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CHAPTER ONE

Introduction to *Cognitive and Social Neuroscience of Aging*

Learning Objectives

- What are some of the theories that explain how cognition changes with age?
- How have cognitive neuroscience data led to new theories of cognitive aging?
- What are some of the overall ways in which the patterns of brain activity change with age?
- Which methods are employed to study the aging brain?
- What are some of the current trends in the study of aging?

1.1 Introduction

Studying the brain has dramatically altered how scientists think about aging. Initially, the study of aging presented a gloomy picture, with most behavioral research illustrating losses in cognitive ability. These included poorer vision and audition, poorer attentional control and ability to ignore distractions, and declines in the accuracy, amount, and quality of information in memory. Although there are some notable exceptions, such as suggestions that wisdom increases in old age (Baltes, 1993) and consideration of gains and optimization of function (Baltes & Lindenberger, 1997), most of the literature emphasized impairments and losses that occur with age. Cognitive neuroscience methods, however, have highlighted the reorganization and even compensatory gains that can occur with age. Early papers showed that older adults could engage the brain *more* than younger adults, with additional brain regions activated for tasks compared to younger adults. This was a surprising finding, indicating that older adults' brains are more active than those of their younger adult counterparts. There were many attempts to establish that these additional activations of the brain indicate **compensation** such that older adults boost task performance, or stave off further declines, by recruiting brain regions more flexibly than younger adults. Literature

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consistent with, and in opposition to, this interpretation will be reviewed throughout the book. At the very least, neuroscience methods opened up new ways of considering questions of how cognitive, social, and affective abilities change with age.

In this chapter, I will briefly review theories of cognitive aging. These are largely based on behavioral data accumulated over years of research; the rest of the book will allow the reader to explore ways in which neuroscience data converge with these theories, or have led to the development of new ways of thinking about the process of cognitive aging. The chapter will then present the cognitive neuroscience methods that are commonly employed to study brain activity with age, and discuss recent advances.

1.2 Theories of Cognitive Aging

Much research has been devoted to attempts to identify a single mechanism that explains cognitive changes with age. These approaches are reviewed briefly here; readers are urged to consult other edited volumes on the topic (Craik & Salthouse, 2007; Lemaire, 2016; D. C. Park & Schwarz, 2000; Perfect & Maylor, 2000).

Processing speed theory purports that aging is associated with slowing, possibly reflecting reduced neural transmission speed due to the demyelination, or loss of white matter, that occurs with age (Salthouse, 1996; Salthouse & Babcock, 1991). More than simply slowing down how long it takes to reach a solution for a problem or retrieve information from memory, speed of processing also could impact the *quality* of information processing. This also has implications for cognitive abilities that are not under time pressure. For example, information may be degraded to the point that it is no longer useful, or outcomes from earlier stages of processing may no longer be available by the time the later stages are complete.

Working memory research considers the amount of cognitive resources that are available to accomplish challenging tasks (Craik & Byrd, 1982; D. C. Park et al., 2002; D. C. Park et al., 1996). Classic models of working memory focus on the ways in which we store visuospatial or verbal information alongside a central executive system that coordinates processes and an episodic buffer that integrates and orders information (Baddeley, 2000; Baddeley & Hitch, 1974). For example, information must be taken in from the environment, comprehended, and transmitted to brain regions or other processes that allow one to formulate a goal or response, and then a response must be

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executed. Theories focused on working memory ability suggest that the amount of information one can keep in mind and coordinate at a time differs across individuals, and this resource accounts for differences across individuals in a number of different abilities such as long-term memory and reasoning. Because working memory capacity decreases with age, individuals become more limited in a variety of cognitive abilities. The fluid nature of working memory differs from world knowledge, which is accumulated over a lifetime and is intact, or even enhanced, with age.

Inhibition theory also emphasizes the importance of the ability to keep multiple pieces of information in mind simultaneously, but highlights the competition or interference that is in play (Hasher & Zacks, 1988; Zacks & Hasher, 1997). Being able to focus on target information, while ignoring irrelevant information, becomes more difficult with age, and this may underlie a host of cognitive declines that occur with age. Early research critiqued inhibition theory for not being distinct enough from working memory theory, but recent work with neural measures emphasizes the importance of **cognitive control** (the ability to control how one uses information, perhaps ignoring some information while focusing on other aspects), particularly with age.

Rather than focusing on specific cognitive abilities, such as speed, working memory, or inhibition, another theory purports that **sensory function** reflects the integrity of the brain and cognitive processes. Early data revealed striking relationships between how well one performs on acuity measures for vision and audition and performance on a variety of cognitive abilities, spanning from speed of processing to memory to world knowledge (Lindenberger & Baltes, 1994). These connections led Baltes and Lindenberger (1997) to propose the **common cause hypothesis** of aging. This theory suggests that aging has a widespread and consistent impact on the brain, which may be detected by measures of these sensory abilities.

Although each of the reviewed approaches highlights a single ability, many of the abilities are associated with each other (e.g., individuals with the fastest speed of processing may also have the best working memory performance). Findings of relationships between performance on different tasks have led to appreciation of domain-general aspects of cognitive aging. Such an approach emphasizes that declines occur consistently across multiple abilities rather than affecting distinct abilities to greater or lesser degrees (e.g., Salthouse, 2017; Tucker-Drob, 2011; Tucker-Drob et al., 2014).

1.3 Cognitive Neuroscience of Aging Theories

An initial brain-based theory of cognitive aging, the **frontal aging hypothesis**, predated much of the cognitive neuroscience movement. This emerged from a neuropsychological approach, guided largely by older adults' impaired pattern of performance on tasks thought to be mediated by the frontal lobes, in conjunction with observations of exaggerated structural decline in the frontal lobes and reduced dopamine in the region (West, 1996). The literature has largely moved away from this hypothesis. This shift has occurred because cognitive neuroscience methods have uncovered complex patterns with age, sometimes indicating reorganization and change, in the conditions under which frontal lobes are engaged by tasks. There is also great variability in the rates at which different regions of the frontal lobes decline.

1.3.1 Increased Activity and Compensation with Age

One of the initial observations identified changes in the **bilaterality** of brain activation patterns with age (Cabeza et al., 1997; Grady et al., 1995; Reuter-Lorenz et al., 2000). That is, whereas younger adults largely activate the left *or* right prefrontal cortex during tasks, older adults tend to activate the same region in both hemispheres. Roberto Cabeza and colleagues identified two frameworks to characterize the pervasive patterns of changes in neural activity with age. The hemispheric asymmetry reduction in older adults, or **HAROLD**, model (Cabeza, 2002) emphasizes the increased bilaterality with age. Another change in the pattern of brain activity with age, a posterior–anterior shift in aging, or **PASA**, links age-related increases in frontal lobe activity with age-related decreases in occipital lobe activation (S. W. Davis et al., 2008).

Initially, there was much debate over the function of these patterns of activation, with some researchers claiming they were compensatory. That is, by recruiting the other hemisphere, older adults are able to harness additional cognitive resources and thus improve their performance relative to what it would be if supported by the younger adult pattern of unilateral activation. Data comparing high and low performers (e.g., Cabeza et al., 2002), differences in reaction time (e.g., Madden et al., 1997), and successful versus unsuccessful performance (e.g., Gutchess et al., 2005) were interpreted as supporting the notion that increased activation with aging is compensatory (see Figure 1.1). The claim of compensation is substantiated by a method that allows for the

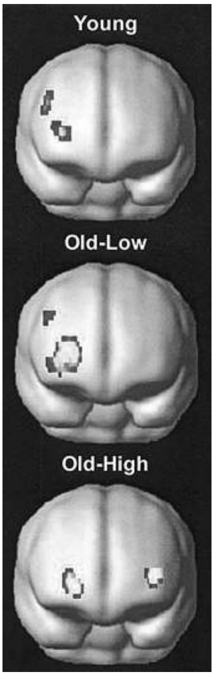

Figure 1.1 During a memory recall task, high-performing older adults (bottom) showed more bilateral prefrontal activity than lower-performing older adults (middle). This was interpreted as evidence that bilaterality is compensatory, as the pattern was linked to better performance for older adults, despite differing from the unilateral prefrontal activations seen in young adults (top).
Adapted from Cabeza et al. (2002), *NeuroImage*, Figure 2.

disruption of neural activity in a region. Older adults' performance is impaired when the second hemisphere is targeted (Rossi et al., 2004).

Whether increased activation serves a compensatory function became a more complicated question due to diverging findings in the literature when comparing across groups, including those with disorders associated with aging (e.g., Alzheimer's disease (AD)). Thus, models of cognitive aging began to consider task demands and differences across individuals and groups. This led Cabeza and Dennis (2013) to delineate criteria to differentiate successful compensation from mere *attempts* at compensation. Specifically, neural activity may initially increase as the brain atrophies, reflecting a compensatory attempt to respond to cognitive decline. As the brain continues to deteriorate with age, or as task demands exceed one's ability, it will no longer be possible to continue to increase activity in an attempt to compensate, so neural activity will decline. Furthermore, for neural activity to be considered evidence of successful compensation, the activity must be related to improved task performance and occur in neural regions known to support task performance in older adults. With limited ability to test the *causal* role of brain activity on behavioral outcomes (e.g., what happens to behavior when a region is impaired versus intact), it has been difficult to conclusively substantiate claims of compensation (for further discussion, see Section 1.4.2).

1.3.2 Changing Neural Responses to Task Demands

Whereas initial frameworks largely described the patterns of neural activity that occur with age, other frameworks emerged that emphasized how the demands on cognitive resources change with age. For example, the compensation-related utilization of neural circuits hypothesis (**CRUNCH**) purports that increased task demands should necessitate increased neural activity for older adults at lower levels of difficulty than is the case for younger adults (Reuter-Lorenz & Cappell, 2008). The scaffolding theory of aging and cognition (**STAC**) incorporates a similar perspective, whereby cognitive and neural challenges that accompany aging require additional resources (D. C. Park & Reuter-Lorenz, 2009). Life experience factors, such as fitness and social or intellectual engagement over the life span, can also shape the availability and engagement of resources (Reuter-Lorenz & Park, 2014). When these resources are available, through recruitment of additional neural regions or other processes that enhance neural systems (such as cognitive training and exercise), older adults will harness them to support cognitive performance. The STAC framework goes beyond the others in considering individual differences and contextual factors. For example, individuals may differ in how they respond to the challenges of aging or other neural insults (e.g., head injury, AD). This idea is encapsulated in the concept of **cognitive reserve**, whereby individual differences in neural systems or cognitive abilities, developed as a function of nature or nurture (e.g., educational attainment, leisure activities), could serve a protective function for those individuals with higher capacity (Stern, 2002, 2009). Another model suggests that age groups differ in *when* they engage resources to encounter task demands. This could allow younger adults to manage task challenges more successfully than older adults. Whereas younger adults engage in proactive control, planning ahead for

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challenging conditions, older adults display reactive control in response to task demands (Braver et al., 2009; Velanova et al., 2007).

1.3.3 Reduced Specificity of Neural Responses with Age

A final set of models proposed to account for cognitive changes with age focuses on the ways in which aging reduces the clarity of information processing with age. There is substantial evidence for **dedifferentiation** with age, meaning that neural regions respond in a less specific way for older than younger adults. This has largely been established for sensory regions, such that regions for processing visual information that are narrowly tuned in younger adults to respond to certain classes of stimuli, like faces or houses (places), respond more generally across categories for older adults (D. C. Park et al., 2004). Similarly, motor cortex response tends to be lateralized for each side of the body, with the left motor cortex responding to movement of the right side of the body, and vice versa. With aging, however, motor cortices respond bilaterally to movement on either side of the body, reflecting a loss of specialization with age (Carp, Park, Hebrank, Park, & Polk, 2011). Findings of greater dedifferentiation with age also extend to memory (e.g., St-Laurent et al., 2014). These findings are discussed further in Chapters 3 and 4.

Other processes also exhibit a loss of specificity with age. The **default network** is so named because these neural regions tend to be more engaged when at rest than when performing cognitive tasks (e.g., solving math problems presented on a computer screen). Older adults do not suppress this network as much as younger adults during tasks that demand external attention (Grady et al., 2010; Persson et al., 2007). This may indicate difficulty in alternating between cognitive states with age. In addition, neural transmission may be noisier in older adults, with a reduced signal-to-noise ratio (Backman et al., 2006; S. C. Li et al., 2001). This could make it difficult to distinguish representations, such as one item from another similar one. Failure to suppress the default network during tasks or to distinguish the relevant neural signal from noise could increase older adults' vulnerability to making errors as a result of poorer-quality representations of information.

1.4 Cognitive Neuroscience Methods

There are two broad classes of measures: those that measure the physical structure of the brain, and others that measure the function or dynamic engagement of the brain over time or task demands.

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1.4.1 Measures of Structural Integrity of the Brain

One approach to studying the brain is to investigate the integrity of and changes in structural measures of anatomy. This includes measures of gray matter (consisting of the cell bodies of neurons) as well as white matter (consisting of bundles of myelinated axons from neurons and glial cells). By considering structural measures, one can assess the physical changes of the brain and relate these to performance on cognitive tasks. Such comparisons largely adopt an individual differences approach to determine whether greater loss of volume in a specific region is related to poorer cognitive performance.

Magnetic Resonance Imaging (MRI)

This technique involves imaging the anatomy of the brain with magnetic fields and radio waves. Because the magnetic properties of soft tissue allow it to be differentiated from bone, blood, or other substances within the head, high-resolution images can be produced that distinguish gray from white matter in the brain. MRI is preferred to other 3D imaging measures, such as CT (X-ray computed tomography), because it has higher resolution and is safer due to the lack of ionizing radiation. Measures of brain structure have the longest history of application to the study of cognitive aging, and have illustrated the ways in which aging impacts gray and white matter. As will be discussed in Chapter 2, individual differences in the volume of particular regions can be linked to how well individuals perform on a task (e.g., is a bigger brain region associated with better performance on a memory task?). But because these measures convey static information about an individual's anatomy, MRI cannot be directly linked to trial-by-trial task performance.

Diffusion Tensor Imaging (DTI)

Diffusion is a measure of how much water spreads from a point, and is used to assess white matter pathways. When unconstrained, water is equally likely to flow in all directions from a point. White matter fiber tracts restrict the flow along that pathway, much as paved roads direct the flow of traffic; the presence of white matter fibers is inferred through diffusion measures. One measure of diffusion is fractional anisotropy (FA), which characterizes how strongly water molecules diffuse in a particular direction. Aging can break down the microstructure of tissue, decreasing FA (Alexander et al., 2007; Gunning-Dixon et al., 2009).

Although the study of aging has a longer history of focusing on measures of gray matter, there is increasing recognition that white matter changes can be profound, and may explain much age-related decline in cognition (Gunning-Dixon et al., 2009).

1.4.2 Measures of Brain Function

Measures of brain function provide information about what parts of the brain are engaged over time. The approach typically is used to investigate which regions of the brain are involved during tasks (e.g., viewing attractive versus unattractive faces), but some of these methods are used to evaluate which regions communicate with each other, with or without an ongoing task. One of the limitations that applies to all of the methods discussed in this section is the fact that the data are largely correlational. This means that the results of different studies illustrate how the brain responds for younger adults versus older adults, but the current methods are largely unable to establish causality (e.g., is this region responsible for memory impairments with age?). In order to determine causality, it would be necessary to independently increase or decrease levels of neural activity and then measure the effect on behavior. The inability to determine causality is an important caveat to keep in mind when reading about studies relying on methods such as fMRI and ERP, as well as recognizing the difficulty posed for testing theories based on neural data.

Functional magnetic resonance imaging (fMRI) relies on the same imaging properties as MRI, but requires additional hardware and software that allow the scanner to track neural activity over time. This allows us to assess brain activity during cognitive tasks, such as attending to some information while ignoring other information, or holding a series of numbers in mind. Thus, neural activity can be linked with tasks, and the resulting performance (e.g., success or failure on a trial; better or worse performance than other individuals). The technique does not directly measure the activity of the brain (e.g., the firing of neurons) but instead capitalizes on the differences in the magnetic properties of oxygenated versus deoxygenated blood. The BOLD (blood oxygenation level dependent) signal detects active brain regions based on the inference that oxygenated blood is drawn to active regions of the brain and deoxygenated blood flows away. Although fMRI has reasonable temporal sensitivity, on the order of seconds, it is not instantaneous because the BOLD response is slow, allowing a signal to peak approximately 6 s after the neural activity occurred. Despite its imperfect temporal resolution, the method has good spatial resolution, on the order of mm (and this can be increased with methods such as high-resolution imaging).

fMRI methods are the most common in the study of cognitive aging, due to their good spatial resolution, relative cheapness, and ready availability, compared to some other methods. Still, it is important to realize the shortcomings of this method, including the potential for age-related changes in the very signal that is being measured. For example, research suggests that the BOLD response may lag with age, or even reach a flatter peak for older than younger adults (D'Esposito et al., 1999; Huettel et al., 2001). Studies comparing the effects of aging across conditions (e.g., difficult versus easy) sidestep this concern to some extent, because the overall effects of aging should impact both conditions. The comparison across conditions also highlights the fact that fMRI does not produce an absolute value that can be compared across conditions or individuals. Rather, it relies on *relative* comparisons, using subtractions of different conditions, such as assessing whether the neural response to a difficult arithmetic problem is *more* affected by aging than the neural response to an easy problem.

Positron emission tomography (PET) is a functional imaging technique much like fMRI in that it relies on blood flow to localize regions that are engaged during performance of cognitive tasks. The method involves injecting a participant with a radioactive tracer. Regions that use more or less of the compound (e.g., oxygen, glucose) labeled with the tracer can be identified as radioisotopes are emitted. These data can be used to create 2D or 3D images, showing the distribution of the tracer across brain regions. PET has been largely replaced by fMRI, which is a cheaper method that is less invasive for human participants (no injections of radioactive substances), while also offering superior spatial resolution and flexibility in the timing of experimental designs. Because PET can target specific neurotransmitter systems (e.g., dopamine), the method is having a resurgence, used even in combination with other methods.

Event-related potentials (ERP) use electrodes positioned on the scalp to measure electrical activity, typically reflecting the postsynaptic potentials emitted when neurotransmitters bind to receptors (Luck, 2014). These can be measured at the scalp when they are emitted simultaneously from many neurons that are oriented the same way. ERPs have particularly good temporal resolution, and this timing information can be used to identify specific components. Components are linked to specific mental processes (e.g., perceiving an oddball tone, committing an error when responding), and are identified by their timing, polarity (i.e.,