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# Development holds the key to understanding the interplay of nature versus nurture in shaping the individual



This special issue is dedicated to the late Annette Karmiloff-Smith, a passionate and far-sighted thinker and scientist whose ground-breaking work helped give the nascent field of developmental cognitive neuroscience onto solid, theoretical grounding. Annette's life and work has had true impact, and touched and inspired many. Annette was a pioneer, an inspiration and a wonderful role model, and she will be sorely missed.

One of the key questions in developmental cognitive neuroscience is how nature and nurture interact to shape the individual. In particular, studying how and when the quality of the environment influences the maturing brain at specific points in development, to produce the types of social, cognitive and affective functions and behaviours that can be observed, is one of the most important challenges in developmental neuroscience. Sensitive periods refer to a time window in development during which the brain is especially susceptible to certain environmental stimuli, responding to the input in an experience-expectant manner (Johnson et al., 2015). Annette Karmiloff-Smith was one of the first researchers to point out the considerable potential contribution of developmental research for mapping behaviour and brain functions in health and disease (Karmiloff-Smith, 1998)

Yet studying sensitive periods presents a plethora of theoretical and methodological challenges, ranging from developing comprehensive descriptions of environmental experience to limits in experimentally controlled designs. Technological advances in brain imaging research over the past three decades have brought us closer to understanding how the brain controls behaviour and how this unfolds over development. Development is being increasingly conceptualised as a life-long process, best investigated in longitudinal, behavioural and cognitive training interventions or environment enrichment paradigms (e.g. (Fuhrmann et al., 2016; Mills and Tamnes, 2014; Nithianantharajah and Hannan, 2006; Tamnes et al., 2013)).

This special issue reports some of the most recent experimental approaches to studying sensitive periods using a range of methodologies (including fMRI, fNIRS, animal models, latent class models), psychological domains (including attachment, executive functions, language learning) and theoretical frameworks (including interactive specialisation, dual-systems models of adolescent development).

### 1. Understanding the dynamics of development

Annette's research approach was beautifully encapsulated in her article from 1975: "If you want to get ahead, get a theory!" (Karmiloff-Smith and Inhelder, 1975). And indeed, in many publications that followed this ground-breaking work (e.g., (Johnson et al., 2002; Karmiloff-Smith, 1998; Karmiloff-Smith et al., 2003)), Annette carefully laid out how understanding the dynamics of development could hold the key for understanding trajectories of typical and atypical development. Subsequent theories have further extended this view. For example, theories of interactive specialisation (Johnson, 2011; Johnson et al., 2009) propose that, through an interplay of genetic processes and environmental factors, specific regions of the developing brain assume increasingly specific cognitive functions. This suggests that, early in life, brain activity acts as a neural signature to a wider range of cognitive functions.

Johnson's opinion paper in this issue proposes that autism should be viewed, not as a disorder of neurodevelopment, but rather as an adaptive common variant pathway of human functional brain development (Johnson, 2017). Such a research approach moves away from focusing on recovery of function following focal perinatal lesions by encouraging scientists to investigate the processes of brain adaptation resulting from mild but widespread disturbances to neural processing over the early years (such as alterations in synaptic efficiency). Specifically, Johnson suggests that, rather than being viewed as a direct, behavioural consequence of life-long neural dysfunction, autism is better viewed as the end result of engaging adaptive processes during a sensitive period.

Thinking about sensitive periods in development, Byrne and colleagues (Byrne et al., 2017), draw our attention to adrenarche, the relatively understudied developmental period at the beginning of puberty. Based on a systematic review, they show that earlier timing of adrenarche is associated with greater mental health symptoms, and there is emerging evidence that brain development plays a role in this relationship. Jordan and Anderson's review comes to a similar conclusion (Jordan and Anderson, 2017), based on evidence showing that early substance abuse in adolescence increases the risk for developing substance abuse disorders later in life. Following this, Reynell and Harris (Harris and Reynell, 2017) highlight how the use of medication during adolescence, and particularly the use of antidepressants, may produce neurobiological changes, some of which may outlast the course of treatment. In particular, this paper explores the ways in which neurovascular coupling and brain energy use may be altered by

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antidepressant medication given during adolescence. This discussion is not only important to cognitive neuroscientists studying depression, but also more generally to any neuroscientist using fMRI to compare neural activity between medicated and non-medicated groups of people.

# 2. New methodological approaches

Further methodological insights for interpreting functional magnetic resonance imaging results in paediatric populations come from a study by Engelhardt and colleagues (Engelhardt et al., 2017). This group examined the factors affecting scanner motion in a population-based twin sample of 73 participants (ages 7–12 years) and a case-control sample of 32 non-struggling readers and 78 struggling readers (ages 8–11 years), of whom 30 were scanned multiple times. They found that age, but not ADHD symptoms, was significantly related to scanner movement, suggesting that movement acts as a relatively stable, heritable phenotype that serves as a marker for other genetically influenced phenotypes.

Bunge and colleagues (Eckstein et al., 2017) flag up the unique suitability of using eye-tracking measures, particularly pupil dilation and spontaneous blink rate, to study cognitive development and plasticity. Looking at cognitive development more generally, Lloyd-Fox and colleagues (Lloyd-Fox et al., 2017) conducted an fNIRS to map cognitive function in both resource-poor and resource-rich environments. Cortical mapping of cognitive function during infancy is poorly understood in resource-poor settings due to the lack of transportable and low-cost neuroimaging methods. Having established a signature cortical response to social versus non-social visual and auditory stimuli in infants from 4 to 6 months of age in the UK, they then went on to apply this fNIRS paradigm to investigate social responses in infants from the first postnatal days to the second year of life in two contrasting environments: rural Gambian and urban UK. Results reveal localized socially-selective brain responses from 9 - 24 months of life to both the visual and auditory stimuli. These findings demonstrate a robust developmental curve of cortical specialization over the first two years of life.

#### 3. Affective development and mental health

In the psychiatric literature, adolescence has long been viewed as a period of vulnerability: age-of-onset data suggest that first symptoms of many psychiatric disorders, including (social) anxiety, depression, bipolar disorder and psychosis emerge during adolescence juncture and young adulthood (Kessler et al., 2007; Lee et al., 2014; Wittchen et al., 2011). Dual-systems theories (Somerville et al., 2010) (and their more recent extensions of triadic- and imbalance models (Crone and Dahl, 2012; Nelson et al., 2005)) propose that developmental discrepancies between brain regions coding for motivation and affect on the one hand, and self-regulation on the other, are marked during adolescence. The 'mismatch' in the maturation of these two systems is proposed to render adolescence a period of heightened vulnerability for developing mental health disorders. It has been suggested that the timing of adolescence-associated transformational processes may serve to bring out and compound risk for mental health disorders in this developmental period (Haller et al., 2013; Haller et al., 2015; Keshavan et al., 2014; Paus et al., 2008).

In this issue, a number of papers have looked at affective behaviour during development. Flannery et al., depart from the classic approach of studying affective development using static emotional adult faces by introducing a paradigm asking 10–23 year old female participants to view and label dynamic emotional expressions of peers (Flannery et al., 2017). Whereas core circuitry of emotion regulation is activated using this paradigm, the developmental trends particularly in lateral prefrontal cortex were non-linear. This is in contrast to the dominant view of linear increases in prefrontal cortical activation throughout development (Mills et al., 2016; Mills and Tamnes, 2014). Silvers et al. (Silvers et al., 2017) incorporate new methodologies in studying the development of affective reactivity and regulation, by showing faces displaying neutral as well as negative affect to participants aged 6 to 23 years. Whereas over the entire sample response of the amygdala was greater for negative compared to neutral stimuli, children were more sensitive to both compared to older age groups. The transition from childhood to adolescence was marked by a shift in activity to negative stimuli from ventral to dorsal medial prefrontal cortical regions.

To investigate earlier brain development, Li et al. used fNIRS in 3–5-year-old children to study the link between activity of dorsolateral prefrontal cortex and executive functions, such as attentional control and also emotional behaviour such as irritability (Li et al., 2017). They showed that activity in the left dorsolateral prefrontal cortex relates to individual differences in attentional control as well as in irritability. This common neural link between the two at a relatively early developmental time point suggests a point of intervention to treat developmental irritability.

# 4. Attachment

The study of the attachment system has provided some of the strongest evidence for sensitive periods. After all, the phenomenon of imprinting first reported by Konrad Lorenz, captures the power of the attachment system in shaping the development of the visual system in young chicks.

In this Issue, Opendak et al., review the rodent literature on attachment and early-life trauma, both in the presence of and caused by the primary caregiver (Opendak et al., 2017). Opendak et al. provide a compelling synthesis of evidence suggesting that trauma and attachment interact during a sensitive period early in life, highlighting the role of caregivers' presence in enhancing attachment and attenuating threat-related brain circuitry. Flannery et al., report effects of early caregiving adversity on the hypo-thalamic-pituitary (HPA)-axis and cortisol responses and how these play out differentially across development (Flannery et al., 2017). Focussing on the classic finding of blunted cortisol response in children following previous institutionalization, the authors investigated whether this pattern is also found in adolescents. Indeed, adolescents do not show such a blunted cortisol response, suggesting that the transition from childhood to adolescence marks a sensitive period for diurnal cortisol patterning. This might offer opportunities for timing interventions. As shown by Opendak et al., animal models have been vital in laying the foundation to and expanding our knowledge of the underlying mechanisms of sensitive periods at various points in development. Goepfricha et al. illustrate this beautifully by studying the endocannabinoid system and its modulatory role in the development of cognitive processing from childhood to adolescence in male rats (Goepfricha et al., 2017). The authors show that, through the specific modulation of cannabinoid receptor function (CB1), performance on recognition memory was affected only in adolescent rats but not at other ages tested. These findings highlight the role of the endocannabinoid system and shaping cognitive differentially across development.

# 5. Language

The field of early language comprehension has long been an arena of understanding sensitive periods of sensory development, with much research highlighting not only the importance but also the timing of early exposure and experience (Kuhl et al., 2003; Kuhl et al., 1992)). In this issue, Issard and Gervain look at compressed speech in newborns using functional near infrared spectroscopy techniques (fNIRS) (Issard and Gervain,

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