedigree-derived relatedness (**Figure 3.2c**), suggesting there are substantial heritable factors contributing to life expectancy of rhesus monkeys. Specifically, we estimate that monkeys with frailty terms that are one standard deviation above the mean had a mortality risk that is least 1.6 times the average monkeys, meaning that these monkeys have a 60% increase in mortality rates due to heritable effects. Future work performing sequencing analyses on animals from the extreme tails of the frailty distribution will help to inform genetic risk factors for increased mortality rates or that promote longevity.

Rearing experience and BioBehavioral measures modify risks and resilience towards psychosocial stressors across the lifespan

To assess how infants monkeys' behaviors promoted risks and resilience towards psychosocial stressors over their lives, we computed two important time-varying socioaffective measures that, based on previous literature (Charbonneau et al., 2021; Gottlieb et al., 2013, 2018), we hypothesized would impact mortality rates: the cumulative number of relocations into another social environment (*relocations)* that the monkey has experienced and the monkey's *social state* (i.e., housed in large social groups outdoors, indoors with another pairmate, or singly housed indoors). Each of these time-varying predictors were entered into a time-dependent Cox proportional hazards model using methods described in the Methods below. Interactions between social state at a given time point, the cumulative number of moves up until that time point, rearing condition, and the BioBehavioral measures discussed above were entered into the model.

On average, the (standardized) cumulative number of relocations an animal experienced was significantly associated with mortality (*HR* = 1.27, 95% CI: [1.12, 1.43], *P* = 1.0 x 10^{-4}), consistent with past research indicating that an unstable social environment causes psychological duress for monkeys (Gottlieb et al., 2018). That is, the stressful impact of relocations is clearly demonstrated here through increased risk for mortality. Further, the association between the number of relocations and mortality rates was not significantly modified by rearing condition (*P* = 0.21) or any other measures indicating that relocations are invariably associated with elevated mortality rates across all monkeys regardless of rearing environment or behavioral responsiveness to psychosocial stressors as infants.

Monkeys' momentary social state (group housed outdoors, paired indoors, or singly-housed indoors) was additionally associated with survival ($X^2(2) = 14.3$, $P = 7.6 \times 10^{-4}$), however this association was modified by both rearing condition and monkeys' Day 1 holding cage Affective Reactivity ($X^2(2) = 7.06$, $P = 0.03$) (**Figure 3.3**). For simplicity, we present contrasts between mortality rates across social states in two ways: the first being indoors (singly housed or paired) vs outdoors (group housed outdoors) (**Figure 3.3a,b**) and singly housed vs paired (that is, conditional on being housed indoors, how do mortality rates differ between singly housed vs paired animals?) (**Figure 3.3c,d**).

Being housed indoors had opposite effects on mortality rates for animals raised under normal compared to adverse rearing conditions, however animals' age and Day 1 holding cage Affective reactivity modified this effect. For animals reared in normal social environments, mortality rates were higher among animals that were housed indoors compared to animals that were housed outdoors ($HR = 1.55$, 95% CI: [1.30, 1.85], $P = 8.7 \times 10^{-7}$), irrespective of Day 1 holding cage Affective Reactivity as an infant (low reactivity: $HR = 1.46$, 95% CI: [1.19, 1.79], $P = 2.5 \times 10^{-4}$, high reactivity: $HR = 1.60$, 95% CI: [1.33, 1.92], $P = 4.9 \times 10^{-7}$) (**Figure 3.3a**). Moreover, increased mortality rates as a function of being indoors vs. outdoors were particularly pronounced in the youngest and oldest animals that were raised under normal rearing conditions (**Figure 3.3b**). Although mortality rates did not differ between indoor and outdoor housed monkeys that were reared under adverse conditions and that evidence low Day 1 holding cage Affective reactivity ($HR = 1.17$, 95% CI: [0.79, 1.75], $P = 0.44$), monkeys reared under adverse conditions and that evidence high Day 1 holding cage Affective Reactivity lived longer if housed indoors compared to outdoors ($HR = 0.60$, 95% CI: [0.43, 0.84], $P = 0.003$) (**Figure 3.3a**). However, critically, the protective effect of indoor housing against mortality was only true in infancy and indoor housing increased mortality rates in early adulthood (**Figure 3.3b**). Together, these results demonstrate that being housed indoors was typically correlated with increased mortality rates.

Among animals that were housed indoors, we were surprised to find that being singly housed was correlated with lower mortality rates overall. This effect was surprising given the large literature showing negative impacts of being singly housed on normative monkey behavior (Charbonneau et al., 2021; Gottlieb et al., 2013, 2018). Specifically, for animals reared in normal social environments, mortality rates were lower among animals that were singly housed compared to animals that were paired (*HR* = 0.73, 95% CI: [0.55, 2.66], *P* = 0.031), largely irrespective of Day 1 holding cage Affective Reactivity as an infant (low reactivity: *HR* = 0.75, 95% CI: [0.53, 1.06], *P* = 0.12, high reactivity: *HR* = 0.72, 95% CI: [0.53, 0.98], *P* = 0.033) (**Figure 3.3c**). The protective effect that being singly housed had against mortality was most pronounced in the youngest animals that were raised under normal rearing conditions (**Figure 3.3d**). Among animals raised under adverse conditions, only animals that evidence high Day 1 holding cage Affective Reactivity scores showed decreased mortality rates when singly housed compared to paired (low reactivity: *HR* = 1.11, 95% CI: [0.52, 2.39], *P* = 0.92, high reactivity: *HR* = 0.36, 95% CI: [0.13, 0.94], *P* = 0.034) (**Figure 3.3c**). That said, we in *no way* advocate for singly housing monkeys given the substantial evidence that such social isolation results in psychological duress (Charbonneau et al., 2021; Hennessy et al., 2014b; M. A. Novak, 2003) and further research is needed to determine the mechanisms by which this mortality effect emerges. We interpret these data to mean extra care needs to be taken when selecting pair mates, such as matching on features of each monkey's temperament to promote pair success (Capitanio et al., 2017) and improve longevity.

Discussion

Our results demonstrate that aspects of infant monkeys' physiology and behavior predict their risk for dying from infancy to old age. These general effects were exacerbated by some social environments. In general, infant monkeys with higher affective reactivity—both behaviorally and physiologically, as evidenced by their cortisol responding—had shorter life expectancies following initial removal from their home environment and relocation into a novel setting. Adjusting for other biobehavioral measures, monkeys that were *less* physically active (e.g., less exploratory of the environment, potentially meaning more behaviorally inhibited (for a discussion on behavioral inhibition in nonhuman primates see Capitanio, 2018)) during the threat responding paradigm (i.e., human intruder) also had shorter life expectancies. Critically, the environment in which monkeys were raised was the single most important predictor of mortality—monkeys raised in impoverished social environments died younger. Rearing environment was also found to modify how features of infant behavior correlated with mortality. Although several of our findings are intuitive, we uncover critical widows across development in which specific aspects of physiology, behavior, and exposure to psychosocial stressors most strongly impact mortality rates in addition to estimating the heritability of mortality—findings made possible by the large scale, high temporal resolution, and intergenerational nature of our study.

Adverse rearing condition is a risk factor for early mortality specifically in adolescence

In line with decades of research demonstrating the crucial role social environments in monkeys' infancy play in the normative development of both socioaffective behavior (Capitanio et al., 1986; Harlow, 1958; Harlow et al., 1965; Harlow & Zimmermann, 1959; Mitchell et al., 1966; Ruppenthal et al., 1976; Suomi & Harlow, 1972) and neurophysiology (Bliss-Moreau et al., 2017; Seraphin et al., 2022; Wood et al., 2021), we find that the social condition in which infant monkeys were reared (i.e., in large and small social groups versus very limited social environments) was the single most important predictor of mortality rates. Surprisingly, rearing condition remained the strongest predictor of mortality rates even after adjusting for the behavioral and physiological properties that we had hypothesized should mediate rearing condition's impact on mortality (e.g., affective reactivity and cortisol response) and which are known to be disrupted following adverse rearing experiences (Nelson et al., 2009; Suomi, 1991, 2006; Vandeleest et al., 2019). Potential mechanisms through which rearing condition influences mortality rates may be illuminated by focusing on *when* in development we observed excess mortality as a function of rearing condition—namely, during adolescence and early adulthood.

Like humans (Bethlehem et al., 2022; Delevich et al., 2021; Vijayakumar et al., 2021), adolescence and early adulthood is a time of massive reconfiguration to prefrontal cortical structure and function for rhesus monkeys (Bourgeois et al., 1994; Fuster, 2002) and also a time during which monkeys exhibit a breadth of changes to their social behavior. In the wild, males disperse from their natal social groups in search of new groups (Colvin, 1983), females attempt to gain social status in their existing social networks (Bernstein & Ehardt, 1986), and monkeys encounter elevated levels of physical conflict (Bernstein & Ehardt, 1986). Our data suggest that the widely established negative impacts of adverse rearing on monkeys' social processing in adolescence (for a review see Suomi, 1991) directly translate to increased mortality rates and this may be due to aberrant development in neurophysiological systems critical for normative socioaffective processing. Specifically, we know that monkeys raised under adverse rearing conditions have disrupted dopaminergic (Seraphin et al., 2022) and serotonergic (Wood et al., 2021) systems, which are critical for engaging in species-typical behaviors, such as processing dominance signals in social interactions (Morgan et al., 2013; Nader et al., 2012) and also widely implicated in affective processing generally (for reviews see Floresco, 2015; Goschke & Bolte, 2014; Liu et al., 2020; Wise & Rompre, 1989). Adverse rearing experiences may thus directly contribute to excess mortality as a result of maladaptive development in these neural systems.

The finding that monkeys raised under adverse rearing conditions face excess mortality in adolescence draws parallels to psychological health outcomes during the teen years of people who had adverse childhood experiences (ACEs). For example, adolescents who experienced ACEs are at increased risk of substance abuse (Dube et al., 2003), have hypoactive adrenocortical function (L. E. Johnson et al., 2021), and overall poor health (Kabiru et al., 2014). Interestingly, somatic complaints are a common feature of many of the maladaptive behaviors that adolescents who experienced ACEs (Flaherty et al., 2013), which, by definition, implies involvement of interoception (i.e., the sensation of signals arising from the body). Although much of the work in maladaptive behaviors in adolescence have been conceptualized around disruption to self-control (i.e., prefrontal regulatory mechanisms) (for a review see Dvir et al., 2014), dysfunction in interoceptive processing (i.e., sensing signals arising from the organs in the body) is an understudied aspect of psychology that may mediate maladaptive behaviors adolescence (see for example Atanasova et al., 2021; Schaan et al., 2019), and contribute to excess mortality in this age range. Given that rhesus monkeys possess interoceptive ability (Charbonneau et al., 2022), assessing the neural mechanisms through which adverse rearing conditions may disrupt interoceptive processing in adolescence will inform the development of treatments and interventions for youth at risk for negative behavioral and health outcomes.

Contributions of cortisol response to infant mortality

Infant monkeys' cortisol reactivity was the second most important impact on mortality rates—specifically in infancy and early childhood—and remained a significant predictor during this time window even after adjusting for other biological and behavioral covariates. The fact that monkeys' cortisol response was only predictive of mortality in infancy is interesting given evidence from nonhuman primates that chronic exposure to glucocorticoids is a risk factor for depression (Qin et al., 2019) and mortality in adulthood (Campos et al., 2021). Increases in mortality due to cortisol in adulthood are thought to be largely a result of disruption to immune function (for a review see Morey et al., 2015) (making animals more susceptible to disease processes (Capitanio et al., 1998)) and to increases in rates of cardiovascular disease (for a review see Iob & Steptoe, 2019). The finding that infants' cortisol response was only predictive of mortality in infancy suggests that different mechanisms may be at play in determining how cortisol affects mortality rates in infancy compared to in adulthood.

We returned to the health records of the animals in this study in order to get a sense of the causes of death in younger animals with high cortisol responses. Gastrointestinal problems (e.g., colitis) as the cause of decline in health resulted in the overwhelming majority of these animals' deaths. Past research from BBA has demonstrated features of infant monkeys' behavior (Gottlieb et al., 2018) and maternal stress while in utero (Elfenbein et al., 2016) can influence rates of gastrointestinal problems throughout monkeys' lives. Critically, the findings that gastrointestinal problems are observed in infant monkeys following stressors is consistent with research in human children and adults, who are at increased risk for diseases such as irritable bowel disorder which may be mediated by cortisol-induced inflammatory dysregulation and immune dysfunction (Gao et al., 2018; Sun et al., 2019). These past findings, combined with our mortality work, highlight the importance of understanding and investigating further mechanisms though which stress alters gastrointestinal function in infancy as we demonstrate this to be a severe risk factor for early mortality.

Risks and resilience towards psychosocial stressors across development

Our analyses reveal a nuanced relationship between how infant monkeys' behavioral responsiveness and rearing environment correlated with resilience towards psychosocial stressors across the lifespan. The most consistent finding was that an unstable social environment (indexed by the number of times monkeys were moved to new living quarters) was invariably associated with increased mortality rates. This finding is consistent with past work in monkeys demonstrating that frequent relocations is a stress induction, observed through increases in self-injurious behavior (Davenport et al., 2008; Gottlieb et al., 2013; Novak, 2003), cortisol concentrations in hair cortisol (Davenport et al., 2008; Dettmer et al., 2012), and risk for developing gastrointestinal problems (Gottlieb et al., 2018) following many relocations (for a review on how housing practices influence monkeys' wellbeing see Hannibal et al., 2017) and we demonstrate that this stress has measurable impacts on mortality rates across the entire lifespan.

In contrast to social environment stability, measures regarding features of the social environment itself had a more nuanced correlation with mortality rates. Regardless of infant temperament, monkeys raised in normal rearing conditions were uniformly and negatively affected by being moved indoors into relatively impoverished physical and social environments—with older monkeys and infants having significantly higher mortality rates when housed indoors compared to outdoors. A combination of access to physical exercise in addition to rich social relationships likely drives reduced mortality rates in outdoors-housed compared to indoor-housed animals, as we know that in humans, exercise (for a meta-analysis see Reimers et al., 2012) and strong social networks (for a meta-analysis see Holt-Lunstad et al., 2010) promote longevity. We find the difference in life expectancy between indoor and outdoor animals to be especially interesting because although monkeys are clearly at risk for being the target of aggression when in large social settings outside, this risk pales in comparison to the *benefits* monkeys gain by being in large outdoors enclosures in which they have access to physical activity and the positive psychological benefits of interacting with social partners.

The reduction in mortality rates as a result of being housed outdoors was not universally true, however. Animals that were highly reactive in infancy and were raised in adverse rearing conditions had increased mortality rates when housed outdoors—at least in infancy. Increased mortality rates for these animals may be driven by a combination of the fact infants have low rank when moved to a new social network (Wooddell et al., 2017) and that because these infants were raised under adverse conditions they have impaired social processing (for reviews see Suomi, 1991, 2005) and thus likely faced major psychosocial challenges integrating into and navigating their new robust social environments. Thus, extreme care should be taken when integrating infant monkeys with adverse rearing experiences to novel social networks. Critically, our data also suggest that these animals should be integrated into larger social networks, as they have increased mortality rates in adulthood when housed in pairs or alone (indoors) compared to being housed in social groups (outdoors). We note that at our center, very little group housing occurs indoors and when it does it is typically for developmental experiments (and those infants were excluded from this analysis) – as a result, we are unable to disentangle the effects of indoor versus outdoor housing from robust versus impoverished social environments. Our sense given the literature, however, and our own team's ability to rear normal healthy infants in groups indoors, is that the determining factor is not where the animals are housed physically but the extent to which those housing conditions provide robust social contexts.

Our evidence suggests that not all indoor housing conditions (i.e., being paired or living alone) provide the same benefits with regards to lifespan. We were surprised to find that being paired indoors was correlated with *increased* mortality rates compared to being singly housed among animals housed indoors. This was surprising to us given the substantial evidence that housing monkeys alone results in the development of depressive-like behaviors (Hennessy et al., 2017; Suomi et al., 1975), dysfunctional reactivity to psychosocial stressors (Charbonneau et al., 2021), and has negative impacts on monkeys' cardiovascular health (Shively et al., 1989). There has and continues to be discussion (and disagreement) regarding how to best house monkeys indoors given the delicate balance between promoting species-typical behaviors (and presumably wellbeing) via socialization but minimizing adverse outcomes such as aggression/trauma (for commentaries see DiVincenti & Wyatt, 2011; Hannibal et al., 2017; Novak, 2004). Our data underscore the importance of existing research into how to optimize monkey pair formation, such as matching on features of temperament (Capitanio et al., 2017; Truelove et al., 2017), and points to the need for further research into optimal pair formation practices.

Why these data matter for understanding the human condition

Our results corroborate research in people demonstrating a relationship between their socioemotional experiences and mortality rates (e.g., Holt-Lunstad et al., 2010; Steptoe et al., 2013; Steptoe & Wardle, 2011) and provide evidence that biopsychological risk factors for mortality are evolutionarily conserved between rhesus monkeys and humans. Similar to our findings, people with abnormal affective reactivity—namely anxiety and depression—face increased mortality rates (Meier et al., 2016; Meng et al., 2020; Pratt et al., 2016), whereas people with larger and more meaningful social connections live longer (Holt-Lunstad et al., 2010; Steptoe et al., 2013). One interesting aspect of predictors of survival in the human literature is that, among older adults, levels of positive affect are predictive of longevity above and beyond levels of negative affect (Chida & Steptoe, 2008; Steptoe & Wardle, 2011). Given that the presence of positive affect is not necessarily the same as the absence of negative affect (Deci & Ryan, 2008), separate mechanisms may underlie differential effects of positive and negative affective experiences and risks for mortality. Age-related changes to behavior in addition to preservation of autonomic nervous system function may be one such mechanism for promoting longevity in aging populations. Specifically, respiratory sinus arrhythmia—a cardiovascular measure of parasympathetic nervous system activity which is known to be disrupted in normal aging (Jandackova et al., 2016, 2019), is implicated in the processing of positively valenced affective stimuli in both humans and monkeys (Bliss-Moreau et al., 2013; Cacioppo et al., 2000; Santistevan et al., 2022; however see Behnke et al., 2022), and is a measure of cardiovascular health (Mantantzis et al., 2020) is a likely target. That said, the relationship between positive affect and longevity in aging humans is all correlational work that would benefit from performing experiments in which aspects of biology and social environments are manipulated—work that is unethical in humans. Such studies should take place in aging rhesus monkeys, which demonstrate similarities to humans in age-related changes to visual processing of social signals (Santistevan, Fiske, et al., submitted) and autonomic function (Santistevan, Moadab, et al., submitted).

Conclusions

Our results demonstrate that aspects of infant monkeys' physiology and behavior predict their risks and resilience towards mortality from infancy to old age. In general, infant monkeys that were more reactive following removal from their home environments to a novel testing environment had shorter life expectancies. Monkeys raised under adverse rearing conditions had increased mortality rates and were differentially affected by psychosocial stressors across their lifespans relative to monkeys raised in enriched social environments. Our data have far-reaching implications for when in development targeted interventions should take place to promote health and wellbeing for individuals exposed to adverse childhood experiences, with adolescence and old age as particularly important periods for intervention. Future work causally manipulating aspects of monkeys' social environments specifically during adolescence and old age is necessary for uncovering true causal impact such interventions may carry in reducing mortality rates.

Materials and Methods

Subjects included 4,939 rhesus macaques (*Macaca mulatta*) (2,695 female). Monkeys that were born and reared at the California National Primate Research Center (CNPRC) between the years of 2001 and 2019 and that underwent the BioBehavioral assessment were included in the analysis. Subjects were reared in either large social groups (~60-180 members) in 0.2 hectare (hA) outdoor encloses (*field corral*: N = 3,853), outdoors in smaller social groups in approximately 400 square foot enclosures (~7-22 members) (*corn crib*: N = 398), indoors in standard primate caging with their mothers (and, at most, an additional adult-infant pair) (*indoor mother reared*: N = 371), or reared by humans in a nursery with another infant pairmate (*nursery reared*: N = 317). These subjects represent all animals at the CNPRC that underwent the BioBehavioral assessment (BBA) (Capitanio, 2017) and were deemed useable for this analysis (e.g., were not part of invasive developmental studies). All procedures were approved by the UC Davis Institutional Animal Care and Use Committee (IACUC) and were in compliance with the National Institutes of Health guide for the care and use of Laboratory animals.

BioBehavioral Assessment

For a detailed description of the BioBehavioral program see (Capitanio, 2021). All subjects underwent an extensive 25-hour-long behavioral and physiological evaluation between 3-4 months of age (Average days old at assessment: 106.8, interquartile range *[IQR]* = 17 days) aimed at quantifying various measures of BioBehavioral variation. Details of the assessment have been previously described (Capitanio, 2017; Golub, Hogrefe, Widaman, & Capitanio, 2009). Briefly, infants were temporarily relocated from their home environment to individual indoor cages (*holding cage*) for the 25-hr testing period, where they took part in multiple behavioral and physiological assessments which assayed affective reactivity to threat and underwent blood draws for measuring endogenous cortisol as a measure of hypothalamic-adrenal-pituitary (HPA) axis function, and additional genetic, metabolic, and immunological measures not used in this analysis. This study focuses on two composite behavioral measures collected during the assessment—*holding cage observations* and the *human intruder task*—and on cortisol assayed from blood draws at four different time points during the 25-hr assessment. Although the BBA program assays a number of other different behavioral and biological measures, we focused on home cage observations, the human intruder task, and cortisol as these measures are most directly related to infants' stress response.

Holding Cage Observations

We performed focal observations after the animals were relocated to the holding cages on the first day of testing (Day 1) and again approximately 22hrs later (Day 2) in order to evaluate monkeys' behavioral responsivity to the acute stressor of being relocated into a novel environment. These focal observations were used to compute "Activity" and "Affective Reactivity"[6] scores (hereafter referred to as "holding cage Activity" and "holding cage Affective Reactivity") derived from factor analysis as previously described (Golub et al., 2009). Holding cage Activity scores correspond to exploratory behavior and the proportion of time in locomotion. Holding cage Affective Reactivity scores were derived from rates of cooing, barking, and whether or not the animal scratched (all of which are anxiety-like behaviors in monkeys; Coleman & Pierre, 2014). Holding cage Activity and Affective Reactivity scores were Z-scored within each year.

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[6] We again note we change nomenclature from "Emotionality" in the original reference to "Affective Reactivity". See previous footnote on page 92 for more details.

Human Intruder Task

Next, to assess how the monkeys responded to an ostensibly threating stimulus, they experienced the "human intruder" (HI) task (Gottlieb et al., 2013). HI is a standard task used in nonhuman primate research in which a novel human ("intruder") stands in progressively more threatening positions towards the animal. Initially inspired by classic work evaluating behavioral inhibition in human children (Ainsworth & Bell, 1970), variation in reactivity in the HI task has been shown to correlate with numerous behavioral and physiological outcomes in nonhuman primates—highlighting translational validity of our approach and findings to inform human health.

The test proceeds as follows: After a brief 1-min acclimation, an unfamiliar human entered the room and presented themselves to the monkey for 1-min intervals in four different positions (4 minutes total). The various positions were presented in the following order: 1) *profile-far*: human standing ~ 1 m from cage facing 90 degrees away from cage; 2) *profile-near*: human standing ~ 0.5 m from cage, facing 90 degrees away from the cage; 3) *stare-far*: human standing ~ 1 m from cage, facing cage, and making eye contact with subject; 4) *stare-near*: human standing ~ 0.5 m from cage, facing cage and making eye contact with subject.

A previous factor analysis of the behaviors performed during this task demonstrated a four-factor structure: *Activity* (proportion of time spent active; rate of environment exploration; whether cage shake was recorded or not), *Affective Reactivity* (rate of silent bared tooth display (often referred to as a "fear grimace"); rate of coo vocalization; and dichotomized codes of whether convulsive jerk or self-clasp was recorded), *Aggression* (rate of threat; rate of bark; whether other vocalizations were recorded), and *Displacement* (rate of tooth grind; whether yawn was recorded) (Gottlieb & Capitanio, 2013). These four measures, or derivatives therefrom, were used in the analyses.

Hypothalamic-Pituitary-Adrenal (HPA) Axis Function

Blood measurements were taken at four time points during the BBA assessment, from which plasma cortisol measures are assayed. The first samples were taken approximately two hours following relocation to the holding cage and after the focal observations described above. The second were taken approximately five hours after the first (after several behavioral experiments had been performed). The final two cortisol samples represent physiological probes of the hypothalamic-pituitary-adrenal (HPA) axis. Sample 3 involved a performance on the dexamethasone (DEX) suppression test, which serves as a measure of negative feedback sensitivity in the HPA axis function. Dexamethasone is a synthetic glucocorticoid that should normally lead to lower levels of circulating cortisol in the blood via negative feedback mechanisms—therefore a reduction in circulating cortisol levels following dexamethasone administration indicate normal HPA function. The fourth sample reflects stimulation of the HPA axis by Adrenocorticotropic hormone (ACTH), was administered at the last time point and which probes the evaluated the rebound of the adrenal cortex from the earlier dexamethasone blockade—abnormally low cortisol response to ACTH administration suggests HPA dysfunction.

Psychosocial & Environmental changes through life

The unique resources available at the CNPRC allowed us to compute changes in each animal's social environment throughout their entire life (e.g., changes to where the animal lived and changes to the number of social partners with which the animal could interact) and to ultimately correlate these changes with mortality rates.

Given previous results indicating that instability in one's social environment (e.g., frequently being moved into different rooms with new social partners) can lead to abnormal behaviors in rhesus monkeys (Gottlieb, Capitanio, & McCowan, 2013), we used our database to compute the number of times an animal was relocated throughout their life. A "relocation" was defined as being physically moved to another room/outdoor enclosure and staying in that same location for one week or longer. We ignored relocations to the veterinary hospital for the purposes of this variable.

A large literature additionally points to physiological and behavioral benefits of having access to a pair mate compared to being housed alone (for a review see Hannibal, Bliss-Moreau, Vandeleest, McCowan, & Capitanio, 2017)—for example, rhesus monkeys that are singly housed display abnormal behavioral reactivity in response to a social stressor (Charbonneau et al., 2021). We therefore computed changes to social housing status across each monkey’s life to evaluate the degree to which social housing condition influenced mortality risk. At any point in time, an animal could be in one of three mutually exclusive social environments: group housed (housed in the large outdoors enclosures including field corrals and corn cribs), paired with another social partner indoors, or singly housed indoors.

Statistical analyses

All statistical analyses were performed in R version 4.0.3 (R Core Team, 2020). Cox proportional hazards models were used to test for associations between baseline behavioral responsiveness measures, cortisol response, and all-cause mortality. All models were tested for the proportional hazards assumption (i.e., that the effect of the covariate is constant across all age groups) using the *cox.zph* function in the *Survival* package, and time-varying effects (e.g., violations of the proportional hazards assumption) are shown where appropriate. Because *cox.zph* only formally tests for significant linear trends of departure of the proportional hazards assumption, we additionally plotted graphs of the Schoenfeld residuals to identify non-linear departures of the proportional hazards assumption. Models incorporating pedigree information in order to estimate heritability were fit using the *coxme* package (Therneau, 2020).

Censoring

Survival analyses are often performed on data from humans in longitudinal studies in which subjects either drop out of the study or are still alive at the end of the study. These participants are said to be *censored*—that is, we know that they lived at least as long as they had been followed up, but we don't know their actual survival time. Survival analysis models take this censoring process into account when computing hazards ratios and allow for using all of the data that the subjects contribute (even the subjects that dropped out) to obtain unbiased estimates of differences in life expectancy between groups of interest. Given that the CNPRC is a research institute and breeding facility, some animals lives are ended for experimental purposes and not due to natural causes. As a result, treating deaths from animals who were a part of experiments with terminal endpoints would lead to biased estimates of how early life behavioral responsiveness—and adversity trough life—are associated with mortality. To address this issue, four raters were trained to review each animal's records to determine if and when animals should be considered *censored* (i.e., we only include portions of animals' lives during which they were not enrolled on projects that interfered with their life expectancy). For example, if a monkey was put on a project that significantly altered its life trajectory/had a terminal endpoint, then we recorded the date on which that monkey was placed on that project and indicated that this monkey was still alive on that date. We ignore everything that happened to the monkey after that date (i.e., treat it as missing data). Projects with a terminal endpoint or that otherwise interfered with the monkeys' health, social environment, and wellbeing resulted in an animal being censored if they were placed on that project. Raters were required to reach > 90% accuracy (as measured by intraclass correlation) on identifying whether or not a given animal should be censored and on what date they should be censored. Animals that were shipped to other research facilities were censored on the date they were shipped (as we have no information about how long they lived thereafter).

Relatedness

Each monkey's dam and sire were determined genetically using a panel of 29 short tandem repeats (STR's) by the UC Davis Veterinary Genetics Lab (for details see Andrade et al., 2004, Kanthaswamy et al., 2006). Parentage was then used to construct a familial pedigree for all animals at the primate center going back to up to 12 generations. This pedigree was used to compute a kinship matrix, Φ, in which entries ϕ_{ij}

represent the estimated probability that two random alleles drawn with replacement from subjects *i* and *j* are identical by descent (IBD)—that is, that the alleles have the same ancestral origin (Balding et al., 2008). This matrix was then used to inform the covariance structure of the random effects in mixed effect Cox regression models. This allows us to not only adjust for the fact that animals are related to one another at our center, thus adjusting for non-independence in our sample, but to also estimate potential genetic contributions to excess mortality after adjusting for shared environmental and behavioral effects (**Figure 3.2c**).

References

Aaronson, S. T., Sears, P., Ruvuna, F., Bunker, M., Conway, C. R., Dougherty, D. D., Reimherr, F. W., Schwartz, T. L., & Zajecka, J. M. (2017). A 5-Year Observational Study of Patients With Treatment-Resistant Depression Treated With Vagus Nerve Stimulation or Treatment as Usual: Comparison of Response, Remission, and Suicidality. *American Journal of Psychiatry*, *174*(7), 640–648. https://doi.org/10.1176/appi.ajp.2017.16010034

Ainsworth, M. (1967). *Infancy in Uganda: Infant care and the growth of love.*

Ainsworth, M., & Bowlby, J. (1991). An ethological approach to personality development. *American Psychologist*, *46*(4), 333.

Alexander, G. E., Chen, K., Aschenbrenner, M., Merkley, T. L., Santerre-Lemmon, L. E., Shamy, J. L., Skaggs, W. E., Buonocore, M. H., Rapp, P. R., & Barnes, C. A. (2008). Age-Related Regional Network of Magnetic Resonance Imaging Gray Matter in the Rhesus Macaque. *Journal of Neuroscience*, *28*(11), 2710–2718. https://doi.org/10.1523/JNEUROSCI.1852-07.2008

Almeling, L., Hammerschmidt, K., Sennhenn-Reulen, H., Freund, A. M., & Fischer, J. (2016). Motivational shifts in aging monkeys and the origins of social selectivity. *Curr Biol*, *26*(13), 1744–1749. https://doi.org/10.1016/j.cub.2016.04.066

Almeling, L., Sennhenn-Reulen, H., Hammerschmidt, K., Freund, A. M., & Fischer, J. (2017). Social interactions and activity patterns of old Barbary macaques: Further insights into the foundations of social selectivity. *American Journal of Primatology*, *79*(11), e22711. https://doi.org/10.1002/ajp.22711

Amir, I., Zvielli, A., & Bernstein, A. (2016). (De) coupling of our eyes and our mind's eye: A dynamic process perspective on attentional bias. *Emotion*, *16*(7), 978.

Andreano, J. M., Touroutoglou, A., Dickerson, B. C., & Barrett, L. F. (2017). Resting connectivity between salience nodes predicts recognition memory. *Social Cognitive and Affective Neuroscience*, *12*(6), 948–955. https://doi.org/10.1093/scan/nsx026

Asendorpf, J. B., Denissen, J. J., & Van Aken, M. A. (2008). Inhibited and aggressive preschool children at 23 years of age: Personality and social transitions into adulthood. *Developmental Psychology*, *44*(4), 997.

Atanasova, K., Lotter, T., Reindl, W., & Lis, S. (2021). Multidimensional Assessment of Interoceptive Abilities, Emotion Processing and the Role of Early Life Stress in Inflammatory Bowel Diseases. *Frontiers in Psychiatry*, *12*, 680878. https://doi.org/10.3389/fpsyt.2021.680878

Baker, S. E., Limberg, J. K., Dillon, G. A., Curry, T. B., Joyner, M. J., & Nicholson, W. T. (2018). Aging Alters the Relative Contributions of the Sympathetic and Parasympathetic Nervous System to Blood Pressure Control in Women. *Hypertension*, *72*(5), 1236–1242. https://doi.org/10.1161/HYPERTENSIONAHA.118.11550

Balding, D. J., Bishop, M., & Cannings, C. (2008). *Handbook of statistical genetics*. John Wiley & Sons.

Barber, S. J., Lopez, N., Cadambi, K., & Alferez, S. (2020). The limited roles of cognitive capabilities and future time perspective in contributing to positivity effects. *Cognition*, *200*, 104267. https://doi.org/10.1016/j.cognition.2020.104267

Barr, D. J., Levy, R., Scheepers, C., & Tily, H. J. (2013). Random effects structure for confirmatory hypothesis testing: Keep it maximal. *Journal of Memory and Language*, *68*(3), 255–278. https://doi.org/10.1016/j.jml.2012.11.001

Barrett, L. F. (2017). The theory of constructed emotion: An active inference account of interoception and categorization. *Social Cognitive and Affective Neuroscience*, *12*(1), 1–23. https://doi.org/10.1093/scan/nsw154

Barrett, L. F., Adolphs, R., Marsella, S., Martinez, A. M., & Pollak, S. D. (2019). Emotional Expressions Reconsidered: Challenges to Inferring Emotion From Human Facial Movements. *Psychological Science in the Public Interest*, *20*(1), 1–68. https://doi.org/10.1177/1529100619832930

Barrett, L. F., & Bliss-Moreau, E. (2009). Affect as a psychological primitive. *Advances in Experimental Social Psychology*, *41*(08), 167–218. https://doi.org/10.1016/S0065-2601(08)00404-8

Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using lme4. *Journal of Statistical Software*, *67*(1), 1–48. https://doi.org/10.18637/jss.v067.i01

Baxter, M. G. (2001). Cognitive Aging in Nonhuman Primates. In P. R. Hoff & C. V. Mobbs (Eds.), *Functional Neurobiology of Aging* (pp. 407–419). Academic Press.

Bayer, J. K., Hastings, P. D., Sanson, A. V., Ukoumunne, O. C., & Rubin, K. H. (2010). Predicting mid-childhood internalising symptoms: A longitudinal community study. *International Journal of Mental Health Promotion*, *12*(1), 5–17.

Behnke, M., Kreibig, S. D., Kaczmarek, L. D., Assink, M., & Gross, J. J. (2022). Autonomic Nervous System Activity During Positive Emotions: A Meta-Analytic Review. *Emotion Review*, 175407392110730. https://doi.org/10.1177/17540739211073084

Bernstein, I. S., & Ehardt, C. L. (1986). Modification of aggression through socialization and the special case of adult and adolescent male rhesus monkeys (Macaca mulatta). *American Journal of Primatology*, *10*(3), 213–227.

Berntson, G. G., Cacioppo, J. T., & Bosch, J. A. (2016). From Homeostasis to Allodynamic Regulation. In J. T. Cacioppo, L. G. Tassinary, & G. G. Berntson (Eds.), *Handbook of Psychophysiology* (4th ed., pp. 401–426). Cambridge University Press. https://doi.org/10.1017/9781107415782.018

Berntson, G. G., Quigley, K. S., Norman, G. J., & Lozano, D. L. (2016). Cardiovascular Psychophysiology. In J. T. Cacioppo, L. G. Tassinary, & G. G. Berntson (Eds.), *Handbook of Psychophysiology* (4th ed., pp. 183–216). Cambridge University Press. https://doi.org/10.1017/9781107415782.009

Bethlehem, R. A. I., Seidlitz, J., White, S. R., Vogel, J. W., Anderson, K. M., Adamson, C., Adler, S., Alexopoulos, G. S., Anagnostou, E., Areces-Gonzalez, A., Astle, D. E., Auyeung, B., Ayub, M., Bae, J., Ball, G., Baron-Cohen, S., Beare, R., Bedford, S. A., Benegal, V., … Alexander-Bloch, A. F. (2022). Brain charts for the human lifespan. *Nature*. https://doi.org/10.1038/s41586-022-04554-y

Bliss-Moreau, E., Machado, C. J., & Amaral, D. G. (2013a). Macaque cardiac physiology is sensitive to the valence of passively viewed sensory stimuli. *PLoS One*, *8*(8), e71170. https://doi.org/10.1371/journal.pone.0071170

Bliss-Moreau, E., Machado, C. J., & Amaral, D. G. (2013b). Macaque Cardiac Physiology Is Sensitive to the Valence of Passively Viewed Sensory Stimuli. *PLoS ONE*, *8*(8). https://doi.org/10.1371/journal.pone.0071170

Bliss-Moreau, E., & Moadab, G. (2017). The faces monkeys make. *The Science of Facial Expression. New York, NY: Oxford*.

Bliss-Moreau, E., Moadab, G., & Capitanio, J. P. (2017). Maternal rearing environment impacts autonomic nervous system activity. *Developmental Psychobiology*, *59*(4), 551–556. https://doi.org/10.1002/dev.21513

Bliss-Moreau, E., Santistevan, A. C., Bennet, J., Moadab, G., & Amaral, D. G. (2021). Anterior cingulate cortex ablation disrupts affective vigor and vigilance. *Journal of Neuroscience*.

Bliss-Moreau, E., Theil, J. H., & Moadab, G. (2013). Efficient Cooperative Restraint Training With Rhesus Macaques. *Journal of Applied Animal Welfare Science*, *16*(2). https://doi.org/10.1080/10888705.2013.768897

Bourgeois, J.-P., Goldman-Rakic, P. S., & Rakic, P. (1994). Synaptogenesis in the prefrontal cortex of rhesus monkeys. *Cerebral Cortex*, *4*(1), 78–96.

Bowlby, J. (1969). Attachment and loss: Volume I: attachment. In *Attachment and Loss: Volume I: Attachment* (pp. 1–401). London: The Hogarth Press and the Institute of Psycho-Analysis.

Bowlby, J. (1973). Attachment and loss: Volume II: Separation, anxiety and anger. In *Attachment and loss: Volume II: Separation, anxiety and anger* (pp. 1–429). London: The Hogarth press and the institute of psycho-analysis.

Bowlby, J. (1980). Attachment and loss: Volume III: Loss, sadness and depression. In *Attachment and Loss: Volume III: Loss, Sadness and Depression* (pp. 1–462). London: The Hogarth press and the institute of psycho-analysis.

Bowlby, J. (1988). *A secure base: Parent-child attachment and healthy human development*. Basic books.

Bretherton, B., Atkinson, L., Murray, A., Clancy, J., Deuchars, S., & Deuchars, J. (2019). Effects of transcutaneous vagus nerve stimulation in individuals aged 55 years or above: Potential benefits of daily stimulation. *Aging*, *11*(14), 4836–4857. https://doi.org/10.18632/aging.102074

Bretherton, I. (1992). The origins of attachment theory: John Bowlby and Mary Ainsworth. *Developmental Psychology*, *28*(5), 759.

Bruine de Bruin, W., Parker, A. M., & Strough, J. (2020). Age differences in reported social networks and well-being. *Psychology and Aging*, *35*(2), 159.

Bürkner, P.-C. (2017). brms: An R Package for Bayesian Multilevel Models Using Stan. *Journal of Statistical Software*, *80*(1), 1–28. https://doi.org/10.18637/jss.v080.i01

Bürkner, P.-C. (2018). Advanced Bayesian Multilevel Modeling with the R Package brms. *The R Journal*, *10*(1), 395–411. https://doi.org/10.32614/RJ-2018-017

Burr, D. A., Castrellon, J. J., Zald, D. H., & Samanez-Larkin, G. R. (2021). Emotion dynamics across adulthood in everyday life: Older adults are more emotionally stable and better at regulating desires. *Emotion*, *21*(3), 453.

Cacioppo, J. T., Berntson, G. G., Larsen, J. T., Poehlmann, K. M., Ito, T. A., & others. (2000). The psychophysiology of emotion. *Handbook of Emotions*, *2*, 173–191.

Campos, F. A., Archie, E. A., Gesquiere, L. R., Tung, J., Altmann, J., & Alberts, S. C. (2021). Glucocorticoid exposure predicts survival in female baboons. *Science Advances*, *7*(17), eabf6759. https://doi.org/10.1126/sciadv.abf6759

Capitanio, J. P. (2018). Behavioral inhibition in nonhuman primates: The elephant in the room. In *Behavioral inhibition* (pp. 17–33). Springer.

Capitanio, J. P. (2021). Knowledge of biobehavioral organization can facilitate better science: A review of the BioBehavioral Assessment Program at the California National Primate Research Center. *Animals*, *11*(8), 2445.

Capitanio, J. P., Blozis, S. A., Snarr, J., Steward, A., & McCowan, B. J. (2017). Do “birds of a feather flock together” or do “opposites attract”? Behavioral responses and temperament predict success in pairings of rhesus monkeys in a laboratory setting: Temperament and Pairing Success. *American Journal of Primatology*, *79*(1), e22464. https://doi.org/10.1002/ajp.22464

Capitanio, J. P., Mendoza, S. P., Lerche, N. W., & Mason, W. A. (1998). Social stress results in altered glucocorticoid regulation and shorter survival in simian acquired immune deficiency syndrome. *Proceedings of the National Academy of Sciences*, *95*(8), 4714–4719. https://doi.org/10.1073/pnas.95.8.4714

Capitanio, J. P., Miller, L. A., Schelegle, E. S., Mendoza, S. P., Mason, W. A., & Hyde, D. M. (2011). Behavioral inhibition is associated with airway hyper-responsiveness but not atopy in a monkey model of asthma. *Psychosomatic Medicine*, *73*(4), 288.

Capitanio, J. P., Rasmussen, K., Snyder, D., Laudenslager, M., & Reite, M. (1986). Long-term follow-up of previously separated pigtail macaques: Group and individual differences in response to novel situations. *Journal of Child Psychology and Psychiatry*, *27*(4), 531–538.

Carstensen, L. L., & DeLiema, M. (2018). The positivity effect: A negativity bias in youth fades with age. *Current Opinion in Behavioral Sciences*, *19*, 7–12. https://doi.org/10.1016/j.cobeha.2017.07.009

Carstensen, L. L., & Fredrickson, B. L. (1998). *Influence of HIV Status and Age on Cognitive Representations of Others*. 19.

Carstensen, L. L., Isaacowitz, D. M., & Charles, S. T. (1999). Taking Time Seriously: A Theory of Socioemotional Selectivity. *American Psychologist*, 17.

Carstensen, L. L., Turan, B., Scheibe, S., Ram, N., Ersner-Hershfield, H., Samanez-Larkin, G. R., Brooks, K. P., & Nesselroade, J. R. (2011). Emotional experience improves with age: Evidence based on over 10 years of experience sampling. *Psychology and Aging*, *26*(1), 21.

Caspi, A. (1996). Behavioral Observations at Age 3 Years Predict Adult Psychiatric Disorders: Longitudinal Evidence From a Birth Cohort. *Archives of General Psychiatry*, *53*(11), 1033. https://doi.org/10.1001/archpsyc.1996.01830110071009

Caspi, A., Harrington, H., Milne, B., Amell, J. W., Theodore, R. F., & Moffitt, T. E. (2003). Children's Behavioral Styles at Age 3 Are Linked to Their Adult Personality Traits at Age 26: From Age 3 to Age 26. *Journal of Personality*, *71*(4), 495–514. https://doi.org/10.1111/1467-6494.7104001

Cassidy, L. C., Bethell, E. J., Brockhausen, R. R., Boretius, S., Treue, S., & Pfefferle, D. (2021). The dot-probe attention bias task as a method to assess psychological wellbeing after anesthesia: A study with adult female long-tailed macaques (Macaca fascicularis). *European Surgical Research*. https://doi.org/10.1159/000521440

Center for Disease Control. (2011). *Policy Impact: Seat Belts*. 8.

Chapman, A., Devue, C., & Grimshaw, G. M. (2019). Fleeting reliability in the dot-probe task. *Psychological Research*, *83*(2), 308–320. https://doi.org/10.1007/s00426-017-0947-6

Charbonneau, J. A., Amaral, D. G., & Bliss-Moreau, E. (2021). *Social housing status impacts rhesus monkeys' affective responding in classic threat processing tasks* [Preprint]. Animal Behavior and Cognition. https://doi.org/10.1101/2021.05.16.444352

Charbonneau, J. A., Maister, L., Tsakiris, M., & Bliss-Moreau, E. (2022). Rhesus monkeys have an interoceptive sense of their beating hearts. *Proceedings of the National Academy of Sciences*. In press.

Charles, S. T. (2010). Strength and vulnerability integration: A model of emotional well-being across adulthood. *Psychological Bulletin*, *136*(6), 1068–1091. https://doi.org/10.1037/a0021232

Charles, S. T., & Carstensen, L. L. (2010). Social and emotional aging. *Annual Review of Psychology*, *61*, 383–409.

Charles, S. T., Mather, M., & Carstensen, L. L. (2003). Aging and emotional memory: The forgettable nature of negative images for older adults. *Journal of Experimental Psychology: General*, *132*(2), 310–324. https://doi.org/10.1037/0096-3445.132.2.310

Chatterji, S., Byles, J., Cutler, D., Seeman, T., & Verdes, E. (2015). Health, functioning, and disability in older adults—Present status and future implications. *The Lancet*, *385*(9967), 563–575.

Chida, Y., & Steptoe, A. (2008). Positive psychological well-being and mortality: A quantitative review of prospective observational studies. *Psychosomatic Medicine*, *70*(7), 741–756.

Chun, K., Miller, L. A., Schelegle, E. S., Hyde, D. M., & Capitanio, J. P. (2013). Behavioral inhibition in rhesus monkeys (Macaca mulatta) is related to the airways response, but not immune measures, commonly associated with asthma. *PloS One*, *8*(8), e71575.

Cohen, A., & Einav, L. (2003). The effects of mandatory seat belt laws on driving behavior and traffic fatalities. *Review of Economics and Statistics*, *85*(4), 828–843.

Coleman, K., & Pierre, P. J. (2014). Assessing anxiety in nonhuman primates. *ILAR Journal*, *55*(2), 333–346.

Colman, R. J., Anderson, R. M., Johnson, S. C., Kastman, E. K., Kosmatka, K. J., Beasley, T. M., Allison, D. B., Cruzen, C., Simmons, H. A., Kemnitz, J. W., & Weindruch, R. (2009). Caloric Restriction Delays Disease Onset and Mortality in Rhesus Monkeys. *Science*, *325*(5937), 201–204. https://doi.org/10.1126/science.1173635

Colvin, J. (1983). Familiarity, rank and the structure of rhesus male peer networks. *Primate Social Relationships: An Integrated Approach. Oxford: Blackwell Scientific Publications*, 190–199.

Cornwell, B., Laumann, E. O., & Schumm, L. P. (2008). The social connectedness of older adults: A national profile. *American Sociological Review*, *73*(2), 185–203.

Corr, J. (2003). Social behavior in aged rhesus macaques. *Collegium Antropologicum*, *27*(1), 87–94.

Csibra, G., Hernik, M., Mascaro, O., Tatone, D., & Lengyel, M. (2016). Statistical treatment of looking-time data. *Developmental Psychology*, *52*(4), 521–536. https://doi.org/10.1037/dev0000083

Cypryańska, M., Krejtz, I., Jaskó\lowska, A., Kulawik, A., Żukowska, A., De Zavala, A. G., Niewiarowski, J., & Nezlek, J. B. (2014). An experimental study of the influence of limited time horizon on positivity effects among young adults using eye-tracking. *Psychological Reports*, *115*(3), 813–827.

Damasio, A. R., Everitt, B. J., & Bishop, D. (1996). The Somatic Marker Hypothesis and the Possible Functions of the Prefrontal Cortex. *Philosophical Transactions: Biological Sciences*, *351*(1346,), 1413–1420.

Davenport, M. D., Lutz, C. K., Tiefenbacher, S., Novak, M. A., & Meyer, J. S. (2008). A rhesus monkey model of self-injury: Effects of relocation stress on behavior and neuroendocrine function. *Biological Psychiatry*, *63*(10), 990–996.

Deci, E. L., & Ryan, R. M. (2008). Hedonia, eudaimonia, and well-being: An introduction. *Journal of Happiness Studies*, *9*(1), 1–11. https://doi.org/10.1007/s10902-006-9018-1

Delevich, K., Klinger, M., Okada, N. J., & Wilbrecht, L. (2021). Coming of age in the frontal cortex: The role of puberty in cortical maturation. *Seminars in Cell & Developmental Biology*, *118*, 64–72.

Demeyer, I., & De Raedt, R. (2013). Attentional bias for emotional information in older adults: The role of emotion and future time perspective. *PloS One*, *8*(6), e65429.

Demeyer, I., & De Raedt, R. (2014). The effect of future time perspective manipulation on affect and attentional bias. *Cognitive Therapy and Research*, *38*(3), 302–312.

Dettmer, A. M., Novak, M. A., Suomi, S. J., & Meyer, J. S. (2012). Physiological and behavioral adaptation to relocation stress in differentially reared rhesus monkeys: Hair cortisol as a biomarker for anxiety-related responses. *Psychoneuroendocrinology*, *37*(2), 191–199. https://doi.org/10.1016/j.psyneuen.2011.06.003

DiVincenti, L. D., & Wyatt, J. D. (2011). Pair Housing of Macaques in Research Facilities: A Science-Based Review of Benefits and Risks. *Journal of the American Association for Laboratory Animal Science*, *50*(6), 8.

Dube, S. R., Felitti, V. J., Dong, M., Chapman, D. P., Giles, W. H., & Anda, R. F. (2003). Childhood Abuse, Neglect, and Household Dysfunction and the Risk of Illicit Drug Use: The Adverse Childhood Experiences Study. *Pediatrics*, *111*(3), 564–572. https://doi.org/10.1542/peds.111.3.564

Dvir, Y., Ford, J. D., Hill, M., & Frazier, J. A. (2014). Childhood maltreatment, emotional dysregulation, and psychiatric comorbidities. *Harvard Review of Psychiatry*, *22*(3), 149.

Eldesouky, L., & English, T. (2018). Another year older, another year wiser? Emotion regulation strategy selection and flexibility across adulthood. *Psychology and Aging*, *33*(4), 572–585. https://doi.org/10.1037/pag0000251

Elfenbein, H. A., Rosso, L. D., McCowan, B., & Capitanio, J. P. (2016). Effect of indoor compared with outdoor location during gestation on the incidence of diarrhea in indoor-reared rhesus macaques (Macaca mulatta). *Journal of the American Association for Laboratory Animal Science*, *55*(3), 277–290.

Emery Thompson, M., Fox, S. A., Berghänel, A., Sabbi, K. H., Phillips-Garcia, S., Enigk, D. K., Otali, E., Machanda, Z. P., Wrangham, R. W., & Muller, M. N. (2020). Wild chimpanzees exhibit humanlike aging of glucocorticoid regulation. *Proceedings of the National Academy of Sciences*, *117*(15), 8424–8430. https://doi.org/10.1073/pnas.1920593117

English, T., & Carstensen, L. L. (2014). Selective narrowing of social networks across adulthood is associated with improved emotional experience in daily life. *International Journal of Behavioral Development*, *38*(2), 195–202. https://doi.org/10.1177/0165025413515404

English, T., & Carstensen, L. L. (2016). Socioemotional Selectivity Theory. In N. A. Pachana (Ed.), *Encyclopedia of Geropsychology* (pp. 1–6). Springer Singapore. https://doi.org/10.1007/978-981-287-080-3_110-1

Esler, M., Rumantir, M., Kaye, D., Jennings, G., Hastings, J., Socratous, F., & Lambert, G. (2001). Sympathetic nerve biology in essential hypertension. *Clinical and Experimental Pharmacology and Physiology*, *28*(12), 986–989.

Ferrari, A. U., Radaelli, A., & Centola, M. (2003). Invited review: Aging and the cardiovascular system. *J Appl Physiol*, *95*(6), 2591–2597. https://doi.org/10.1152/japplphysiol.00601.2003

Finello, K. M., Terteryan, A., & Riewerts, R. J. (2016). Home visiting programs: What the primary care clinician should know. *Current Problems in Pediatric and Adolescent Health Care*, *46*(4), 101–125.

Fiske, A., Wetherell, J. L., & Gatz, M. (2009). Depression in Older Adults. *Annual Review of Clinical Psychology*, *5*(1), 363–389. https://doi.org/10.1146/annurev.clinpsy.032408.153621

Flaherty, E. G., Thompson, R., Dubowitz, H., Harvey, E. M., English, D. J., Proctor, L. J., & Runyan, D. K. (2013). Adverse Childhood Experiences and Child Health in Early Adolescence. *JAMA Pediatrics*, *167*(7), 622. https://doi.org/10.1001/jamapediatrics.2013.22

Floresco, S. B. (2015). The nucleus accumbens: An interface between cognition, emotion, and action. *Annual Review of Psychology*, *66*, 25–52.

Fooden, J. (2000). Systematic review of the rhesus macaque, Macaca mulatta (Zimmermann, 1780) / Jack Fooden. In *Systematic review of the rhesus macaque, Macaca mulatta (Zimmermann, 1780) / Jack Fooden.* Field Museum of Natural History,. https://doi.org/10.5962/bhl.title.7192

Fox, A. S., Harris, R. A., Rosso, L. D., Raveendran, M., Kamboj, S., Kinnally, E. L., Capitanio, J. P., & Rogers, J. (2021). Infant inhibited temperament in primates predicts adult behavior, is heritable, and is associated with anxiety-relevant genetic variation. *Molecular Psychiatry*, *26*(11), 6609–6618. https://doi.org/10.1038/s41380-021-01156-4

Fox, N. A., Almas, A. N., Degnan, K. A., Nelson, C. A., & Zeanah, C. H. (2011). The effects of severe psychosocial deprivation and foster care intervention on cognitive development at 8 years of age: Findings from the Bucharest Early Intervention Project: Institutionalization, foster care and IQ. *Journal of Child Psychology and Psychiatry*, *52*(9), 919–928. https://doi.org/10.1111/j.1469-7610.2010.02355.x

Fung, H. H., & Carstensen, L. L. (2006). Goals Change When Life's Fragility is Primed: Lessons Learned From Older Adults, the September 11 Attacks and Sars. *Social Cognition*, *24*(3), 248–278. https://doi.org/10.1521/soco.2006.24.3.248

Fung, H. H., Carstensen, L. L., & Lang, F. R. (2001). Age-related patterns in social networks among European Americans and African Americans: Implications for socioemotional selectivity across the life span. *The International Journal of Aging and Human Development*, *52*(3), 185–206.

Fung, H. H., Lai, P., & Ng, R. (2001). Age differences in social preferences among Taiwanese and Mainland Chinese: The role of perceived time. *Psychology and Aging*, *16*(2), 351.

Fuster, J. M. (2002). Frontal lobe and cognitive development. *Journal of Neurocytology*, *31*(3), 373–385.

Gao, X., Cao, Q., Cheng, Y., Zhao, D., Wang, Z., Yang, H., Wu, Q., You, L., Wang, Y., Lin, Y., Li, X., Wang, Y., Bian, J.-S., Sun, D., Kong, L., Birnbaumer, L., & Yang, Y. (2018). *Chronic stress promotes colitis by disturbing the gut microbiota and triggering immune system response*. 10.

Gerhardsson, A., Fischer, H., Lekander, M., Kecklund, G., Axelsson, J., Åkerstedt, T., & Schwarz, J. (2019). *Positivity Effect and Working Memory Performance Remains Intact in Older Adults After Sleep Deprivation* [Preprint]. Open Science Framework. https://doi.org/10.31219/osf.io/nkaqr

Goncharova, N. D., Chigarova, O., Rudenko, N., & Oganyan, T. (2019). Glucocorticoid Negative Feedback in Regulation of the Hypothalamic-Pituitary-Adrenal Axis in Rhesus Monkeys With Various Types of Adaptive Behavior: Individual and Age-Related Differences. *Frontiers in Endocrinology*, *10*, 24. https://doi.org/10.3389/fendo.2019.00024

Goncharova, N. D., & Oganyan, T. E. (2018). Age-related differences in stress responsiveness of the hypothalamic-pituitary-adrenal axis of nonhuman primates with various types of adaptive behavior. *General and Comparative Endocrinology*, *258*, 163–172. https://doi.org/10.1016/j.ygcen.2017.08.007

Goschke, T., & Bolte, A. (2014). Emotional modulation of control dilemmas: The role of positive affect, reward, and dopamine in cognitive stability and flexibility. *Neuropsychologia*, *62*, 403–423. https://doi.org/10.1016/j.neuropsychologia.2014.07.015

Gothard, K. M., Erickson, C. A., & Amaral, D. G. (2004). How do rhesus monkeys (Macaca mulatta) scan faces in a visual paired comparison task? *Anim Cogn*, *7*(1), 25–36. https://doi.org/10.1007/s10071-003-0179-6

Gottlieb, D. H., & Capitanio, J. P. (2013). Latent variables affecting behavioral response to the human intruder test in infant rhesus macaques (Macaca mulatta). *American Journal of Primatology*, *75*(4), 314–323.

Gottlieb, D. H., Capitanio, J. P., & McCowan, B. (2013). Risk factors for stereotypic behavior and self-biting in rhesus macaques (*Macaca mulatta*): Animal's history, current environment, and personality: Stereotypic Behavior and Self-Biting. *American Journal of Primatology*, *75*(10), 995–1008. https://doi.org/10.1002/ajp.22161

Gottlieb, D. H., Del Rosso, L., Sheikhi, F., Gottlieb, A., McCowan, B., & Capitanio, J. P. (2018). Personality, environmental stressors, and diarrhea in *Rhesus macaques*: An interactionist perspective. *American Journal of Primatology*, *80*(12), e22908. https://doi.org/10.1002/ajp.22908

Graham, E. K., Weston, S. J., Gerstorf, D., Yoneda, T. B., Booth, T., Beam, C. R., Petkus, A. J., Drewelies, J., Hall, A. N., Bastarache, E. D., Estabrook, R., Katz, M. J., Turiano, N. A., Lindenberger, U., Smith, J., Wagner, G. G., Pedersen, N. L., Allemand, M., Spiro, A., … Mroczek, D. K. (2020). Trajectories of Big Five Personality Traits: A Coordinated Analysis of 16 Longitudinal Samples. *European Journal of Personality*, *34*(3), 301–321. https://doi.org/10.1002/per.2259

Gross, J. J., Carstensen, L. L., Pasupathi, M., Tsai, J., Götestam Skorpen, C., & Hsu, A. Y. C. (1997). Emotion and aging: Experience, expression, and control. *Psychology and Aging*, *12*(4), 590–599.

Gurel, N. Z., Carek, A. M., Inan, O. T., Levantsevych, O., Abdelhadi, N., Hammadah, M., O'Neal, W. T., Kelli, H., Wilmot, K., Ward, L., Rhodes, S., Pearce, B. D., Mehta, P. K., Kutner, M., Garcia, E., Quyyumi, A., Vaccarino, V., Raggi, P., Bremner, J. D., & Shah, A. J. (2019). Comparison of autonomic stress reactivity in young healthy versus aging subjects with heart disease. *PLOS ONE*, *14*(5), e0216278. https://doi.org/10.1371/journal.pone.0216278

Hannibal, D. L., Bliss-Moreau, E., Vandeleest, J., McCowan, B., & Capitanio, J. (2017). Laboratory rhesus macaque social housing and social changes: Implications for research: Macaque Laboratory Housing Changes and Research. *American Journal of Primatology*, *79*(1), e22528. https://doi.org/10.1002/ajp.22528

Harlow, H. F. (1958). The nature of love. *American Psychologist*, *13*(12), 673.

Harlow, H. F., Dodsworth, R. O., & Harlow, M. K. (1965). Total social isolation in monkeys. *Proceedings of the National Academy of Sciences of the United States of America*, *54*(1), 90.

Harlow, H. F., & Zimmermann, R. R. (1959). Affectional response in the infant monkey: Orphaned baby monkeys develop a strong and persistent attachment to inanimate surrogate mothers. *Science*, *130*(3373), 421–432.

Hauser, M. D., & Tyrrell, G. (1984). Old age and its behavioral manifestations: A study on two species of macaque. *Folia Primatologica*, *43*(1), 24–35.

He, X., Qin, W., Liu, Y., Zhang, X., Duan, Y., Song, J., Li, K., Jiang, T., & Yu, C. (2014). Abnormal salience network in normal aging and in amnestic mild cognitive impairment and Alzheimer's disease. *Human Brain Mapping*, *35*(7), 3446–3464.

Hennessy, M. B., Chun, K., & Capitanio, J. P. (2017). Depressive-like behavior, its sensitization, social buffering, and altered cytokine responses in rhesus macaques moved from outdoor social groups to indoor housing. *Social Neuroscience*, *12*(1), 65–75. https://doi.org/10.1080/17470919.2016.1145595

Hennessy, M. B., McCowan, B., Jiang, J., & Capitanio, J. P. (2014a). Depressive-like behavioral response of adult male rhesus monkeys during routine animal husbandry procedure. *Frontiers in Behavioral Neuroscience*, *8*, 309.

Hennessy, M. B., McCowan, B., Jiang, J., & Capitanio, J. P. (2014b). Depressive-like behavioral response of adult male rhesus monkeys during routine animal husbandry procedure. *Frontiers in Behavioral Neuroscience*, *8*. https://doi.org/10.3389/fnbeh.2014.00309

Home Visiting Accountability Act of 2012, 699, 2012 Regular Session, Children.

Hoffman, C. L., Higham, J. P., Mas-Rivera, A., Ayala, J. E., & Maestripieri, D. (2010). Terminal investment and senescence in rhesus macaques (Macaca mulatta) on Cayo Santiago. *Behav Ecol*, *21*(5), 972–978. https://doi.org/10.1093/beheco/arq098

Holt-Lunstad, J., Smith, T. B., & Layton, J. B. (2010). Social relationships and mortality risk: A meta-analytic review. *PLoS Medicine*, *7*(7), e1000316.

Hotta, H., & Uchida, S. (2010). Aging of the autonomic nervous system and possible improvements in autonomic activity using somatic afferent stimulation: Aging of the autonomic nervous system. *Geriatrics & Gerontology International*, *10*, S127–S136. https://doi.org/10.1111/j.1447-0594.2010.00592.x

Iob, E., & Steptoe, A. (2019). Cardiovascular disease and hair cortisol: A novel biomarker of chronic stress. *Current Cardiology Reports*, *21*(10), 1–11.

Isaacowitz, D. M., Allard, E. S., Murphy, N. A., & Schlangel, M. (2009). The Time Course of Age-Related Preferences Toward Positive and Negative Stimuli. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *64B*(2), 188–192. https://doi.org/10.1093/geronb/gbn036

Isaacowitz, D. M., Toner, K., Goren, D., & Wilson, H. R. (2008). Looking while unhappy: Mood-congruent gaze in young adults, positive gaze in older adults. *Psychological Science*, *19*(9), 848–853.

Isaacowitz, D. M., Wadlinger, H. A., Goren, D., & Wilson, H. R. (2006a). *Is There an Age-Related Positivity Effect in Visual Attention? A Comparison of Two Methodologies*. https://doi.org/10.1037/1528-3542.6.3.511

Isaacowitz, D. M., Wadlinger, H. A., Goren, D., & Wilson, H. R. (2006b). Selective preference in visual fixation away from negative images in old age? An eye-tracking study. *Psychol Aging*, *21*(1), 40–48. https://doi.org/10.1037/0882-7974.21.1.40

James, W. (1884). What is an Emotion? *Mind*, *9*(34), 188–205.

Jandackova, V. K., Scholes, S., Britton, A., & Steptoe, A. (2016). Are Changes in Heart Rate Variability in Middle-Aged and Older People Normative or Caused by Pathological Conditions? Findings From a Large Population-Based Longitudinal Cohort Study. *Journal of the American Heart Association*, *5*(2). https://doi.org/10.1161/JAHA.115.002365

Jandackova, V. K., Scholes, S., Britton, A., & Steptoe, A. (2019). Healthy Lifestyle and Cardiac Vagal Modulation Over 10 Years: Whitehall II Cohort Study. *Journal of the American Heart Association*, *8*(19). https://doi.org/10.1161/JAHA.119.012420

Johnson, D. R. (2009). Goal-directed attentional deployment to emotional faces and individual differences in emotional regulation. *Journal of Research in Personality*, *43*(1), 8–13.

Johnson, L. E., Parra, L. A., Ugarte, E., Weissman, D. G., Han, S. G., Robins, R. W., Guyer, A. E., & Hastings, P. D. (2021). Patterns of poverty across adolescence predict salivary cortisol stress responses in Mexican-origin youths. *Psychoneuroendocrinology*, *132*, 105340. https://doi.org/10.1016/j.psyneuen.2021.105340

Joiner, R. J., Bergeman, C. S., & Wang, L. (2018). Affective experience across the adult lifespan: An accelerated longitudinal design. *Psychology and Aging*, *33*(3), 399.

Jokela, M., Ferrie, J., & Kivimäki, M. (2009). Childhood Problem Behaviors and Death by Midlife: The British National Child Development Study. *Journal of the American Academy of Child & Adolescent Psychiatry*, *48*(1), 19–24. https://doi.org/10.1097/CHI.0b013e31818b1c76

Joubert, C., Davidson, P. S. R., & Chainay, H. (2018). When Do Older Adults Show a Positivity Effect in Emotional Memory? *Experimental Aging Research*, *44*(5), 455–468. https://doi.org/10.1080/0361073X.2018.1521498

Judd, C. M., Westfall, J., & Kenny, D. A. (2012). Treating stimuli as a random factor in social psychology: A new and comprehensive solution to a pervasive but largely ignored problem. *Journal of Personality and Social Psychology*, *103*(1), 54–69. https://doi.org/10.1037/a0028347

Kabiru, C. W., Elung'ata, P., Mojola, S. A., & Beguy, D. (2014). Adverse life events and delinquent behavior among Kenyan adolescents: A cross-sectional study on the protective role of parental monitoring, religiosity, and self-esteem. *Child and Adolescent Psychiatry and Mental Health*, *8*(1), 1–11.

Kagitcibasi, C., Sunar, D., & Bekman, S. (2001). Long-term effects of early intervention: Turkish low-income mothers and children. *Journal of Applied Developmental Psychology*, *22*(4), 333–361. https://doi.org/10.1016/S0193-3973(01)00071-5

Kalin, N., & Shelton, S. E. (1989). Defensive behaviors in infant rhesus monkeys: Environmental cues and neurochemical regulation. *Science*, *243*(4899), 1718–1721.

Kappenman, E. S., Farrens, J. L., Luck, S. J., & Proudfit, G. H. (2014). Behavioral and ERP measures of attentional bias to threat in the dot-probe task: Poor reliability and lack of correlation with anxiety. *Frontiers in Psychology*, *5*. https://doi.org/10.3389/fpsyg.2014.01368

Kawashima, T., Sato, K., Akita, K., & Sasaki, H. (2005). Comparative anatomical study of the autonomic cardiac nervous system in macaque monkeys. *Journal of Morphology*, *266*(1), 112–124. https://doi.org/10.1002/jmor.10371

Kennedy, B. L., Huang, R., & Mather, M. (2020). Age differences in emotion-induced blindness: Positivity effects in early attention. *Emotion*, *20*(7), 1266–1278. https://doi.org/10.1037/emo0000643

Kennedy, Q., Mather, M., & Carstensen, L. L. (2004). The Role of Motivation in the Age-Related Positivity Effect in Autobiographical Memory. *Psychological Science*, *15*(3), 208–214. https://doi.org/10.1111/j.0956-7976.2004.01503011.x

King, H. M., Kurdziel, L. B., Meyer, J. S., & Lacreuse, A. (2012). Effects of testosterone on attention and memory for emotional stimuli in male rhesus monkeys. *Psychoneuroendocrinology*, *37*(3), 396–409. https://doi.org/10.1016/j.psyneuen.2011.07.010

Kinnally, E. L., Capitanio, J. P., Leibel, R., Deng, L., LeDuc, C., Haghighi, F., & Mann, J. J. (2010). Epigenetic regulation of serotonin transporter expression and behavior in infant rhesus macaques. *Genes, Brain and Behavior*, no-no. https://doi.org/10.1111/j.1601-183X.2010.00588.x

Kleckner, I. R., Zhang, J., Touroutoglou, A., Chanes, L., Xia, C., Simmons, W. K., Quigley, K. S., Dickerson, B. C., & Feldman Barrett, L. (2017). Evidence for a large-scale brain system supporting allostasis and interoception in humans. *Nature Human Behaviour*, *1*(5), 0069. https://doi.org/10.1038/s41562-017-0069

Kolk, S. M., & Rakic, P. (2022). Development of prefrontal cortex. *Neuropsychopharmacology*, *47*(1), 41–57. https://doi.org/10.1038/s41386-021-01137-9

Kret, M. E., Jaasma, L., Bionda, T., & Wijnen, J. G. (2016). Bonobos (*Pan paniscus*) show an attentional bias toward conspecifics' emotions. *Proceedings of the National Academy of Sciences*, *113*(14), 3761–3766. https://doi.org/10.1073/pnas.1522060113

Krum, H., Schlaich, M., Whitbourn, R., Sobotka, P. A., Sadowski, J., Bartus, K., Kapelak, B., Walton, A., Sievert, H., Thambar, S., & others. (2009). Catheter-based renal sympathetic denervation for resistant hypertension: A multicentre safety and proof-of-principle cohort study. *The Lancet*, *373*(9671), 1275–1281.

Kuehn, E., Perez-Lopez, M. B., Diersch, N., Döhler, J., Wolbers, T., & Riemer, M. (2018). Embodiment in the aging mind. *Neuroscience and Biobehavioral Reviews*, *86*(January 2017), 207–225. https://doi.org/10.1016/j.neubiorev.2017.11.016

Kuraoka, H., Kurosaka, C., Wada, C., & Miyake, S. (2018). Effect of Age on Heart Rate Responses and Subjective Mental Workload During Mental Tasks. *Congress of the International Ergonomics Association*, 316–321.

Kuznetsova, A., Brockhoff, P. B., & Christensen, R. H. B. (2017). lmerTest Package: Tests in Linear Mixed Effects Models. *Journal of Statistical Software*, *82*(13), 1–26. https://doi.org/10.18637/jss.v082.i13

Kyröläinen, A.-J., Keuleers, E., Mandera, P., Brysbaert, M., & Kuperman, V. (2021). Affect across adulthood: Evidence from English, Dutch, and Spanish. *Journal of Experimental Psychology: General*, *150*(4), 792.

La Corte, V., Sperduti, M., Malherbe, C., Vialatte, F., Lion, S., Gallarda, T., Oppenheim, C., & Piolino, P. (2016). Cognitive Decline and Reorganization of Functional Connectivity in Healthy Aging: The Pivotal Role of the Salience Network in the Prediction of Age and Cognitive Performances. *Frontiers in Aging Neuroscience*, *8*. https://doi.org/10.3389/fnagi.2016.00204

Labouvie-Vief, G., Grühn, D., & Studer, J. (2010). *Dynamic integration of emotion and cognition: Equilibrium regulation in development and aging.*

Lakatta, E. (1993). Deficient neuroendocrine regulation of the cardiovascular system with advancing age in healthy humans. *Circulation*, *87*(2), 631–636.

Lansford, J. E., Sherman, A. M., & Antonucci, T. C. (1998). Satisfaction with social networks: An examination of socioemotional selectivity theory across cohorts. *Psychol Aging*, *13*(4), 544–552.

Laubach, M., Amarante, L. M., Swanson, K., & White, S. R. (2018). What, If Anything, Is Rodent Prefrontal Cortex? *Eneuro*, *5*(5), ENEURO.0315-18.2018. https://doi.org/10.1523/ENEURO.0315-18.2018

Lee, L. O., & Knight, B. G. (2009). Attentional bias for threat in older adults: Moderation of the positivity bias by trait anxiety and stimulus modality. *Psychology and Aging*, *24*(3), 741–747. https://doi.org/10.1037/a0016409

Lee, T.-H., Kim, S. H., Katz, B., & Mather, M. (2020). The Decline in Intrinsic Connectivity Between the Salience Network and Locus Coeruleus in Older Adults: Implications for Distractibility. *Frontiers in Aging Neuroscience*, *12*, 2. https://doi.org/10.3389/fnagi.2020.00002

Levy, R. (1994). Aging-associated cognitive decline. Working Party of the International Psychogeriatric Association in collaboration with the World Health Organization. *International Psychogeriatrics*, *6*(1), 63–68.

Liu, Z., Lin, R., & Luo, M. (2020). *Reward Contributions to Serotonergic Functions*. 24.

Luong, G., Charles, S. T., & Fingerman, K. L. (2011). Better with age: Social relationships across adulthood. *Journal of Social and Personal Relationships*, *28*(1), 9–23.

Luong, G., Rauers, A., & Fingerman, K. L. (2015). *The multifaceted nature of late-life socialization: Older adults as agents and targets of socialization.*

Machado, C. J., Bliss-Moreau, E., Platt, M. L., & Amaral, D. G. (2011). Social and Nonsocial Content Differentially Modulates Visual Attention and Autonomic Arousal in Rhesus Macaques. In *PLoS One* (Vol. 6). http://dx.plos.org/10.1371/journal.pone.0026598.g003 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3202553/pdf/pone.0026598.pdf

Machanda, Z. P., & Rosati, A. G. (2020). Shifting sociality during primate ageing. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *375*(1811), 20190620. https://doi.org/10.1098/rstb.2019.0620

MacLeod, C., Mathews, A., & Tata, P. (1986). Attentional Bias in Emotional Disorders. *Journal of Abnormal Psychology*, *95*(1), 15–20. https://doi.org/10.1037/0021-843X.95.1.15

Maestripieri, D. (1997). Gestural communication in macaques: Usage and meaning of nonvocal signals. *Evolution of Communication*, *1*(2), 193–222.

Maestripieri, D., & Wallen, K. (1997). Affiliative and submissive communication in rhesus macaques. *Primates*, *38*(2), 127–138.

Mammarella, N., Di Domenico, A., Palumbo, R., & Fairfield, B. (2016). When green is positive and red is negative: Aging and the influence of color on emotional memories. *Psychology and Aging*, *31*(8), 914–926. https://doi.org/10.1037/pag0000122

Mantantzis, K., Schlaghecken, F., & Maylor, E. A. (2020). Heart Rate Variability Predicts Older Adults' Avoidance of Negativity. *The Journals of Gerontology: Series B*, *75*(8), 1679–1688. https://doi.org/10.1093/geronb/gby148

Mather, M., & Carstensen, L. L. (2003). Aging and attentional biases for emotional faces. *Psychological Science*, *14*(5), 409–415.

Mather, M., & Carstensen, L. L. (2005). Aging and motivated cognition: The positivity effect in attention and memory. *Trends Cogn Sci*, *9*(10), 496–502. https://doi.org/10.1016/j.tics.2005.08.005

Mather, M., & Knight, M. R. (2006). Angry Faces Get Noticed Quickly: Threat Detection is not Impaired Among Older Adults. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *61*(1), P54–P57. https://doi.org/10.1093/geronb/61.1.P54

Matheson, G. J. (2019). We need to talk about reliability: Making better use of test-retest studies for study design and interpretation. *PeerJ*, *7*, e6918. https://doi.org/10.7717/peerj.6918

Mayr, E. (1993). Proximate and ultimate causations. *Biology and Philosophy*, *8*(1).

McCoy, D. C., Jones, S., Roy, A., & Raver, C. C. (2018). Classifying trajectories of social–emotional difficulties through elementary school: Impacts of the Chicago School Readiness Project. *Developmental Psychology*, *54*(4), 772.

McPherson, M., Smith-Lovin, L., & Brashears, M. E. (2006). Social isolation in America: Changes in core discussion networks over two decades. *American Sociological Review*, *71*(3), 353–375.

Meier, S. M., Mattheisen, M., Mors, O., Mortensen, P. B., Laursen, T. M., & Penninx, B. W. (2016). Increased mortality among people with anxiety disorders: Total population study. *British Journal of Psychiatry*, *209*(3), 216–221. https://doi.org/10.1192/bjp.bp.115.171975

Mendes, W. B. (2010). Weakened links between mind and body in older age: The case for maturational dualism in the experience of emotion. *Emotion Review*, *2*(3), 240–244. https://doi.org/10.1177/1754073910364149

Meng, R., Yu, C., Liu, N., He, M., Lv, J., Guo, Y., Bian, Z., Yang, L., Chen, Y., Zhang, X., Chen, Z., Wu, T., Pan, A., Li, L., & for the China Kadoorie Biobank Collaborative Group. (2020). Association of Depression With All-Cause and Cardiovascular Disease Mortality Among Adults in China. *JAMA Network Open*, *3*(2), e1921043. https://doi.org/10.1001/jamanetworkopen.2019.21043

Menon, V., & Uddin, L. Q. (2010). Saliency, switching, attention and control: A network model of insula function. *Brain Structure and Function*, *214*(5–6), 655–667.

Mikkelsen, M. B., O'Toole, M. S., Lyby, M. S., Wallot, S., & Mehlsen, M. (2019). Emotional reactivity and interoceptive sensitivity: Exploring the role of age. *Psychonomic Bulletin & Review*. https://doi.org/10.3758/s13423-019-01603-y

Miladinov, G. (2020). Socioeconomic development and life expectancy relationship: Evidence from the EU accession candidate countries. *Genus*, *76*(1), 2. https://doi.org/10.1186/s41118-019-0071-0

Miloyan, B., Bulley, A., Bandeen-Roche, K., Eaton, W. W., & Gonçalves-Bradley, D. C. (2016). Anxiety disorders and all-cause mortality: Systematic review and meta-analysis. *Social Psychiatry and Psychiatric Epidemiology*, *51*(11), 1467–1475. https://doi.org/10.1007/s00127-016-1284-6

Mitchell, G. D., Raymond, E. J., Ruppenthal, G. C., & Harlow, H. F. (1966). Long-Term Effects of Total Social Isolation Upon Behavior of Rhesus Monkeys. *Psychological Reports*, *18*(2), 567–580. https://doi.org/10.2466/pr0.1966.18.2.567

Morey, J. N., Boggero, I. A., Scott, A. B., & Segerstrom, S. C. (2015). Current directions in stress and human immune function. *Current Opinion in Psychology*, *5*, 13–17. https://doi.org/10.1016/j.copsyc.2015.03.007

Morgan, D., Grant, K. A., Gage, H. D., Mach, R. H., Kaplan, J. R., Nader, S. H., Buchheimer, N., Ehrenkaufer, R. L., Nader, M. A., & others. (2013). Social dominance in monkeys: Dopamine D2 receptors and cocaine self-administration. In *Social Neuroscience* (pp. 243–252). Psychology Press.

Mroczek, D. K. (2001). Age and emotion in adulthood. *Current Directions in Psychological Science*, *10*(3), 87–90.

Nader, M. A., Nader, S. H., Czoty, P. W., Riddick, N. V., Gage, H. D., Gould, R. W., Blaylock, B. L., Kaplan, J. R., Garg, P. K., Davies, H. M., & others. (2012). Social dominance in female monkeys: Dopamine receptor function and cocaine reinforcement. *Biological Psychiatry*, *72*(5), 414–421.

Nakamichi, M. (1984). Behavioral characteristics of old female Japanese monkeys in a free-ranging group. *Primates*, *25*(2), 192–203.

Nelson, E. E., Herman, K. N., Barrett, C. E., Noble, P. L., Wojteczko, K., Chisholm, K., Delaney, D., Ernst, M., Fox, N. A., Suomi, S. J., & others. (2009). Adverse rearing experiences enhance responding to both aversive and rewarding stimuli in juvenile rhesus monkeys. *Biological Psychiatry*, *66*(7), 702–704.

Nelson III, C. A., Zeanah, C. H., Fox, N. A., Marshall, P. J., Smyke, A. T., & Guthrie, D. (2007). Cognitive recovery in socially deprived young children: The Bucharest Early Intervention Project. *Science*, *318*(5858), 1937–1940.

Niedenthal, P. M. (2007). Embodying Emotion. *Science*, *316*(5827), 1002–1005. https://doi.org/10.1126/science.1136930

Nikitin, J., & Freund, A. M. (2011). Age and motivation predict gaze behavior for facial expressions. *Psychol Aging*, *26*(3), 695–700. https://doi.org/10.1037/a0023281

Noh, S. R., Lohani, M., & Isaacowitz, D. M. (2011). Deliberate real-time mood regulation in adulthood: The importance of age, fixation and attentional functioning. *Cognition & Emotion*, *25*(6), 998–1013. https://doi.org/10.1080/02699931.2010.541668

Novak, M. (2004). Housing for captive nonhuman primates: The balancing act. *The Development of Science-Based Guidelines for Laboratory Animal Care: Proceedings of the November 2003 International Workshop*, 79.

Novak, M. A. (2003). Self-injurious behavior in rhesus monkeys: New insights into its etiology, physiology, and treatment. *American Journal of Primatology: Official Journal of the American Society of Primatologists*, *59*(1), 3–19.

Orgeta, V. (2011). Avoiding threat in late adulthood: Testing two life span theories of emotion. *Experimental Aging Research*, *37*(4), 449–472.

Otte, C., Hart, S., Neylan, T. C., Marmar, C. R., Yaffe, K., & Mohr, D. C. (2005). A meta-analysis of cortisol response to challenge in human aging: Importance of gender. *Psychoneuroendocrinology*, *30*(1), 80–91.

Parr, L. A., Modi, M., Siebert, E., & Young, L. J. (2013). Intranasal oxytocin selectively attenuates rhesus monkeys' attention to negative facial expressions. *Psychoneuroendocrinology*, *38*(9), 1748–1756.

Pediatrics, C. on C. (2009). The role of preschool home-visiting programs in improving children's developmental and health outcomes. *Pediatrics*, *123*(2), 598–603.

Peirce, J., Gray, J. R., Simpson, S., MacAskill, M., Höchenberger, R., Sogo, H., Kastman, E., & Lindeløv, J. K. (2019). PsychoPy2: Experiments in behavior made easy. *Behavior Research Methods*, *51*(1), 195–203.

Petrican, R., Moscovitch, M., & Grady, C. (2014). Proficiency in positive vs. Negative emotion identification and subjective well-being among long-term married elderly couples. *Frontiers in Psychology*, *5*, 338.

Phillips, K. A., Bales, K. L., Capitanio, J. P., Conley, A., Czoty, P. W., t Hart, B. A., Hopkins, W. D., Hu, S.-L., Miller, L. A., Nader, M. A., Nathanielsz, P. W., Rogers, J., Shively, C. A., Voytko, M. L., 't Hart, B. A., Hopkins, W. D., Hu, S.-L., Miller, L. A., Nader, M. A., … Voytko, M. L. (2014). Why primate models matter. *American Journal of Primatology*, *76*(9), 801–827. https://doi.org/10.1002/ajp.22281

Piazza, J. R., Charles, S. T., Stawski, R. S., & Almeida, D. M. (2013). Age and the association between negative affective states and diurnal cortisol. *Psychology and Aging*, *28*(1), 47.

Plant, T. M., Ramaswamy, S., Simorangkir, D., & Marshall, G. R. (2005). Postnatal and pubertal development of the rhesus monkey (Macaca mulatta) testis. *Annals of the New York Academy of Sciences*, *1061*(1), 149–162.

Poller, U., Nedelka, G., Radke, J., Pönicke, K., & Brodde, O.-E. (1997). Age-dependent changes in cardiac muscarinic receptor function in healthy volunteers. *Journal of the American College of Cardiology*, *29*(1), 187–193.

Power, C., & Elliott, J. (2006). Cohort profile: 1958 British birth cohort (National Child Development Study). *International Journal of Epidemiology*, *35*(1), 34–41. https://doi.org/10.1093/ije/dyi183

Pratt, L. A., Druss, B. G., Manderscheid, R. W., & Walker, E. R. (2016). Excess mortality due to depression and anxiety in the United States: Results from a nationally representative survey. *General Hospital Psychiatry*, *39*, 39–45.

Preston, S. H. (2007). The changing relation between mortality and level of economic development. *International Journal of Epidemiology*, *36*(3), 484–490. https://doi.org/10.1093/ije/dym075

Preuss, T. M., & Wise, S. P. (2021). Evolution of Prefrontal Cortex. *Neuropsychopharmacology*, 1–17. https://doi.org/10.1038/s41386-021-01076-5

Preuss, T. M., & Wise, S. P. (2022). Evolution of prefrontal cortex. *Neuropsychopharmacology*, *47*(1), 3–19. https://doi.org/10.1038/s41386-021-01076-5

Qin, D., Li, Z., Li, Z., Wang, L., Hu, Z., Lü, L., Wang, Z., Liu, Y., Yin, Y., Li, Z., & Hu, X. (2019). Chronic Glucocorticoid Exposure Induces Depression-Like Phenotype in Rhesus Macaque (Macaca Mulatta). *Frontiers in Neuroscience*, *13*, 188. https://doi.org/10.3389/fnins.2019.00188

Reed, A. E., Chan, L., & Mikels, J. A. (2014). Meta-analysis of the age-related positivity effect: Age differences in preferences for positive over negative information. *Psychology and Aging*, *29*(1), 1–15. https://doi.org/10.1037/a0035194

Reimers, C. D., Knapp, G., & Reimers, A. K. (2012). Does Physical Activity Increase Life Expectancy? A Review of the Literature. *Journal of Aging Research*, *2012*, 1–9. https://doi.org/10.1155/2012/243958

Reutter, M., Hewig, J., Wieser, M. J., & Osinsky, R. (2017). The N2pc component reliably captures attentional bias in social anxiety: N2pc and attentional bias in social anxiety. *Psychophysiology*, *54*(4), 519–527. https://doi.org/10.1111/psyp.12809

Roelofs, K. (2017). Freeze for action: Neurobiological mechanisms in animal and human freezing. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *372*(1718), 20160206. https://doi.org/10.1098/rstb.2016.0206

Rosati, A. G., Arre, A. M., Platt, M. L., Santos, L. R., Amici, F., & Widdig, A. (2018). Developmental shifts in social cognition: Socio-emotional biases across the lifespan in rhesus monkeys. *Behavioral Ecology and Sociobiology*, *72*, 163. https://doi.org/10.1007/s00265-018-2573-8

Rosati, A. G., Hagberg, L., Enigk, D. K., Otali, E., Emery Thompson, M., Muller, M. N., Wrangham, R. W., & Machanda, Z. P. (2020). Social selectivity in aging wild chimpanzees. *Science*, *370*(6515), 473–476. https://doi.org/10.1126/science.aaz9129

Rosati, A. G., & Santos, L. R. (2017). Tolerant Barbary macaques maintain juvenile levels of social attention in old age, but despotic rhesus macaques do not. *Animal Behaviour*, *130*, 199–207.

Ruppenthal, G. C., Arling, G. L., Harlow, H. F., Sackett, G. P., & Suomi, S. J. (1976). A 10-year perspective of motherless-mother monkey behavior. *Journal of Abnormal Psychology*, *85*(4), 341.

Russell, J. A. (2003). Core affect and the psychological construction of emotion. *Psychol Rev*, *110*(1), 145–172.

Santistevan, A. C., Fiske, O., Moadab, G., Isaacowitz, D. M., & Bliss-Moreau, E. (2022). *See no evil: Attentional bias towards threat is diminished in aged monkeys*.

Santistevan, A. C., Kinnally, E. L., Capitanio, J. P., & Bliss-Moreau, E. (2022). *From womb-to-tomb: Infant monkeys' BioBehavioral profile predicts mortality across two decades of follow-up*.

Santistevan, A. C., Moadab, G., Fiske, O., Isaacowitz, D. M., & Bliss-Moreau, E. (2022). *Cardiac psychophysiological tuning to socioaffective content is disrupted in aged rhesus monkeys (Macaca mulatta)*.

Schaan, V. K., Schulz, A., Rubel, J. A., Bernstein, M., Domes, G., Schächinger, H., & Vögele, C. (2019). Childhood Trauma Affects Stress-Related Interoceptive Accuracy. *Frontiers in Psychiatry*, *10*, 750. https://doi.org/10.3389/fpsyt.2019.00750

Schachter, S., Fd, A., & Singer, J. E. (1962). *COGNITIVE, SOCIAL, AND PHYSIOLOGICAL DETERMINANTS OF EMOTIONAL STATE*. *69*(5), 21.

Scheibe, S., English, T., Tsai, J. L., & Carstensen, L. L. (2013). Striving to feel good: Ideal affect, actual affect, and their correspondence across adulthood. *Psychology and Aging*, *28*(1), 160–171. https://doi.org/10.1037/a0030561

Schmukle, S. C. (2005). Unreliability of the dot probe task. *European Journal of Personality*, *19*(7), 595–605.

Schulz, R., Beach, S. R., Ives, D. G., Martire, L. M., Ariyo, A. A., & Kop, W. J. (2000). Association between depression and mortality in older adults: The Cardiovascular Health Study. *Archives of Internal Medicine*, *160*(12), 1761–1768.

Seals, D. R., & Bell, C. (2004). Chronic sympathetic activation: Consequence and cause of age-associated obesity? *Diabetes*, *53*(2), 276–284.

Seals, D. R., & Esler, M. D. (2000). Human ageing and the sympathoadrenal system. *The Journal of Physiology*, *528*(3), 407–417.

Seeley, W. W. (2019). The salience network: A neural system for perceiving and responding to homeostatic demands. *Journal of Neuroscience*, *39*(50), 9878–9882.

Seraphin, S. B., Sanchez, M. M., Whitten, P. L., & Winslow, J. T. (2022). The behavioral neuroendocrinology of dopamine systems in differently reared juvenile male rhesus monkeys (Macaca mulatta). *Hormones and Behavior*, *137*, 105078. https://doi.org/10.1016/j.yhbeh.2021.105078

Shively, C. A., Appt, S. E., Chen, H., Day, S. M., Frye, B. M., Shaltout, H. A., Silverstein-Metzler, M. G., Snyder-Mackler, N., Uberseder, B., Vitolins, M. Z., & Register, T. C. (2020). Mediterranean diet, stress resilience, and aging in nonhuman primates. *Neurobiology of Stress*, *13*, 100254. https://doi.org/10.1016/j.ynstr.2020.100254

Shively, C. A., Clarkson, T. B., & Kaplan, J. R. (1989). Social deprivation and coronary artery atherosclerosis in female cynomolgus monkeys. *Atherosclerosis*, *77*(1), 69–76.

Slade, A., Sadler, L. S., & Mayes, L. C. (2005). *Minding the Baby: Enhancing Parental Reflective Functioning in a Nursing/Mental Health Home Visiting Program.*

Smith, T. W., Uchino, B. N., Berg, C. A., Florsheim, P., Pearce, G., Hawkins, M., Henry, N. J. M., Beveridge, R. M., Skinner, M. A., Ko, K. J., & Olsen-Cerny, C. (2009). Conflict and collaboration in middle-aged and older couples: II. Cardiovascular reactivity during marital interaction. *Psychology and Aging*, *24*(2), 274–286. https://doi.org/10.1037/a0016067

Staugaard, S. R. (2009). Reliability of two versions of the dot-probe task using photographic faces. *Psychology Science Quarterly*, *51*(3), 339–350.

Steptoe, A., Kunz-Ebrecht, S. R., Wright, C., & Feldman, P. J. (2005). Socioeconomic position and cardiovascular and neuroendocrine responses following cognitive challenge in old age. *Biological Psychology*, *69*(2), 149–166. https://doi.org/10.1016/j.biopsycho.2004.07.008

Steptoe, A., Shankar, A., Demakakos, P., & Wardle, J. (2013). Social isolation, loneliness, and all-cause mortality in older men and women. *Proceedings of the National Academy of Sciences*, *110*(15), 5797–5801. https://doi.org/10.1073/pnas.1219686110

Steptoe, A., & Wardle, J. (2011). Positive affect measured using ecological momentary assessment and survival in older men and women. *Proceedings of the National Academy of Sciences*, *108*(45), 18244–18248. https://doi.org/10.1073/pnas.1110892108

Stonebarger, G. A., Bimonte-Nelson, H. A., & Urbanski, H. F. (2021). The Rhesus Macaque as a Translational Model for Neurodegeneration and Alzheimer's Disease. *Frontiers in Aging Neuroscience*, *13*, 581. https://doi.org/10.3389/fnagi.2021.734173

Stratton, J. R., Levy, W. C., Caldwell, J. H., Jacobson, A., May, J., Matsuoka, D., & Madden, K. (2003). Effects of aging on cardiovascular responses to parasympathetic withdrawal. *Journal of the American College of Cardiology*, *41*(11), 2077–2083. https://doi.org/10.1016/S0735-1097(03)00418-2

Strauss, G. P., Allen, D. N., Jorgensen, M. L., & Cramer, S. L. (2005). Test-retest reliability of standard and emotional stroop tasks: An investigation of color-word and picture-word versions. *Assessment*, *12*(3), 330–337.

Sun, Y., Li, L., Xie, R., Wang, B., Jiang, K., & Cao, H. (2019). Stress Triggers Flare of Inflammatory Bowel Disease in Children and Adults. *Frontiers in Pediatrics*, *7*, 432. https://doi.org/10.3389/fped.2019.00432

Suomi, S. J. (1991). Early stress and adult emotional reactivity in rhesus monkeys. *The Childhood Environment and Adult Disease*, *156*, 171–183.

Suomi, S. J. (2005). Mother-Infant Attachment, Peer Relationships, and the Development of Social Networks in Rhesus Monkeys. *Human Development*, *48*(1–2), 67–79. https://doi.org/10.1159/000083216

Suomi, S. J. (2006). Risk, resilience, and gene$\times$ environment interactions in rhesus monkeys. *Annals of the New York Academy of Sciences*, *1094*(1), 52–62.

Suomi, S. J., Eisele, C. D., Grady, S. A., & Harlow, H. F. (1975). Depressive behavior in adult monkeys following separation from family environment. *Journal of Abnormal Psychology*, *84*(5), 576.

Suomi, S. J., & Harlow, H. F. (1972). Social rehabilitation of isolate-reared monkeys. *Developmental Psychology*, *6*(3), 487.

Talbot, C. E., Ksander, J. C., & Gutchess, A. (2018). Aging Impairs Disengagement From Negative Words in a Dot Probe Task. *Frontiers in Psychology*, *9*, 2361. https://doi.org/10.3389/fpsyg.2018.02361

Tang, A., Crawford, H., Morales, S., Degnan, K. A., Pine, D. S., & Fox, N. A. (2020). Infant behavioral inhibition predicts personality and social outcomes three decades later. *Proceedings of the National Academy of Sciences*, *117*(18), 9800–9807. https://doi.org/10.1073/pnas.1917376117

Therneau, T. M. (2020). *coxme: Mixed Effects Cox Models*. https://CRAN.R-project.org/package=coxme

Thierry, B. (2007). Unity in diversity: Lessons from macaque societies. *Evolutionary Anthropology: Issues, News, and Reviews: Issues, News, and Reviews*, *16*(6), 224–238.

Thomas, M. L., Kaufmann, C. N., Palmer, B. W., Depp, C. A., Martin, A. S., Glorioso, D. K., Thompson, W. K., & Jeste, D. V. (2016). Paradoxical trend for improvement in mental health with aging: A community-based study of 1,546 adults aged 21-100 years. *The Journal of Clinical Psychiatry*, *77*(8), 0–0.

Tinbergen, N. (1963). On aims and methods of ethology. *Zeitschrift Für Tierpsychologie*, *20*(4), 410–433.

Tomaszczyk, J. C., & Fernandes, M. A. (2014). Age-related differences in attentional bias for emotional faces. *Aging, Neuropsychology, and Cognition*, *21*(5), 544–559.

Touroutoglou, A., Bliss-Moreau, E., Zhang, J., Mantini, D., Vanduffel, W., Dickerson, B. C., & Barrett, L. F. (2016). A ventral salience network in the macaque brain. *NeuroImage*. https://doi.org/10.1016/j.neuroimage.2016.02.029

Touroutoglou, A., Zhang, J., Andreano, J. M., Dickerson, B. C., & Barrett, L. F. (2018). Dissociable effects of aging on salience subnetwork connectivity mediate age-related changes in executive function and affect. *Frontiers in Aging Neuroscience*, *10*, 410. https://doi.org/10.3389/fnagi.2018.00410

Truelove, M. A., Martin, A. L., Perlman, J. E., Wood, J. S., & Bloomsmith, M. A. (2017). Pair housing of macaques: A review of partner selection, introduction techniques, monitoring for compatibility, and methods for long-term maintenance of pairs. *American Journal of Primatology*, *79*(1), e22485.

Uchino, B. N., Birmingham, W., & Berg, C. A. (2010). Are Older Adults Less or More Physiologically Reactive? A Meta-Analysis of Age-Related Differences in Cardiovascular Reactivity to Laboratory Tasks. *The Journals of Gerontology: Series B*, *65B*(2), 154–162. https://doi.org/10.1093/geronb/gbp127

Uchino, B. N., Holt-Lunstad, J., Bloor, L. E., & Campo, R. A. (2005). Aging and Cardiovascular Reactivity to Stress: Longitudinal Evidence for Changes in Stress Reactivity. *Psychology and Aging*, *20*(1), 134–143. https://doi.org/10.1037/0882-7974.20.1.134

Uchino, B. N., Holt-Lunstad, J., Uno, D., & Flinders, J. B. (2001). Heterogeneity in the Social Networks of Young and Older Adults: Prediction of Mental Health and Cardiovascular Reactivity During Acute Stress. *Journal of Behavioral Medicine*, 22.

Uchino, B. N., Uno, D., Holt-Lunstad, J., & Flinders, J. B. (1999). Age-related differences in cardiovascular reactivity during acute psychological stress in men and women. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *54*(6), P339–P346.

Uddin, L. Q. (2014). Salience processing and insular cortical function and dysfunction. In *Nat Rev Neurosci*. http://www.nature.com/nrn/journal/vaop/ncurrent/full/nrn3857.html

Ueno, D., Matsuoka, T., Kato, Y., Ayani, N., Maeda, S., Takeda, M., & Narumoto, J. (2020). Individual differences in interoceptive accuracy are correlated with salience network connectivity in older adults. *Frontiers in Aging Neuroscience*, *12*, 592002. https://doi.org/10.3389/fnagi.2020.592002

United Nations, Department of Economic and Social Affairs, & Population Division. (2020). *World population ageing, 2019 highlights.*

Upright, N. A., & Baxter, M. G. (2021). Prefrontal cortex and cognitive aging in macaque monkeys. *American Journal of Primatology*. https://doi.org/10.1002/ajp.23250

Urry, H. L., & Gross, J. J. (2010). Emotion Regulation in Older Age. *Current Directions in Psychological Science*, *19*(6), 352–357. https://doi.org/10.1177/0963721410388395

van der Horst, F. C. P., LeRoy, H. A., & van der Veer, R. (2008). “When Strangers Meet”: John Bowlby and Harry Harlow on Attachment Behavior. *Integrative Psychological and Behavioral Science*, *42*(4), 370–388. https://doi.org/10.1007/s12124-008-9079-2

van Rooijen, R., Ploeger, A., & Kret, M. E. (2017). The dot-probe task to measure emotional attention: A suitable measure in comparative studies? *Psychonomic Bulletin & Review*, *24*(6), 1686–1717. https://doi.org/10.3758/s13423-016-1224-1

van Rosmalen, L., van der Veer, R., & van der Horst, F. C. (2020). The nature of love: Harlow, Bowlby and Bettelheim on affectionless mothers. *History of Psychiatry*, *31*(2), 227–231. https://doi.org/10.1177/0957154X19898997

Vandeleest, J. J., Capitanio, J. P., Hamel, A., Meyer, J., Novak, M., Mendoza, S. P., & McCowan, B. (2019). Social stability influences the association between adrenal responsiveness and hair cortisol concentrations in rhesus macaques. *Psychoneuroendocrinology*, *100*, 164–171. https://doi.org/10.1016/j.psyneuen.2018.10.008

Vijayakumar, N., Youssef, G. J., Allen, N. B., Anderson, V., Efron, D., Hazell, P., Mundy, L., Nicholson, J. M., Patton, G., Seal, M. L., & others. (2021). A longitudinal analysis of puberty-related cortical development. *Neuroimage*, *228*, 117684.

Waechter, S., Nelson, A. L., Wright, C., Hyatt, A., & Oakman, J. (2014). Measuring attentional bias to threat: Reliability of dot probe and eye movement indices. *Cognitive Therapy and Research*, *38*(3), 313–333.

Waechter, S., & Stolz, J. A. (2015). Trait anxiety, state anxiety, and attentional bias to threat: Assessing the psychometric properties of response time measures. *Cognitive Therapy and Research*, *39*(4), 441–458.

Wang, J., Xie, F., He, L., Meadmore, K. L., Paterson, K. B., & Benson, V. (2020). Eye movements reveal a similar positivity effect in Chinese and UK older adults. *Quarterly Journal of Experimental Psychology*, *73*(11), 1921–1929. https://doi.org/10.1177/1747021820935861

Wei, J., Lu, Y., Li, K., Goodman, M., & Xu, H. (2021). The Associations of Late-life Depression with All-cause and Cardiovascular Mortality: The NHANES 2005-2014. *Journal of Affective Disorders*, S0165032721014233. https://doi.org/10.1016/j.jad.2021.12.104

Weinstein, T. A. R., & Capitanio, J. P. (2008). Individual differences in infant temperament predict social relationships of yearling rhesus monkeys, Macaca mulatta. *Animal Behaviour*, *76*(2), 455–465. https://doi.org/10.1016/j.anbehav.2008.01.024

White, L. K., Britton, J. C., Sequeira, S., Ronkin, E. G., Chen, G., Bar-Haim, Y., Shechner, T., Ernst, M., Fox, N. A., Leibenluft, E., & others. (2016). Behavioral and neural stability of attention bias to threat in healthy adolescents. *Neuroimage*, *136*, 84–93.

Wise, R. A., & Rompre, P.-P. (1989). Brain dopamine and reward. *Annual Review of Psychology*, *40*(1), 191–225.

Wolf, V., Kühnel, A., Teckentrup, V., Koenig, J., & Kroemer, N. B. (2021). Does transcutaneous auricular vagus nerve stimulation affect vagally mediated heart rate variability? A living and interactive Bayesian meta-analysis. *Psychophysiology*, *58*(11). https://doi.org/10.1111/psyp.13933

Wood, E. K., Gabrielle, N., Hunter, J., Skowbo, A. N., Schwandt, M. L., Lindell, S. G., Barr, C. S., Suomi, S. J., & Higley, J. D. (2021). Early Rearing Conditions Affect Monoamine Metabolite Levels During Baseline and Periods of Social Separation Stress: A Non-human Primate Model (Macaca mulatta). *Frontiers in Human Neuroscience*, *15*.

Wooddell, L. J., Kaburu, S. S. K., Murphy, A. M., Suomi, S. J., & Dettmer, A. M. (2017). Rank acquisition in rhesus macaque yearlings following permanent maternal separation: The importance of the social and physical environment. *Developmental Psychobiology*, *59*(7), 863–875. https://doi.org/10.1002/dev.21555

Wrzus, C., Hänel, M., Wagner, J., & Neyer, F. J. (2013). Social network changes and life events across the life span: A meta-analysis. *Psychological Bulletin*, *139*(1), 53.

Yu, B., Steptoe, A., Chen, L.-J., Chen, Y.-H., Lin, C.-H., & Ku, P.-W. (2020). Social isolation, loneliness, and all-cause mortality in patients with cardiovascular disease: A 10-year follow-up study. *Psychosomatic Medicine*, *82*(2), 208–214.

Figures

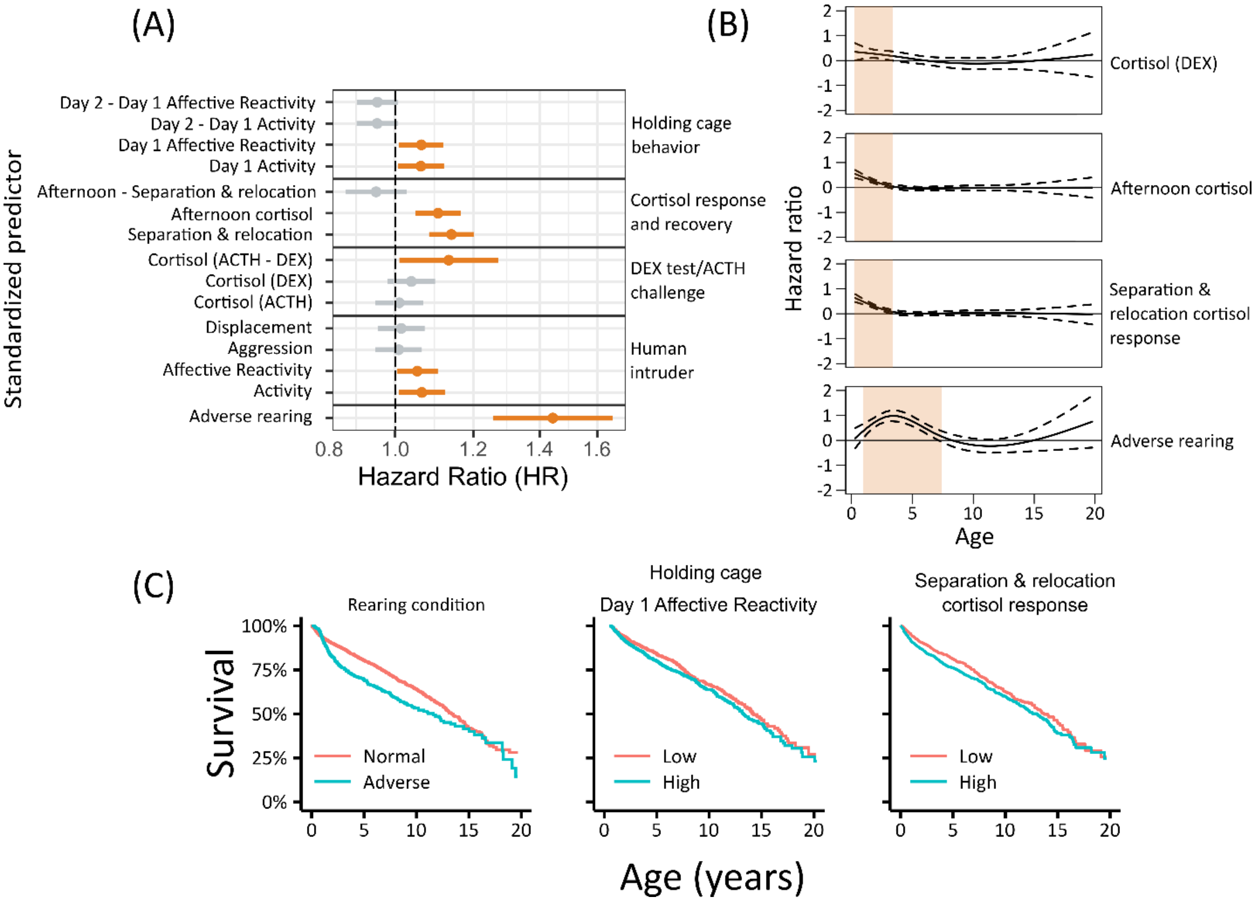

Figure 3.4 Association between BioBehavioral measures in infancy and longevity. (A) Hazard ratios (HR) for mortality. Significant HR's ($p < 0.05$) that are greater than 1 (i.e., associated with increased mortality) are shown in orange. (B) Time-varying HR's for predictors that violated the proportional hazards assumption. Shaded areas show ages at which these predictors were significantly associated with mortality. (C) Survival curves for rearing condition, holding cage Affective Reactivity, and cortisol response after initial separation and relocation to the novel testing environment. Low = lower 33rd percentile, high = upper 66th percentile, and continuous measures were split for display purposes only. All intervals represent 95% confidence intervals.

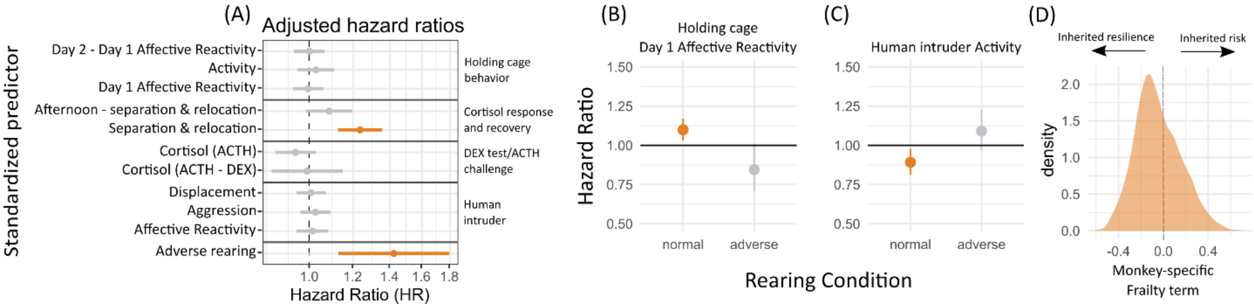

Figure 3.2 Adjusted hazards ratios and heritability of longevity. (A) Adjusted hazard ratios of infant BioBehavioral measures indicated morning cortisol and adverse rearing were positively associated with mortality. (B) Monkeys that were raised under normal rearing conditions evidenced a positive association between reactivity in the holding cage and mortality, but this association was blunted and almost reversed in monkeys raised under adverse rearing conditions. (C) Monkeys that were raised under normal rearing conditions evidenced a negative association between activity during human intruder and mortality and this association was almost reversed in monkeys raised under adverse rearing conditions. (D) There was substantial heritability of longevity, shown in the distribution of monkey-specific frailty terms (log HR’s) that were estimated by incorporating relatedness between monkeys into the model using pedigree information. Frailty terms represent monkey-specific risks/residences that are due to inherited effects.

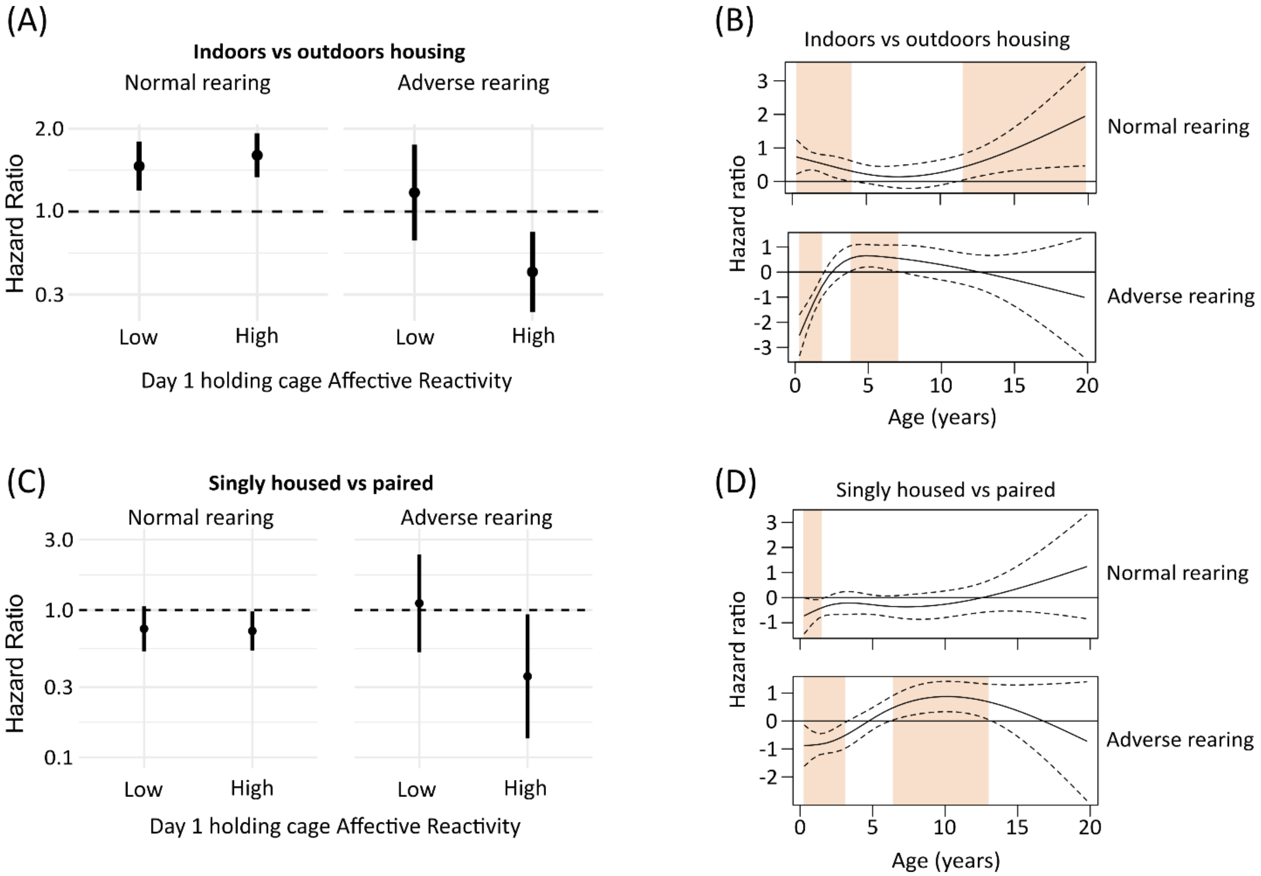

Figure 3.3 Effects of social environment on mortality. (A) Animals that were raised in normal rearing conditions had elevated mortality rates when housed indoors compared to outdoors, regardless of Day 1 holding cage Affective Reactivity. On average, animals that had adverse rearing experiences and had high Day 1 holding cage Affective Reactivity scores had lower mortality rates when housed indoors, however (B) this was only true in infancy. (C) Both animals that were raised under normal rearing conditions and animals that were raised under adverse rearing conditions and that had high Day 1 holding cage Affective Reactivity scores lived longer if singly housed, compared to being paired. However, (B) this was predominantly driven by protective effects in infancy. We do not advocate for singly housing monkeys solely on the merit of decreasing mortality rates as there are likely tradeoffs between quantity and quality of life—please see the discussion for further details.

Conclusion

These studies further our current understanding of how aging impacts the psychological processing of socioaffective stimuli across the nonhuman primate lifespan and additionally point to the important role socioaffective processing—even as early as infancy—plays in determining health and wellbeing. Results point to phylogenetically conserved features of socioaffective aging between rhesus monkeys and humans but also highlight important species differences. Integrating findings across the studies helps to inform biological, psychological, and evolutionary mechanisms though which age-related changes to socioaffective processing occur.

The first chapter demonstrated that, like humans, middle-aged monkeys display a potent bias in visual attention towards threatening faces; however, the bias towards threatening stimuli was not present in older monkeys. Unlike humans, older monkeys did not display an age-related bias in visual attention *towards* putatively positive facial stimuli. These results suggest that the avoidance of negative socioaffective stimuli—at least in the context in which these experiments were performed—is evolutionarily conserved between rhesus monkeys and humans, indicating that age-related reduction in attending to threatening stimuli potentially confers fitness advantages for aged primates. Results of the second and third chapters help to inform the potential fitness advantages that avoiding negative socioaffective stimuli confers to aged monkeys.

Specifically, in the second chapter, we found an age-related reduction in monkeys' parasympathetic nervous system responsivity (as indexed through respiratory sinus arrhythmia) to socioaffective stimuli. Put another way, older monkeys displayed reduced autonomic flexibility and were less able to physiologically adapt to changes in environmental demands. Therefore, avoiding threatening situations promotes survival for older monkeys because engaging with such stimuli carries a physiological price that their bodies cannot afford to pay. As a result, we believe that threat avoidance—at least in the context in which our experiments were carried out—promotes survival in aged animals and was thus selected for evolutionarily. Whether or not threat avoidance in aging primates is causally mediated by changes to the vagal system remains an open question and is a future avenue of research.

The final chapter demonstrated that aspects of monkeys' temperament and biology in infancy were predictive of longevity. Critical windows across development were identified, with physiological features carrying most predictive power in early life and behavioral features being most predictive of mortality in adolescence and adulthood. Behaviorally, we find that monkeys that were more reactive as a result of being removed from their home environment and animals that were less physically activity in the presence of a threatening stimuli had shorter life expectancies. Therefore, in the context in which our studies have been carried out (at a research institute/breeding facility), measures of efficient affective regulation in infancy carry predictive ability for survival.

Future work directly assessing features of neurophysiology as animals age is necessary for truly uncovering causal mechanisms through which changes to the body, brain, and social environment mediate changes to behavior in aging but such work is critical for promoting wellbeing in an aging world.