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Introduction to the special issue: advances in understanding the cognitive neuroscience of aging with multivariate methods

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As the aging population across the world continues to grow, there is an ever-increasing need to understand how age and factors associated with aging impact cognition. Cognitive aging research has expanded rapidly over the past several decades focusing on the inherent relationship between the brain and subsequent behavior across the lifespan. For example, early work in structural neuroimaging focused on identification of age-related volumetric declines in the hippocampus and frontal cortices (Raz, 2000; Raz et al., 2005; for a recent review, see, Lockhart & DeCarli, 2014), linking these declines to age-related declines in cognitive performance (Fjell & Walhovd, 2020; Raz & Rodrigue, 2006). Early functional neuroimaging studies largely focused on cross-sectional differences between young and older adults in univariate measures of regional brain structure and function (e.g., amplitude and location of the fMRI BOLD signal) and their relationship to cognition. This foundational work has led to theories and conclusions regarding age-related deficits in the engagement of core cognitive processes as well as age-related shifts in neural engagement and cognitive operations.

One of the prominent findings in early functional neuroimaging work in aging is that of functional reorganization. Specifically, under-recruitment, or an age-related reduction in BOLD activation in a given brain region, has led to the idea of neural deficits in engaging necessary cognitive resources for completing a behavioral task (e.g., attention or memory; Grady, 2008). At the same time, over-recruitment, or an age-related increase in BOLD activation with a given brain region, has been met with the idea of compensatory processing in aging (Cabeza et al., 2002; Cabeza & Dennis, 2013). For example, a consistent poster-to-anterior-shift in aging activation across perceptual, attentional, and memory tasks has led to the conclusion that older adults engage in less overall processing within sensory cortices (e.g., occipital cortex), while over recruiting regions (e.g., frontal cortex) involved in higher-order cognition compared to younger adults (Davis et al., 2008). Other work has focused on age-related decreases in the overall BOLD signal within highly specialized brain regions when viewing or processing discrete categories of stimuli (e.g., fusiform gyrus activity when viewing face stimuli; Park et al., 2004). The

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results from this research have led to the conclusion that the brain loses specificity, or becomes more dedifferentiated, with increasing age and, in turn, compromises cognitive function in older adults (Koen & Rugg, 2019; Li et al., 2001; Li & Rieckmann, 2014).

More recently these, and other longstanding theories of cognitive aging, have been investigated using multivariate statistical modeling techniques applied to behavioral, psychophysiological, and neuroimaging data. While multivariate techniques have been a mainstay in basic cognitive neuroscience research over the past 15 years, there has recently been a surge of interest in applying multivariate techniques to test longstanding theories of cognitive aging. Multivariate techniques can identify and/or leverage the spatial and temporal information inherent in behavioral and neural data to identify patterns that are associated with human cognition. Some of these methods, such as partial-least squares, can be used to identify covariances between combinations of structural and functional brain variables to identify structure–function–behavior relationships. These techniques work by finding combinations of variables and summarizing them into a "latent" factor. Given the many changes in both brain and behavior that accompany aging, these methods are well suited to identify the brain–behavior relationships that differ across the lifespan. Multivariate pattern analysis (MVPA) has perhaps become one of the most dominant analysis methods in task-based fMRI and psychophysiological (i.e., EEG and eye tracking) studies. Broadly speaking, MVPA techniques take into account the spatial and temporal patterns of neural signals in order to extract information about the type of information that is represented in specific brain regions. One common version of MVPA, namely pattern (or representational) similarity analysis, computes the (dis)similarity between both behavioral and neural patterns across categories of trials and can detect multidimensional features in data (Kriegeskorte, 2008; for a recent tutorial review, see, Dimsdale-Zucker & Ranganath, 2018). An advantage of MVPA approaches, when compared to traditional univariate analyses and even other multivariate techniques like partial least squares, is that MVPA can relate trial-by-trial neural patterns to behavior. Importantly, the foregoing techniques have been increasingly applied to cognitive aging studies to examine how neural representations differ across the lifespan and are associated with age-related cognitive decline.

This special issue of *Aging, Neuropsychology, & Cognition*, Advances in understanding the cognitive neuroscience of aging with multivariate methods, highlights recent work from some of the top labs that are leveraging multivariate analysis of psychophysiological and/or neuroimaging data to advance our understanding of the neural bases of cognitive aging. The papers in this special issue include both new empirical investigations and review papers that highlight how multivariate techniques can be used to investigate cognitive aging across a variety of cognitive domains, including executive function, memory encoding and retrieval, false memory, empathy, and emotion regulation.

Four research papers in this special issue applied multivariate analyses to behavioral and psychophysiological indices of cognition, such as neuropsychological tests and eye movements in memory encoding, in order to elucidate the relationship between these measures and neural processes. Lin and McDonough (2022) used multivariate statistics to investigate the relationship between measures of cognition and brain metrics in both middle aged and older adults. Specifically, research sought to elucidate the brain mechanisms underlying Intra-Individual Cognitive Variability (IICV), or the variation in performance across multiple neuropsychological tests. Using multivariate partial least-squares analysis, they found that lower mean and higher IICV variability were linked to lower connectivity in the sensorimotor and default mode networks, whereas higher mean and higher IICV variability were linked to lower volume in cognitive control regions including the default mode and limbic networks. This dissociation across neural networks suggests a heterogenous relationship across neural networks, signaling widespread network dysfunction. The implementation of the partial least-squares analysis allowed for a multivariate analysis that accounted for the shared variance among multiple neural networks in a way that a univariate approach to the data simply could not support. This ability to elucidate dysfunction within neural networks will help expand the usefulness of using IICV in identifying cognitive decline in clinical settings and using this metric as a possible indicator of both structural and functional neural alterations in aging.

In another study focusing on behavioral indices of cognition, John et al. (2022) used canonical correlation analyses to examine the relationship between different stages of learning and latent constructs of executive functioning and MTL subregion structure. In a heterogeneous sample of healthy older adults and patients with MCI, researchers found that MTL volume and verbal memory demonstrate a graded relationship across early learning, late learning, and delayed recall. While executive function and attention also exhibited a significant relationship between learning and recall, researchers did not find that the relationships differed across memory phases. The foregoing work highlights the importance of sample characteristics in age-related analyses and introduces the use of multivariate statistics to the investigation of complex cognitive relationships in aging. Specifically, the inclusion of latent factors in measuring these relationships allows more precise accuracy in the estimation of domain-general cognitive functions as opposed to a single measure of cognition.

Ryan et al. (2022) reviewed work from their lab and others that applied multi-model and multivariate approaches to the study of eye movements in aging as a means to understand age-related changes in memory. The approach used is similar to that of pattern similarity analyses used in conjunction with neuroimaging data (see below for examples), whereby moment-to moment alterations in eye movements are tracked and characterized as part of a larger pattern. These larger patterns of visual exploration are then linked to alterations in neural functioning. The conclusion reached by this review is that age-related changes in momentary fluctuations in oculomotor behavior are linked with that of MTL structure and function. When relating these findings to age-related deficits in episodic memory, researchers suggest that the alternative way in which older adults are engaging in visual exploration may be non-optimal and lend itself to a reduction in the amount of information the visual system encodes. This in turn can affect encoding even before neural processing of the visual scene begins. This work has implications for understanding not only age-related memory deficits, but also downstream deficits in neural processing and memory representations in aging.

Ziaei and colleagues (2022) examined the neural correlates of young and older adults' ability to share another's emotional state, a process referred to as affective empathy. The authors addressed this open question using DTI, fMRI, and behavioral data in conjunction with a partial- least squares analysis to investigate the structure-function correlates of anterior and posterior cingulate brain networks associated with affective empathy. In older, but not young, adults faster responses on the Multifacted Empathy Task, which reflects better empathic responding, was associated with increased functional activation in the anterior cingulate network and with higher fractional anisotropy in the uncinate fasiculus for both negative and positive emotions. Moreover, empathy for negative emotions was associated with functional activation in the anterior cingulate network and white matter integrity of the anterior cingulum bundle. Older adults also showed increased activation and white matter integrity in the posterior cingulate network during positive affective empath, although this was not related to performance. These results suggest that the neural correlates of affective empathy show a posterior-to-anterior shift with increasing age, which might be due to age-related increases in difficulty for engaging affective empathy for negative emotions.

The remaining papers included in this special issue focus on MVPA techniques, primarily pattern similarity analyses, to investigate cognitive and memory aging. Sommer and Sander (2022) review recent research that has used MVPA techniques applied to fMRI and EEG to investigate age differences in the specificity of neural representations supporting memory. They argue that neural specificity is determined by a combination of representational distinctiveness and stability. Distinctiveness reflects the similarity between the neural representation for stimuli or broad categories of stimuli, whereas representational stability captures the degree of "change," or consistency, of neural representations for events over time. The authors review evidence that aging is associated with decreases in both representational distinctiveness and stability, and thus an overall decline in neural specificity. These age-related reductions in neural specificity are proposed to compromise both the encoding and retrieval processes critical to episodic memory.

Investigating perceptual and categorical similarity in memory was undertaken by a study by Davison et al. (2022). Building off strong behavioral work in cognitive aging theory, their work applied the principles of the inhibitory deficit hypothesis (Hasher & Zacks, 1988) to examine differences among the neural similarity of activity patterns between relevant and irrelevant stimulus categories and how these differences impact visual working memory in aging. Consistent with the inhibition deficit theory, the paper found that younger adults outperformed older adults with respect to recognition accuracy in the face of interference. This behavioral finding was met with evidence for neural similarity between the cued and uncued categories in young, but not older adults, predicted memory success. Interestingly, older adults' overall memory performance improved as the similarity of their neural representations of the categories increased. This benefit was specific to match trials in the N-back working memory task. In contrast, on mismatch trials, older adults' performance was negatively impacted by increases in target-distractor neural category similarity. Together results suggest that, in aging, precision opposed to recognition memory strength, is more impacted by interference in memory.

Expanding upon what we know about neural dedifferentiation in aging, Simmonite and Polk (2022) investigated age differences in neural distinctiveness across the visual, auditory, and motor cortices using pattern similarity analyses. Supporting the previous univariate findings, researchers observed age-related reductions in neural distinctiveness across all three regions. They further observed that these reductions were driven by both decreases in within-category similarity and increases in between category similarity. This nosier neural signal in aging was correlated across regions, meaning that the reliability of neural activation was related to an overall decline in distinctiveness within individuals.

The authors conclude that age-related declines in neural distinctiveness are driven by age-related changes in both the reliability and confusability of neural activity. Given the apparent ubiquitous nature of these changes, they may serve as a possible biomarker for cognitive decline.

Dennis et al. (2022) utilized pattern similarity analyses to examine the neural basis of associative memory errors within a sample of younger and older adults as a means to better understand the cognitive and neural processes that underlie age-related increases in false memories. Researchers found that age-related increases in false memories were accompanied by reduced distinctiveness of the neural signal across hits and false alarms within several brain regions, including the middle occipital cortex, medial temporal gyrus, and superior frontal gyrus. Critically, these three regions have been associated with false memories in the previous univariate work (Kurkela & Dennis, 2016). The current analysis highlights a possible mechanism within these regions accounting for memory errors. To this end, the extent of overlap in neural patterns underlying these two different memory types is correlated with individual differences in false memory rates. The work suggests that with an increase in the correspondence in neural processing between targets and related lures, one is more apt to erroneously identify the lure as previously studied.

Two studies, Folville et al. (2022) and Koen (2022), leveraged across-participant pattern similarity analysis methods to investigate how neural patterns shared across individuals contribute to age differences in memory. In young adults, this approach has revealed that events or stimuli share a common neural pattern across individuals during the initial perception of a stimulus and when the memory is retrieved (Chen et al., 2017; Koch et al., 2020; Oedekoven et al., 2017; Zadbood et al., 2017). Folville et al. (2022) applied this multivariate technique combined with a searchlight analysis to examine stimulus-specific neural patterns during encoding and retrieval of stimuli that were remembered with high subjective vividness. The results demonstrated that across-participant similarity for vividly remembered events was reduced in older relative to younger adults in numerous regions including the middle occipital gyrus, posterior parietal cortex, and in the superior and middle frontal cortex. A similar age-related reduction was observed in the occipital and parietal cortex, including the angular gyrus, when examining across-participant similarity during memory retrieval. These results suggest that older adults' neural representations during encoding and retrieval are less distinct and show more inter-individual variability relative to younger adults.

Koen (2022) used a modification on previous across participant pattern similarity analysis methods to examine age differences in the distinctiveness of stimulus specific and category level neural patterns for scene and object stimuli in relation to subsequent memory. The approach used a subset of participants' data to train a linear mixed effects model to predict the estimated BOLD response for each individual image. The predicted image maps from this approach were then submitted to a multivariate pattern similarity analysis to measure both stimulus specific, or item-level, and category-level specificity within parahippocampal place area and the lateral occipital complex. The results showed that both item and category-level pattern was reduced in older adults which joins a growing literature demonstrating that age-related neural dedifferentiation occurs for multiple levels of neural representations (Kobelt et al., 2021; Sommer & Sander, 2022). Notably, item-level similarity showed graded subsequent memory effects only in younger adults, a finding that suggests older adults do not form memory traces with sufficient distinctiveness to support successful memory retrieval.

In their paper examining autobiographical memories, Martins-Klein et al. (2022) introduce a novel theory linking one's retrieval of self-defining autobiographical memories with the greater tendency for older adults to engage in cognitive reappraisals of to new stressors. The authors propose that dedifferentiation of hippocampal dependent autobiographical memories in older adults promotes generalization across memory episodes. This hypothesis challenges the common view that neural dedifferentiation exclusively comprises cognition in older adults, and suggests that there are situations in which dedifferentiation may benefit cognition. The increase in neural overlap of memories in the hippocampus promotes narrative building across unique, self-defining events through interactions with the ventromedial prefrontal cortex, a region that has been implicated in both the integration of unique episodes and emotion regulation. The authors argue that multivariate analysis techniques, such as multivariate classification, pattern similarity, and informational connectivity analysis (Coutanche & Thompson-Schill, 2013), are uniquely suited to test central assumptions and new predictions from their theoretical model.

Taken together, the papers in this special issue present several advances in our understanding of the underlying mechanisms accounting for cognitive changes that accompany aging. This includes the identification of neural correlates of cognitive variability and emotion processing in young and older adults and age differences in brain–behavior relationships related to neural representations contributing to working, episodic, and autobiographical memories. These papers also highlight the breadth of applications for which multivariate analyses can be used to inform cognitive aging research. The multivariate techniques included in this special issue hold promise for providing a deeper understanding of the neural basis of cognitive aging. This and future work stemming from the foregoing papers will play a critical role in advancing theories of cognitive aging and, potentially, in the development of interventions aimed at slowing cognitive decline and the onset of dementia.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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