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Overview

The behavioral neurosciences and related disciplines have seen spectacular scientific advances that make them rich in scientific opportunity. These advances have made it possible to work toward a mechanistic understanding of behavioral aging and psychopathology, two empirically overlapping fields of great importance to science and society. In both fields, it is of key importance to take a personalized lifespan approach by identifying neural and behavioral parameters that predict more or less favorable trajectories, with the intent to intervene in time when undesirable outcomes are expected.

With these goals in mind, the Max Planck Society (MPS) and University College London (UCL) have established the Max Planck UCL Centre for Computational Psychiatry and Ageing Research. The Centre’s opening ceremony took place in London at the Royal Society on 1 April 2014. MPS and UCL have provided funding for the Centre for an initial period of 5 years. The Centre has two sites, one in London (Russell Square) and the other in Berlin-Dahlem (MPI for Human Development). The Centre’s foundation was preceded by a 3-year preparatory phase, which also included the organization of the First Symposium and Advanced Course on Computational Psychiatry and Ageing Research in 2012 at Ringberg Castle, Bavaria. During the reporting period, the Centre organized two further such symposia in 2014 and 2016, again at Ringberg Castle. In 2016, MPS and UCL jointly launched the International Max Planck Research School on Computational Methods in Psychiatry and Ageing Research (COMP2PSYCH) to extend the Centre’s reach into graduate education (see p. 293 for details).

Below, we summarize the activities of the Centre’s Lifespan Neural Dynamics Group, which is located in Berlin. In addition, the Formal Methods project of the Center for Lifespan Psychology (see pp. 172–174) is affiliated with the Centre. A full overview of the Centre’s activities, including those primarily based in London, can be found on the Centre’s website.

The Lifespan Neural Dynamics Group

Various subdisciplines within neuroscience have long shown that the brain is inherently dynamic and variable across moments at every level of the nervous system. The Lifespan Neural Dynamics Group (LNDG) led by Douglas Garrett pursues the general hypothesis that variability may be highly functional for neural systems, indexing important benefits such as greater dynamic range and systemic flexibility and adaptability (see Garrett et al., 2013). Viewed from this perspective, and in contrast to earlier notions of “neural noise,” normal cognitive aging can be reframed as a generalized process of increasing system rigidity and loss of dynamic range that manifests in reduced brain signal variability. The group tests this conceptualization by examining electroencephalographic (EEG) and functional magnetic resonance imaging (fMRI) brain signal variability and dynamics in relation to lifespan development, cognition, neurochemistry, network dynamics, and brain structure. A brief selection of our current findings and approaches can be found below.

The LNDG continues to build on its work showing that older, poorer performing adults often exhibit less moment-to-moment variability in brain signals under a host of different task conditions (see Garrett et al., 2013). First, the group has taken an explicit interest in how the level of cognitive demand influences the degree of signal variability expressed within an individual. Using multivariate and mixed modeling of fMRI-based parametric face processing data in younger adults, the group showed that the within-person signal variability level responds to incremental adjustments in task difficulty (i.e., increasing noise; see Figure 1) and that difficulty-related reductions in signal variability predicts reduced accuracy and longer reaction times within persons (Garrett, McIntosh, & Grady, 2014). Conversely, follow-up work suggests that older adult levels of signal variability do not

Key References


respond well to differing levels of cognitive demand, indicating muted response dynamics to visual input.

LNDG research has recently expanded to better establish the neurochemical (dopaminergic, DA) basis of age- and performance-graded differences in signal dynamics (Garrett et al., 2015). Given that normal aging is associated with DA decline and poorer cognitive performance, and that poorer cognitive performance characterizes generalized aging-related reductions in brain signal variability, it was predicted that pharmacological agents that boost systemic DA such as amphetamine (AMPH) would restore deficient signal variability levels in older adults during a parametric working-memory task. As hypothesized, older adults expressed lower signal variability on placebo, but matched or exceeded young adult variability levels in the presence of AMPH (see Figure 2). Notably, select older adults also improved in cognitive performance when signal variability was boosted on AMPH. These findings support the hypothesis that age differences in brain signal variability reflect aging-induced changes in DA neuromodulation. LNDG has expanded this work within studies linking DA binding, assessed by positron emission tomography (PET), to (1) blood oxygen level-dependent (BOLD) signal variability in younger and older adults (Guitart-Masip et al., 2016), and continues to link DA PET more broadly to (2) cognition and fMRI (networks, mean signals, moment-to-moment brain dynamics) in the Cognition, Brain, and Aging (COBRA) study of 180 older adults (e.g., Nyberg et al., 2016).

The group has also investigated the notion that age-related changes in brain signal dynamics may not be confined to the variance of BOLD signals. In particular, the entropy (i.e., stochasticity) of a biological system is a purported proxy for a biological system’s ability to adapt and function in an ever-changing environment. In collaboration with the ConMem and Formal Methods projects in the Center for Lifespan Psychology (pp. 148–152 and pp. 172–174, respectively), the group’s latest EEG research has examined age-related brain signal entropy at multiple time scales when participants are at rest. Following in-house development of a novel within-person measure of entropy that compares each subject to randomly shuffled versions of their own brain data, younger adults (n = 40) were found to exhibit higher entropy at nearly all time scales and electrodes than older adults (n = 40). Younger adult brains simply appear more “information-rich” across moments.

Figure 1. (a) Nonlinear, within-person parametric modulation of blood oxygen level-dependent signal variability (SDBOLD) with increasing task difficulty. Upon an initial level of task demand (D20–D30), SDBOLD increased and then continually decreased as participants approached their own limits of face processing (D70). This effect was expressed in (b) yellow/red brain regions. Fix = fixation condition; D0–D70 = increasing difficulty on a face processing task; BSR = bootstrap ratio indicating threshold level for brain regions (adapted from Garrett, McIntosh, & Grady, 2014).

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Other published work on entropy within LNDG (Grandy, Garrett, Schmiedek, & Werkle-Bergner, 2016) has focused on resolving important methodological constraints in the application of multiscale entropy (MSE) to some classes of neural signals, such as the apparent need for long-time series. Using simulated, EEG, and fMRI data, the group found that MSE estimation across discontinuous temporal segments (typical of modern cognitive neuroscience designs) was as precise as if the data were continuously acquired. These findings thus permit a wider range of MSE applications when gauging moment-to-moment dynamics in sparse or discontinuous neurophysiological data.

In further ongoing work, Niels A. Kloosterman completed a simultaneous eyetracking–fMRI project focusing on the role of neural variability in how younger and older individuals explore and recall pictures of everyday scenes, serving as a first examination of real-time coupling between behavioral and neural variability. Iris Wiegand recently embarked on an EEG project examining whether changes in “states” of brain signal entropy can be attentionally cued, both within younger and older adults.

Neuroenergetics theory posits that sustained deviations from cerebral metabolic homeostasis put constraints on neural structure and function, which may be related to important aspects of behavior. In close collaboration with Nils C. Bodammer, the group is using a novel in-vivo imaging method for phosphocreatine, a proxy for such regional homeostasis (Dissertation Julian Q. Kosciessa; see also pp. 170–171). The major goal of the dissertation is to explore potential links between local energy mismatch of supply and demand in the brain under task conditions and the ensuing consequences for neural dynamics and behavioral performance.

Finally, LNDG research has culminated in a successful five-year Emmy Noether grant (2016–2021; to Douglas G. Garrett) from the German Research Foundation (DFG). It allows the group to investigate individual differences and longitudinal change in three key factors (i.e., brain structure, static/dynamic functional connectivity, and dopamine) that may drive age-related brain signal variability.

![Figure 2. Amphetamine (AMPH) boosts SDo2BOLD in older adults in key white-matter regions (e.g., bilateral dorsolateral prefrontal cortex, left putamen/caudate) during an n-back working-memory paradigm. BSR = bootstrap ratio indicating threshold level for brain regions (adapted from Garrett et al., 2015).](image-url)


