WORKING Group 03

CHAPTER



Brain development and maturation in the cont<u>ext of learning</u>_____

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WORKING

CHAPTER

2.1



Why neuroscience is relevant to education

The brain is crucial for learning. Neuroscience, in addition to psychology, can inform education because understanding underlying neural mechanisms can further improve our understanding of how learning works and how learning is constrained by brain function and structure (Thomas, Ansari and Knowland, 2019). In addition, the brain, like every biological organ, requires some specific conditions (e.g. nutrition, stress levels, exercise, sleep, air, social interactions and cultural environment) (Thomas, Ansari and

Knowland, 2019) to be healthy and thus it is relevant for learning to identify these conditions.

Educators are often informed of brain based learning techniques (Simons et al., 2016), but many of these techniques are only commercial programmes that have no actual scientific evidence (WG2ch7). Therefore, it is important that educators and policy-makers are aware of the basic principles of neuroscience and the potential of false promises.



2.2

Brain imaging enables non-invasive investigations of the human brain at rest or during cognitive tasks ... and has provided deep insights into human brain functioning.

Brain, development and learning

2.2 .1

BASICS IN NEUROSCIENCE

2.2 .1 .1

GENERAL PRINCIPLES OF BRAIN FUNCTION AND ORGANIZATION

Understanding of brain functioning has benefited from the development of several domains within neuroscience: cognitive brain imaging, computational neuroscience, integrative/ multiscale neuroscience and cultural neuroscience (WG2-ch7). Brain imaging enables noninvasive investigations of the human brain at rest or during cognitive tasks (see details on brain imaging techniques below) and has provided deep insights into human brain functioning (Toga, 2015). In particular, functional brain imaging has established two fundamental principles of neurophysiological organization: segregation and integration, namely the segregated or modular deployment of functional specialization within interconnected brain regions (Friston, 2009). Brain imaging has also contributed to the development of the concept of neural plasticity (see below), which refers to the anatomical and/or functional changes underlying cognitive and behavioural

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... there is no clear distinction between cognition and emotion: learning is heavily influenced by cognitive, emotional, motivational and social brain processes that are interdependent. changes throughout life or in response to an intervention, for example, learning or training (Rosen and Savoy, 2012; WG1-ch3; WG3-ch3, WG3-ch5, WG3-ch6), Computational neuroscience, which uses mathematical tools and theories to study the brain, has leveraged behavioural and physiological evidence that neurons (the nerve cells in the brain) represent knowledge in the form of probability distributions and acquire new knowledge by following the rules of probabilistic inference (Pouget et al., 2013). Such probabilistic predictions shape how we perceive and comprehend the world (Teufel and Fletcher, 2020): the brain continually generates models of the world to predict the most plausible explanation for what is happening in each moment. The recent development of multiscale neuroscience. integrating the different levels of description, from neurons to behaviour, aims at putting the different pieces of the puzzle together to provide a global picture of brain functioning (van den Heuvel, Scholtens and Kahn, 2019).

Hence, at all levels of organization, connectivity is a central element of nervous system architecture and function: neurons with dendritic and axonal connections form the microscale fabric of brain circuitry,¹ and macroscale brain regions and white matter fibre tracts (bundles of long axons) form the infrastructure for systemlevel communication among brain regions and information integration (**Betzel and Bassett, 2017**).

Different functions are associated with different brain regions, but researchers are increasingly realizing that most complex functions such as learning or memory rely on networks of interconnected – rather than individual – brain regions. In particular, the large amount of information coming from the environment (e.g. listening to someone talking to us) is integrated through multimodal associative regions that are connected to different unimodal networks. Additionally, many cognitive functions are intertwined and rely on similar underlying

¹Dendrites are projections from neurons that receive information and axons are projections from neurons that send information.

...the brain can be regarded as a statistical organ that employs hierarchical (i.e. deep) generative models to accumulate sensory evidence. circuitry (WG1-ch3, WG2-ch7; WG3ch4, ch6). What is also becoming increasingly clear is that there is no clear distinction between cognition and emotion: learning is heavily influenced by cognitive, emotional, motivational and social brain processes that are interdependent (WG3-ch4, WG3-ch5).

Finally, cultural neuroscience studies have reported that culture (e.g. value and belief systems and practices shared by groups) underwrite the functional brain architectures that enable inference and learning (Han and Northoff, 2008; Han, 2013; Chiao et al., 2015; WG2ch7, WG3-ch3, ch5). Throughout the life course, culture affects brain maturation (Li, 2003; Goh et al., 2007; Chiao, 2018). Observed cultural influences on brain activity during development reflect the effect of culture on structural and functional brain changes during development. Culture also modulates the effect of the environment on brain and behavioural changes related to learning. For instance, culture modulates social and emotional processing (Harada et al., 2020).

In summary, the brain can be regarded as a statistical organ that employs hierarchical (i.e. deep) generative models to accumulate sensory evidence. This accumulation or assimilation has separable timescales: (1) inference, mediated by neuronal dynamics and synaptic activity to infer states of the world in the moment; (2) attention, mediated by neuromodulation of synaptic efficacy – to select salient sensory signals for inference; (3) statistical learning, mediated by experiencedependent synaptic plasticity - to encode contingencies and statistical regularities generating sensory signals; (4) structure learning (optimizing the structure of generative models), mediated by neurodevelopment and synapse selection (pruning) - to optimize the structure of the brain's generative model; and (5) encultured learning, mediated by culture and evolutionary psychology - to ensure environmental contingencies are learnable (Friston, 2010).



2.2 .2

BASICS OF BRAIN BIOLOGY

The brain consists of different types of cells that communicate with each other. Neurons consist of a cell body, an axon and one or more dendrites. Axons are used to transmit information to other cells using an electrical signal called an action potential. The axon subdivides into different branches which connect to other cells at synapses. The electric action potential may trigger the synaptic release of different 'neurotransmitters' (chemical substances such as serotonin or dopamine) or be directly transmitted from neuron to neuron electrically through gap junctions. Thus, neurons communicate through both electrical and chemical signals. Neurons receive input from many other neurons, on average 7,000 synaptic connections per neuron.

Glial cells, such as astrocytes and oligodendrocytes, which regulate homeostasis in the brain, provide support and protect the nervous system, aid in recovery from brain damage such as a stroke, and modulate activity within synapses by regulating neurotransmitter, oxygen and ion uptake. For example, oligodendrocytes aid in faster transmission along axons by creating an insulating myelin sheath, consisting mostly of fat, and wrapping that around axons. This fatty layer makes the parts of the brain with many axonal connections look white, which is why those parts are referred to as white matter. Grey matter, on the other hand, contains mostly neuronal cell bodies and glial cells.

Grey matter makes up the folded outer layer of the brain, also called the cortex. The cortex is usually subdivided into different lobes: the frontal lobe, the parietal lobe, the temporal lobe and the occipital lobe. Deeper in the brain, under the cortex, lie subcortical brain structures such as the amygdala and hypothalamus. The hippocampus has a kind of

Cognitive activity is associated with several processes at the cellular level.

transitional architecture, not quite cortical or subcortical, that is referred to as the allocortex.

2.2 .

HOW BRAIN IMAGING METHODS INVESTIGATE THE NEURAL BASIS OF COGNITION

Cognitive activity is associated with several processes at the cellular level. Different techniques are available to measure brain activity, and each technique focuses on a specific cellular process. Briefly and very schematically, for any cognitive task, from perception to higherlevel functions, the brain generates electromagnetic waves that reflect the electrical activity of neurons. This electrical activity propagates along axons and modulates the release of neurotransmitters from the sending (or presynaptic) neuron, which then bind to their receptors on the receiving

(or postsynaptic) neuron. This chemical activity, which can be measured with positron emission tomography (PET), also produces an electromagnetic field. This electromagnetic field can be measured with electroencephalography (EEG) or magnetoencephalography (MEG). EEG and MEG have high temporal resolution (around 10 ms) but their spatial resolution is limited, especially for EEG, which is roughly 20 centimetres³. For cortical structures, MEG has comparable spatial resolution to magnetic resonance imaging (MRI) (i.e. around 1 millimetre), but MEG's spatial resolution for deeper structures is more limited. The activity of neurons requires energy and induces metabolic activity with a local increase in the intake and consumption of glucose and oxygen by neurons. This metabolic activity can be measured with PET. When neurons are more active, the cerebral blood flow to their region increases because neurons need more glucose and oxygen when they are more active; when they are less active, blood flow to them





decreases. This hemodynamic activity can be measured with functional magnetic resonance imaging (fMRI), functional nearinfrared spectroscopy (fNIRS) and PET. Of note, contrary to other 'non-invasive' imaging techniques, PET has limited use to study brain function in healthy participants, especially children, because it uses radioactive substances, or radiotracers, to measure changes in metabolic and hemodynamic processes. It also has less precise spatial resolution than fMRI (roughly 5–10 millimetres3). fNIRS is far cheaper and more portable than fMRI and has better temporal resolution (though not quite as good as EEG or MEG), but it has worse spatial resolution than fMRI (though better than EEG), much shallower penetration depth into the brain, and does fMRI has emerged as a key approach to studying the neural bases of learning, as it can detect activation in the whole brain during sensorimotor, perception and high-level cognitive processes ... not allow for the collection of structural images of brain anatomy (which MRI provides).

fMRI has emerged as a key approach to studying the neural bases of learning, as it can detect activation in the whole brain during sensorimotor, perception and high-level cognitive processes as long as there is not too much movement (Ogawa et al., **1992).** However, the relatively poor spatiotemporal resolution (typically millimeters and seconds) and the indirect nature of the imaging markers to reflect neural activity remain important limitations of fMRI and fNIRS which can be partly overcome by combining different methods (e.g. EEG or MEG). Functional connectivity between brain areas is usually estimated from functional data by calculating the relationship (e.g. correlation) between regional time series. Functional connectivity maps can be obtained either in the context of taskrelated brain activity or in 'resting' conditions through resting-state functional acquisition (Greicius et al., 2003).

For anatomical – as opposed to functional - connectivity the preferred method is diffusionweighted MR imaging (dMRI; Basser, Matiello and Le Bihan, 1994; Le Bihan, 2003), which can produce stunning tridimensional maps of the orientation in space of white matter tracts and brain connections, as well as provide information on white matter and grey matter microstructure and integrity. dMRI has revealed faulty brain connections linked to diverse conditions, including dyslexia, dyscalculia and anxiety disorders (Siugzdaite et al., 2020).

Another relatively recent imaging technique is magnetic resonance spectroscopy (MRS), which is a non-invasive method for measuring biochemical changes in the brain. While MRI can detect the anatomical location of something in the brain (such as a tumor), MRS can detect the chemical composition of that tissue, for example, comparing the chemical composition of normal brain tissue with abnormal tumor tissue.





CHAPTER

2.3



How the brain develops with age

Human brain development is a complex and dynamic process that begins during the first weeks of gestation (embryonic period) and lasts until early adulthood. The availability of non-invasive threedimensional MRI methodologies has changed the paradigm and allows investigation of the living human brain structure. Because of its relative safety, MRI is well adapted for studying individuals at multiple time points and longitudinally following changes in brain structure and function that underlie the early stages of cognitive development. Before the advent of brain imaging tools, structural brain changes were inferred from post mortem data. However, there were major concerns about their generalizability due to the questionable good health of the studied individuals who had died very young.



MRI is well adapted for studying individuals at multiple time points and longitudinally following changes in brain structure and function that underlie the early stages of cognitive development. On the other hand, despite the advantages of in vivo MRI described above, MRI cannot measure structural changes at the cellular or molecular level, and the physiological interpretation of an MRI signal is not straightforward or univocal. In addition, MRI data acquired at the early stage of brain development (before birth) are very noisy due to acquisition constraints (e.g. movement artefacts, short acquisition duration) and difficult to analyse due to low spatial resolution and age-dependent tissue contrast and structure size. Comparing anatomical brain measures derived from MRI across ages after birth is more reliable. The spatial and temporal patterns of developmental changes observed in recent MRI studies reflect patterns that were observed postmortem fetal tissue, demonstrating the validity and compatibility of these methods (Dehaene-Lambertz and Spelke, 2015; Dubois and Dehaene-Lambertz, 2015; Dubois, Kostovicand Judaš, 2015; Dubois et al., 2014).

2.3 .1

FOETAL BRAIN DEVELOPMENT

Most of the cellular and molecular events underlying brain formation and development begin before birth. During prenatal development and after birth, neurons are 'born' (neurogenesis) and new synapses are made (synaptogenesis). Neuronal proliferation (increase in the number of neurons) and migration; cytoarchitectonic aggregation of specific neuronal populations are both completed before birth. On the other hand, the specification of morphological and molecular neuronal phenotypes (growth of dendrites, dendritic spines and axons, continues throughout life); as does establishment of neuronal circuitry and connectivity (growth of axon pathways and synapse creation, i.e. synaptogenesis); proliferation and differentiation of glial cell types;

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and myelination (Kostovic and Judaš, 2015). Almost all neurons in the human brain are born prenatally.

There are distinct developmental phases (Kostovic, Sedmak and Judaš, **2019).** By the end of the early foetal period (ten to sixteen gestational weeks,² GW), all embryonic brain divisions and cell proliferation are visible. During the mid-foetal period (seventeen to twenty-five GW), the subplate contains numerous synapses and represents a transitory substrate for axonal ingrowth and outgrowth. This is the basis of the early foetal circuitry, with the spontaneous generation of functional activity. The hippocampal formation develops while limbic pathways are partly already developed. The first long associative corticocortical pathways start to grow.

During the late foetal to early preterm period (twenty-six to thirty GW), while the intensity of neuronal proliferation decreases, migration continues. This period is characterized by ingrowth of axons, synaptogenesis and dendritic differentiation of neurons. Afferent connections from subcortical structures are relocated from the subplate into the cortical plate, leading to the onset of sensory-expectant cortical functioning that coexists with endogenous activity. Efferent pathways from the cortex (e.g. to the spinal cord, striatum, thalamus, pons) then show accelerated development, which promotes motor activity in particular. The growing long pathways are then particularly vulnerable to hypoxic-ischemic damage.

The late preterm period (thirty-one to thirty-six GW) is characterized by changes in brain architecture (neuron size, density, laminar thickness and spatial arrangement); dendritic differentiation and synaptogenesis in the cortical plate; intense growth of long associative corticocortical pathways; and proliferation of glial cells (astrocytes, oligodendrocytes). The functional status becomes elaborated and immature cortical

Paralleling changes at the microscopic level, early brain development is characterized by dramatic changes in cortex morphology due to the cortical folding process that begins at ten GW.

²Gestation weeks are equal to post conceptional weeks plus two weeks of amenorrhea.

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... subtle variations in the in utero environment, as indexed by birth weight, are accompanied by differences in post natal cognitive abilities.

responses are elicited by sensory inputs.

Paralleling changes at the microscopic level, early brain development is characterized by dramatic changes in cortex morphology due to the cortical folding process that begins at ten GW (Kostovic, Sedmak and Judaš, 2019). The beginnings of gyrification (the birth of gyri, the 'mountains' of the cortex) and the sulcation (the birth of sulci, the 'valleys' of the cortical relief) become manifest after twenty-four GW and greatly heighten during the last weeks before birth. The heritability of the cortical folding is estimated between 0.2 and 0.5 (Le Guen et al., 2018), meaning that early prenatal or perinatal environmental factors like alcohol exposure (De Guio et al., 2014), intrauterine growth restriction or twin pregnancy (Dubois et al., 2008) and birth weight (Kersbergen et al., **2016)** determine 50 per cent to 80 per cent of the cortical folding process.

LONG-TERM EFFECTS OF FETAL BRAIN DEVELOPMENT

2.3 .2

Several studies have reported that subtle variations in the in utero environment, as indexed by birth weight, are accompanied by differences in postnatal cognitive abilities (Raznahan et al., 2012; Walhovd et al., 2012; Shenkin, Starr and Deary, 2004; also see WG3-ch3 on individual differences in brain and learning)). It also seems that the event of birth and the gestational age at birth, even when the birth is not premature, have a major impact on later brain growth as seen in ten-year-old children (El Marroun et al., 2020). In addition to a global proxy measure of 'uterine optimality', analysis of sulcal morphology can provide information on the prenatal constraints imposed by the structure of some specific brain regions on later cognitive development and learning (Cachia et al., 2016). Several studies in



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Different environmental backgrounds, such as bilingualism (after birth) or twin pregnancy (before birth), can modulate the relationships between sulcal patterns and cognitive abilities. typically developing participants report a long-term relationship between cortical sulcation at birth and cognition several years and decades later in several cognitive domains critical for learning, such as cognitive control (Fornito et al., 2004; Borst et al., 2014; Cachia et al., 2014; Tissier et al., 2018) and reading (Borst et al., 2016; Cachia et al., 2018). Different environmental backgrounds, such as bilingualism (after birth) (Cachia et al., 2017; Del Maschio et al., 2018) or twin pregnancy (before birth) (Amiez, Wilson and Procyk, 2018), can modulate the relationships between sulcal patterns and cognitive abilities.

Learning and memory processes in relation to the in utero environment are already beginning to develop in foetuses, as highlighted by early observations of newborns. At birth they show preferences for specific tastes related to the mother's diet during pregnancy (e.g. anise) (Schaal et al., 2000) and for the mother's voice (DeCasper and Fifer, 1980). Their behavioural reactions and brain activity to speech-like auditory sounds differ depending on whether the sounds are familiar or not from when the fetus was in the womb, and greater prenatal speech exposure has been found to be related to enhanced brain activity, with generalization to other types of similar speech sounds (Partanen et al., 2013). Familiar odours and speech rhythms, learned pre- or postnatally, have calming effects during a painful procedure (Rattaz, Goubet and Bullinger, 2005) or during sleep (Lang, Del Giudice and Schabus, 2020). This suggests an important role of memory processes in the newborn's development during the pre- and perinatal period.

2.3 .3

INFANT BRAIN DEVELOPMENT

Birth represents a huge stress for the baby, which shows very high concentrations of stress-related hormones after normal vaginal delivery (Lagercrantz, 2016), but this seems important for its

As infants become more specialized in the language(s) in their environment, their ability to hear sounds unique to other languages gradually recedes. adaptation to the extra-uterine environment. At full-term birth, the proliferation and migration of neurons are complete, the limbic system is relatively mature and some major long projection, commissural and associative pathways have finished their growth, providing the basis for sensory-driven connectivity.

Newborns are able to recognize their mothers' faces (Pascalis et al., 1995; Sai, 2004) and voices (DeCasper and Fifer, 1980) and show an early preference for their native language (Moon, Cooper and Fifer, 1993; Nazzi, Bertoncini and Mehler, **1998).** Their ability to discriminate between phonemes (Kuhl, Tsao and Liu, 2003; Kuhl, 2004) or faces (Kelly et al., 2005) evolves during the first post natal year, in relation to their environment and social interactions, and this allows them to specialize progressively in the stimuli that are relevant to them. During this process, infants perform statistical learning computations that are affected by experiences (Saffran and Kirkham, 2018). During at least the first

six months of life, before this specialization has occurred, infants can discriminate the sounds in all languages (Eimas et al., 1971; Streeter, 1976). As infants become more specialized in the language(s) in their environment, their ability to hear sounds unique to other languages gradually recedes.

Human brain development, compared to that of other species, has one of the slowest rates of development and takes many years to reach maturity (Thompson and Nelson, 2011). The newborn period is characterized by dendritic differentiation, an explosive phase of synaptogenesis, cell death and axon selection (pruning), intense growth of short corticocortical fibres, proliferation of astrocytes and oligodendrocytes, myelination, and the development of tertiary sulci that make the newborn brain resemble the adult brain (Kostovic, Sedmak and Judaš, **2019**). This allows the newborn to enter a new phase of emotional and social interactions with complex multimodal sensory stimulation.

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... during brain development, both generative and degenerative processes take place. During the first post natal year, brain volume increases massively. During early infancy (one to three months of age), synaptogenesis and dendritic differentiation increase rapidly, while other processes develop more smoothly (Kostovic, Sedmak and Judaš, 2019). The growth of axonal pathways slows down, except for intracortical axons that grow until up to six months of age. Mid-infancy (nine to twelve months of age) is characterized by synaptogenesis in both primary and associative cortical regions, relative maturity of pyramidal neurons, disappearance of the subplate remnant, gradual delineation of cortical areas and the beginning of myelination of the cortical pathways (Kostovic, Sedmak and Judaš. 2019). This underlies the development of cognitive functions in interaction with the social environment and the first appearance of advanced cognitive abilities associated with the prefrontal cortex (PFC) (Diamond, 1990, 1991; Fiske and Holmboe, 2019; Fiske et al., 2021).

During the second post natal year, although the number of synapses has reached a temporary plateau, associative areas still show immature cytoarchitecture. Cortical connectivity pathways tend towards adult patterns despite still incomplete myelination, and high-level cognitive, executive, social and emotional functions are still immature.

In summary, during brain development, both generative and degenerative processes take place. During prenatal development and after birth, neurons are 'born' (neurogenesis) and new synapses are made (synaptogenesis). Perhaps surprisingly, degenerative processes such as apoptosis (cell death) and synaptic pruning (elimination of unused or extra synapses) are also crucial for child development. This process is thought to aid in making information processing more efficient by eliminating unnecessary connections and improving the ratio of signal to noise.



Compared to other structures in the brain, the frontal cortex in particular develops more slowly, and keeps developing until around age twentythree.

2.3.4

CHILDHOOD BRAIN DEVELOPMENT

It is important to note that although some influential classic psychological theories often describe child development in terms of accumulative (distinct stages) and linear development, brain research is more supportive of continuous non linear development (see also WG1-ch4, WG3-ch4 for childhood development).

As children develop, white matter connections between brain regions show a steady increase with age (Giedd, 2004). For grey matter, the pattern is a bit different. After birth there are initial increases in grey matter, after which pruning takes place. Importantly, this process does not occur at the same speed in each brain region. Compared to other structures in the brain, the frontal cortex in particular develops more slowly, and keeps developing until around age twenty-three (Giedd, 2004). The most anterior portion of the frontal cortex, the PFC, is linked to processes such as working memory, inhibition and cognitive flexibility (components of what are called 'executive functions' (EF) (Diamond, 2013) that are crucial for the learning process. Every teacher will know that young children find it much more difficult than older children and adults to stay focused on schoolwork and ignore irrelevant stimuli in the classroom. This can in part be explained by the late developing PFC.

Myelination of axonal fibres producing white matter tracts also plays a critical role from late pregnancy to early adulthood in the development of sensory, motor and associative networks, with high variations across regions regarding the age of onset and period length of myelination.

2.3 .5

ADOLESCENT BRAIN DEVELOPMENT



Sensitivities in adolescent brain development can help explain why adolescence seems such a critical turning point, which is highly relevant to education. Although previously most attention on brain development was directed towards the early childhood years, adolescence is now also increasingly recognized as a sensitive period for brain development (Casey, 2015; WG1ch3, WG3-ch4). Adolescence is a key period in life during which development can spiral into positive or negative trajectories (Crone and Dahl, 2012). Sensitivities in adolescent brain development can help explain why adolescence seems such a critical turning point, which is highly relevant to education. As mentioned earlier, brain regions involved in cognitive control, especially the PFC, are late-maturing regions with massive synaptic pruning at puberty (Huttenlocher, 1979). While the PFC is still not completely developed, other brain regions appear to be relatively hyperactive. The brain's 'reward centre', specifically the ventral striatum and nucleus accumbens, shows more activity in mid to late adolescence than in younger children and adults (Silverman, Jedd, and Luciana,

2015). This has led researchers to hypothesize 'imbalance models' of brain development with a hyperactive reward system and an underdeveloped PFC, which is thought to result in an imbalance between cognitive and socioemotional processes (Ernst, Pine and Hardin, 2006; Steinberg 2008; Somerville and Casey, 2010). This theory has been used to explain negative adolescent behaviours such as risk-taking, and use of alcohol and other toxins. This view has now shifted to emphasize more positive aspects: adolescents have the capacity for complex cognitive functions, especially when strong socio-affective stimuli are not interfering (Crone and Dahl, 2012; Casey, 2015; WG3-ch4). Increased striatum activity in adolescence has also been linked to positive behaviours, such as prosocial behaviour (Spaans, Peters and Crone, 2020), better learning from feedback (Davidow, 2016) and better learning in a risky context (McCormick and Telzer, 2017). This may provide interesting pathways to further investigate how to



2.4

Sex differences and similarities in the brain

The question of sex differences in brain structure and function, cognition and academic skills still raises debate in the current scientific literature.

Sex-related differences are apparent across multiple levels of analyses and start from the very early weeks of human prenatal life **(Thomason, 2020)**. For instance, sex differences are apparent in birthweight centile and in foetal and neonatal morbidity and mortality; there are also differential effects of the foetus' sex on the mother, differential susceptibility of male and female foetuses to pathological conditions in pregnancy and, moreover, male foetuses tend to be more vulnerable to detrimental effects from early adversity.



... sex differences in brain development likely evolve dynamically throughout life.

2.4 .1

SEX DIFFERENCES IN BRAIN STRUCTURE AND FUNCTIONING

Sex differences in neurodevelopment have been described for structure, organization and function (Paus, 2010; Giedd, 2012; McCarthy, 2016). The current literature suggests the existence of sex differences in the anatomical development of grey and white matter a (such as brain volume, grey matter density, cortical thickness, cortical surface area and gyrification) (Williams, 2021; WG3-ch6), as well as in anatomical and functional connectivity networks (in white matter tracts and in cerebral blood flow (Kaczkurkin, Raznahan and Satterthwaite, 2019). Although a well-cited seminal study reported that, compared to girls, delayed brain development in boys is likely due to delayed puberty (Lenroot, 2007), some later studies have failed to replicate these findings

(Aubert-Broche et al., 2013; Tamnes et al., 2013; Wierenga et al., 2019). These discrepancies may be related to the fact that sex differences in brain development likely evolve dynamically throughout life (Kaczkurkin, Raznahan and Satterthwaite, 2019). Statistical issues, like the method used to correct for inter-individual differences in body size (Williams, 2021), may also contribute to these discrepancies.

2.4 .2

SEX HORMONES AND THE BRAIN

The literature has also reported the effects of sex hormones on the brain in general (Marrocco and McEwen, 2016; Choleris et al., 2018), and on PFC-related cognition and neuroplasticity more specifically (Shansky, 2004; Hao et al., 2007; Evans, 2015). Sex hormones modulate many neural and cognitive functions due to their action at the whole-brain level (McEwen and Alves, 1999). Sex differences



emerge in many brain regions throughout the life course due to both genetic and epigenetic factors (i.e. environment-dependent gene expression) (McCarthy et al., 2009, McCarthy and Nugent, 2015). For instance, stress that interplays with learning (Vogel and Schwabe, 2016), induces sex-specific effects on brain plasticity (McEwen, Gray and Nasca, 2015), at cellular (Shors, Falduto and Leuner, 2004; Shansky, 2009; Bowers, Waddell and McCarthy, 2010; Goldstein, 2010; Yagi, 2019) and cognitive (Shansky, 2004, 2006) levels.

Because of the indirect and bidirectional relationship between cerebral activity and mental processes, there is a high risk of interpretation bias due to gender stereotypes when translating sex differences in the brain into psychological differences (Fine et al., 2013; WG3-ch6). For instance, purely looking at global volume, boys have on average larger brains than girls, but this is unrelated to cognitive performance (Wierenga et al., 2019).

2.4 .3

SEX DIFFERENCES IN COGNITION AND ACADEMIC SKILLS

The outcome of research on sex differences in cognitive abilities - such as language, spatial orientation and mathematics (Nazareth, 2019: Peragine et al., 2020) – and in emotional and rational processing is still under debate (Schmitz and Höppner, **2014**). Similarly, research on sex differences in academic skills has reported diverging results, despite a growing interest from researchers and policy-makers in recent decades (Guez, Peyre and Ramus, 2020). Meta-analyses on achievement test scores tend to show that girls perform better than boys in language tests (e.g. Hedges and Nowell, 1995; OECD, 2015), while boys perform better than girls in mathematics tests (e.g. OECD, 2015; Reilly, Neumann and Andrews, 2015). But analyses of school exams and marks often report an

... induces sex-specific effects on brain plasticity, at cellular and cognitive levels.



Data also show that each human brain consists of a mosaic of 'female', 'male' and 'mix' features.

advantage of girls in all subjects (Guez, Peyre and Ramus, 2020). The stability and magnitude of these sex differences in academic skills are also highly debated, with some researchers arguing that they have been stable over the decades, while others claim that they are disappearing (Stoet and Geary, **2020**). Understanding the level of stability of these differences would provide valuable insight into another fundamental question, that is, the degree to which sex differences in cognitive abilities are related to environmental and genetic factors.

For note, several neurological disorders associated with learning difficulties such as dyslexia, attention deficit hyperactivity disorder and autism spectrum disorder are diagnosed much more frequently in boys than in girls. Conversely, major depressive disorder, anxiety, panic disorder and anorexia nervosa are much more often diagnosed in adult women than in adult men (McCarthy et al., 2012; WG3-ch6).

2.4 .4

CONTESTED TOPICS

Recent literature has challenged the essentialist view of the human brain and its static sexual dimorphism implying highly dimorphic, internally consistent male and female nervous systems largely fixed by a sexually differentiated genetic blueprint (Rippon et al., 2014; Kaczkurkin, Raznahan and Satterthwaite, 2019

2.4 .4

INTER-INDIVIDUAL VARIABILITY

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Even if inter-group differences (i.e. between males and females) are found when looking at specific anatomical and functional cerebral measures/variables, intra-group differences are often extremely large and the high degree of overlap between distributions of males and females argues against any conclusion at individual level (e.g., Ritchie et al.'s (2018) MRI study on 5,000 adults).





2.4 .4

INTRA-INDIVIDUAL VARIABILITY

.2

Data also show that each human brain consists of a mosaic of 'female', 'male' and 'mix' features. Hence, there is no uniformly 'female' or 'male' brain, since the relative proportion of these characteristics varies substantially between individuals, and possibly changes throughout life (Joel et al., 2015).

2.4 .4 .3

INFLUENCE OF GENETIC AND ENVIRONMENT FACTORS

Since it is currently impossible in most anatomical, functional and behavioural studies to disentangle biological sex differences from those resulting from environmental and social influences throughout life (Kaczkurkin, Raznahan and Satterthwaite, 2019), the sole influence of genetic factors



...the structural and functional organization of the nervous system continuously and dynamically adapts throughout life to environmental conditions and experiences.

is difficult to assess. Studies investigating female/male differences in sex hormones and behaviour are often correlational, and analyses frequently consider hormonal levels as 'purely' biological and causally primary variables without considering the reciprocal influence between biological and environmental factors (**Rippon et al., 2014; WG3-ch6**)

2.4 .4 .4

BRAIN PLASTICITY

The current understanding of human development posits that the structural and functional organization of the nervous system continuously and dynamically adapts throughout life to environmental conditions and experiences, and that the modulation of endocrine function by those factors contributes to its plasticity. Recent data from endocrinology, evolutionary behavioural science and developmental biology raise serious doubts about the popular understanding of female/ male behaviour as rooted in a biological core. Current models of those disciplines do not support the assumption that there is a unidirectional causality link from genes to behaviour via hormones and brain, nor that our behaviours are rooted in some reminiscence of mental processes of our paleolithic ancestors (Fine et al., 2013; WG3-ch3, WG3-ch6).



2.5

Brain plasticity and learning

Neuronal cells and their synapses undergo structural (morphological) and metabolic (biochemical) changes throughout development, as the brain grows, learns and ages in constant, dynamic and adaptive interaction with the external world. Altogether, brain plasticity comprises experience-dependent changes in the size, number and shape of synapses, cells and circuits.

Brain plasticity is present throughout life (for learning, following brain insult, etc.), but these processes are much more important during development, when networks are not yet fully 'stabilized'. This contributes to why learning is so efficient during childhood (WG1-ch4).

2.5 .

BRAIN PLASTICITY AT THE CELLULAR LEVEL

Neurons are formed quite early in the embryo, so that by the end of the first trimester of pregnancy the brain has most of the neurons that will survive into adulthood. Embryonic neurons are small and have few dendrites. in comparison with adult neurons. During development, neurons that are frequently activated by other neurons grow and become progressively more branched, while neurons that are seldom activated loose synapses and eventually are eliminated through a process of programmed cell

2 C H A P T E R

The acquisition and consolidation of memories depend on the formation of new synapses as well as on the strengthening and weakening of previously existing synapses. death (apoptosis). This process selects the most adaptive neuronal pathways and curbs the excess of neurons formed in the embryo.

While most adult neurons are incapable of undergoing further cell division, neurogenesis persists until adolescence (Sorrells eta al., 2021) and perhaps adulthood (Gould et al., 1999, Gage, 2002) in the memoryrelated brain structure called the hippocampus. The acquisition and consolidation of memories depend on the formation of new synapses as well as on the strengthening and weakening of previously existing synapses.

At the functional level, the tagging of a synapse for subsequent remodelling (Frey and Morris, 1997; Morris et al., 2003) depends on neurophysiological phenomena called long-term potentiation (LTP) (Bliss and Lomo, 1973; Bliss and Collingridge, 1993) and longterm depression (LTD) (Fujii et al., 1991; Dudek and Bear, 1992), which account respectively for the strengthening or weakening of a postsynaptic electrical response. Depending on the frequency and intensity of the stimulation used for their induction, LTP and LTD may last for hours, days or even weeks (Barnes, 1979). The link between memory processing and the occurrence of LTP and LTD has been extensively demonstrated (Collingridge, 1985; Malinow et al., 1988; Izquierdo and Medina, 1995; Nicoll and Malenka, 1999, Kandel and Squire, 2000; Whitlock et al., 2006).

2.5 .2

BRAIN PLASTICITY AND MEMORY CONSOLIDATION

After being acquired, memories are stabilized through a series of specific processes termed memory consolidation. The first phase of memory consolidation, which comprises local changes at the synaptic level, coincides with LTP and lasts from several hours

to a few days. The second phase of memory consolidation, which comprises systemic changes at the level of multiple brain regions (e.g. hippocampus and neocortex), coincides with neurophysiological changes lasting from weeks to months to years.

While synaptic changes begin to occur during the waking experience that leads to learning, most of the changes required for memory consolidation take place during post-learning sleep. Slowwave sleep promotes the bulk of sleep-dependent synaptogenesis (Yang et al., 2014), and rapid-eyemovement (REM) sleep triggers most of the synaptic pruning as well as the strengthening of selected new synapses (Li et al., **2017**). During slow-wave sleep, the hippocampal-neocortical circuits activated during learning are reactivated; during REM sleep, consolidation of new learning into long-term memory occurs (Cartwright, 2004).

When consolidated memories are retrieved they must be reactivated

at the electrophysiological level. The different elements of 'a memory' are stored in different areas of the brain and these different elements have to be reassembled when retrieving this memory. This mechanism is part of the reason why the memory can be inaccurate (Lacy, 2013). As first shown by Karim Nader in the late 1990s, reactivated memories go from a latent hardto-change form to a labile, easyto-change form, which reopens the opportunity to strengthen, weaken or otherwise modify the memory contents, leading to the phenomenon known as memory reconsolidation. The biological scaffolding of this process corresponds nicely to one of its putative psychological corollaries, namely that the particular choice of study technique has major implications for learning.

Several students use boring, timeconsuming and inefficient ways of studying (Karpicke, Butler and Roediger, 2009). There is now plenty of evidence that students benefit more from active engagement with the material than passively

The different elements of 'a memory' are stored in different areas of the brain and these different elements have to be reassembled when retrieving this memory.



While repetition is positively correlated with short-term gains, variations in form and context are required to optimize long-term results, avoid habituation and promote integration of new and old knowledge.

receiving information (Roediger and Karpicke, 2006; Freeman et al., 2014; WG2-ch8). In addition, active retrieval of previously learned material can lead to better longterm retention than passive restudy of the material (Hogan and Kintsch, 1971; Whitten and Bjork, 1977). Retrieval practice comprises the resolution of problems, answering or formulating questions about the contents at stake, writing summaries about what was learned in one's own words, and holding peer-to-peer debates (Agarwal et al., 2014; Agarwal et al., 2017). The benefits tend to be proportional to the difficulty level, and they can be obtained even when the students choose incorrect answers, as long as there is clear feedback (Butler, Karpicke and Roediger, 2008). While repetition is positively correlated with short-term gains, variations in form and context are required to optimize long-term results, avoid habituation and promote integration of new and old knowledge (Rosenbaum, Carlson and Gilmore, 2001; WG2-ch5). Students

should have the opportunity to practise content retrieval at least once for every content learned, since the most learning benefits come from the first retrieval practice attempt (**Rowland et al.**, **2015**). When multiple retrieval practices are possible, they should be spaced rather than performed in a block (**Son**, **2004**; **Cepeda et al.**, **2008**).

The feeling of knowing is quite different from being able to remember specific information (Yonelinas. 2002). Rather than actively retrieving contents, students tend to prefer the passive exposure to contents by rereading, which leads to a sense of familiarity that is often just an illusion of competence. While we tend to prefer things that are more familiar (Montoya et al., 2017), 'remembering by recognition' is most often a failed strategy in the classroom. Retrieval practice is feasible in any school, does not involve much extra time and has a negligible cost (Roediger et al.,

³Three quite useful guides on retrieval practice are provided by Henry L. Roediger III (http:// psychnet.wustl.edu/memory/publications/), Jeffrey Karpicke (https://www.purdue.edu/hhs/psy/ directory/faculty/Karpicke_Jeffrey.html) and Pooja K. Agarwal (www.retrievalpractice.org).



2.6

'Brain health': how biological processes influence the brain and learning

2.6

SLEEP

Evidence accumulated over recent decades indicates that sleep is a key mediator of learning (Stickgold and Walker 2005; Diekelmann and Born, 2010), so it is quite worrisome for education that sleep is increasingly sacrificed for the sake of waking activities. The emergence of electro-electronic devices has been very deleterious for sleep (Broman et al., 1996;Lima, Medeiros and Araujo, 2002; Peixot et al., 2009; Moreno et al., 2015), leading to a decrease in the quality and quantity of



Poor sleep is a risk factor for health disorders such as malnutrition, obesity, diabetes and hypertension, and correlates with academic deficits across a wide range of intellectual quotients. sleep, which impacts negatively on approximately one third of the adult population in the United States (USA) (Schoenborn, Adams and Peregoy, 2013). Poor sleep is a risk factor for health disorders such as malnutrition (Beebe et al., 2013), obesity (Jarrin, McGrath and Drake, 2013), diabetes and hypertension (Spiegel et al., 1999), and correlates with academic deficits across a wide range of intellectual quotients (IQ) (Erath et al., 2015). Sleep is an important mediator of socio-economic and health gradients (Teixeira et al., 2004). For instance, the lack of consistent bedtime habits in USA preschoolers is associated with poverty and low maternal education (Hale et al., 2009).

The mechanisms underlying sleepdependent cognitive function involve brain oscillations and calcium-dependent molecular cascades associated with synaptic plasticity (Stickgold and Walker, 2005; Diekelmann and Born, 2010; Mander et al., 2011; Ribeiro, 2012). Sustained waking leads to sleep deprivation, which impacts directly on these cascades impairing learning (Vecsey et al., 2009). Insufficient sleep prevents new learning in the laboratory setting, that is, pre-training sleep is a necessary condition for the acquisition of new memories (Yoo et al., 2007). Post-learning sleep has been shown to improve the learning and memory of declarative and procedural contents in the laboratory (Plihal and Born, 1997; Stickgold and Walker, 2005; Ellenbogen et al., 2006). In recent years these experiments have been successfully extended to the school setting (Kurdziel, Duclos and Spencer, 2013; Lemos, Weissheimer and Ribeiro, 2014; Cabral et al., 2018; Cousins et al., 2019), and may even double reading fluency in first graders (Axelsson, Williams and Horst, 2016; Torres et al., 2020).

It is becoming increasingly clear that schools must offer children and adolescents the opportunity to sleep when needed, either to help the consolidation of newly acquired contents, or to compensate for prior sleep debt and restore the capacity to learn anew (**Ribeiro and Stickgold, 2014; Sigman et al., 2014; Axelsson, Williams**



and Horst, 2016). It is important to embrace naps in the school setting to unleash the full learning potential of students – and teachers as well.

2.6

EXERCISE IN THE SCHOOL SETTING

...schools must offer children and adolescents the opportunity to sleep when needed, either to help the consolidation of newly acquired contents, or to compensate for prior sleep debt and restore the capacity to learn anew. The proliferation of electronic devices in recent decades has contributed to unprecedented pressure on physical activity (Hankonen et al., 2017). Insufficient or ineffective physical activity reaches the entire range of socioeconomic classes, leading to increased body mass and severe health costs (Ng and Popkin, 2012; Fiuza-Luces et al., 2013). Despite recommendations and widespread health campaigns from the World Health Organization (WHO, 2011), and the Physical Activity Guidelines for Americans (U.S. Department of Health and Human Services 2018; Powell et al., 2019),

most children do not perform an adequate amount of physical activity to derive the full health benefits. In fact, fewer than 24 per cent of children ages six to seventeen years engage in the recommended sixty plus minutes of daily moderate-to-vigorous physical activity (National Physical Activity Plan Alliance, 2018). Among its many benefits, physical activity promotes improvement in several variables that impact brain and cognition, such as positive changes in brain structure and function and increases in brain derived neurotrophic factor (BDNF), a key protein involved in plastic changes in the brain related to learning and memory (US Department of Health and Human Services, 2018; Valkenborghs et al., 2019; Lubans et al., 2016). An adequate schedule of regular physical activity is necessary for the cognitive and brain health of children and adolescents (Vavnman and Gomez-Pinilla. 2006: Deslandes et al., 2009; Masley, Roetzheim and Gualtieri, 2009; Chaddock et al., 2011; Lubans et al., 2016; WG3-ch5). Exercise has an acute effect on cognition (Chang et al., 2012; Erickson et al.,





2019; Pontifex et al., 2019), including EF (Ludyga et al., 2016; Moreau, 2019; see also Drollette et al., 2014) and attention (Palmer, Miller and Robinson, 2013), which are important for enhancing learning and academic performance during the school day.

Several studies from neuroscience, psychology and educational science suggest that physical activity and aerobic fitness are beneficial for brain health and well-being (Lubans et al., 2016; Erickson et al., 2019;Valkenborghs et al., 2019). Converging evidence indicates that at every age, people who are more physically active and have better aerobic fitness have better EF; furthermore, children who exercise more and are more physically fit tend to do better in school (Hillman, Castelli and Buck, 2005; Voelcker-Rehage, Godde and Staudinger, 2010; Boucard et al., 2012; Scudder et al., 2014).

What is still debated are questions such as: how much physical activity is enough? Which type of exercise is best? When is the best time in the school day to engage in exercise to best support learning? A difficult problem in this type of research is that much of the literature to date is correlational. In recent years some randomized controlled trials (RCT, the gold standard in intervention research) have indicated that causal relationships link physical activity, EF and memory (Davis et al., 2011; Hillman et al., 2014; Mavilidi et al., 2020), while other studies failed to detect cognitive benefits related to physical activity (see Álvarez-Bueno et al., 2017 and Vazou et al., 2016 for reviews). Regardless, fitter and more active children often score better on cognitive and scholastic tests, and in many cases neuroimaging tools are used to demonstrate brain regions and networks that support better behavioural performance. Alternative explanations also exist; thus it is also possible that these children, for example, have better self-control, which benefits both their ability to engage in regular physical exercise and their schoolwork.

Another important question is how physical activity might benefit cognitive and academic

... it is crucial that

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association with sleep,

nutrition and training

physical activity and

schools provide

contexts.

performance. Animal studies provide evidence for aerobic exercise leading to a cascade of molecular and cellular alterations, including increased growth factor levels, neurogenesis, angiogenesis (growth of blood vessels) and synaptogenesis, which encourages the production of new neurons and blood vessels as well as dendritic complexity and spine density (Gomez-Pinilla and Hillman, 2013; Voss et al., 2013). In humans, benefits are observed in brain structure, including grey matter volume and white matter integrity; brain function including electrophysiological markers, cerebral blood volume and blood flow; and changes in neural network activation during cognitive task performance and while at rest (Voss et al., 2013).

Therefore, it is crucial that schools provide ample opportunity for physical activity and structured exercise, in association with sleep, nutrition and training contexts (Sigman et al., 2014; Ribeiro et al., 2017; Immordino-Yang, Darling-Hammond and Krone, 2019).



CHAPTER

2.7



Nutrition

The nutritional requirements of the human brain depend on the energy needs of several functional systems of the body. With 2 per cent of body mass, the brain consumes around 20 per cent of the body's energy. In particular, neural development is characterized by a complex pattern of nutritional requirements during the whole cycle of life. These requirements are complex and depend on the integration and interdependence of several organ systems involved in the digestion of food and absorption of nutrients into the blood, which are regulated by the brain in interaction with the gut and its microbiota and the modulation of the blood-brain barrier. Optimal brain development depends on a sufficient supply of different nutrients at specific times. While all nutrients are relevant to brain development, proteins, carbohydrates, polyunsaturated fats, iron, copper, zinc, iodine,

...since brain development is a lifelong process, adequate nutrition is critical from conception to late adulthood. folates, and vitamins A, B6 and B12 have important influences beginning in the early stages of development. Potentially, their presence or absence during critical or sensitive periods can affect neural development. In a few cases it has been possible to identify periods during which the absence affects the neural organization of some function, as in the case of iron (Lozoff, 2017). However, in many cases the existence of such periods and their possible effects are still being investigated. Although nutritional requirements are more critical during times of greater brain function organization, brain functions are not all organized at the same time: different neural networks are organized at different times during at least the first two decades of life. For example, by the second year of life glucose consumption in the brain – the main energy source for the brain - is equivalent to that of an adult. But this does not mean that the development of the brain is completed. Besides glucose there are other essential nutrients necessary for several important cellular functions, such as synapse

formation and elimination, that occur well beyond the first 1,000 days (**Goyal et al., 2014**). Meanwhile, in the adult brain, glucose consumption for these and other related functions is approximately 10 per cent of the total metabolized by the brain; during childhood this rate could peak at 30 per cent. Thus, since brain development is a lifelong process, adequate nutrition is critical from conception to late adulthood. WORKING GROUP 3

C H A P T E R



2.8

Early experience, stress and trauma

2.8

EARLY EXPERIENCE

From conception and throughout life, the nervous system is organized and modified based on the dynamic interaction between the individual and the world in which they live. The presence, lack or absence of material, sensory and social stimuli, and threats in developmental contexts, have been repeatedly associated with changes in different aspects of the structure and functioning of the nervous system during its development (Lambert et al., 2016; Farah, 2017; WG2-ch5, WG3-ch4, WG3-ch6). Such changes, which occur due to the

adaptive nature of the components and connections of the nervous system, have been documented at different levels of organization, from the molecular to the structure and function of different neural networks for different kinds of deprivations and threats (Sheridan and McLaughlin, 2014).

2.8 .2

STRESS

Various forms of deprivation and trauma lead to a stress response, which can take many forms and can influence learning in myriad ways. It prepares the body to respond quickly to perceived dangers, by raising heart rate and tensing muscles and preparing for 'fight or flight'. Exposure to moderate stress is important for learning how to handle stress, but severe and/or long-term (i.e. chronic) stress is associated with negative consequences. Severe or prolonged stress in early childhood can have an important impact on later development (for e.g. Anda et

al., 2006; Miller et al., 2009; Yam et al., 2015). Early stress can shape developing neural systems and changes how future stressful events are processed (WG2-ch5, ch7).

Stress can be very present at school for both students and teachers: exams, deadlines, dysregulated student behaviour and interpersonal conflicts are just a few examples of the many events that may result in high levels of stress. Hormones and neurotransmitters released during and after a stressful event are major modulators of human learning and memory processes, with critical implications for educational contexts (see WG2-ch5 for further discussion on neurobiological and neurohormonal responses to stress and their effect on cognition and emotion regulation; WG3-ch4). Stress markedly impairs memory retrieval, bearing, for instance, the risk of underachieving in exams (Vogel and Schwabe, 2016). Recent evidence further indicates that stress may hamper the updating of memories in the light of new information, impair EF and induce a shift

Hormones and neurotransmitters released during and after a stressful event are major modulators of human learning and memory processes, with critical implications for educational contexts.

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Working on social and emotional skills reduces stress by promoting students helping and supporting one another and increasing the sense of community in the classroom.

from a flexible, 'cognitive' form of learning towards rather rigid, 'habit'-like behaviour (Schwabe et al., 2010; Schwabe and Wolf, 2013; Zareyan et al., 2020).

Stress in school can be reduced by consistency, knowing what to expect, and clarity about what is and what is not allowed. Working on EF and self-regulation reduces the stress from having dysregulated students in a class. Working on social and emotional skills reduces stress by promoting students helping and supporting one another and increasing the sense of community in the classroom. Exercise and yoga reduce stress (Lane and Lovejoy, 2001; Williamson, Dewey and Steinberg, 2001; Gothe, Keswani and McAuley, 2016; WG1-ch3, **WG3-ch4**). The representation of stress is also important: students educated on the positive, adaptive benefits of stress arousal improve academic performance and evaluation anxiety in classroom exam situations is reduced Jamieson et al., 2018, 2021).

2.8.3

CHRONIC LIFE STRESS FROM CONDITIONS SUCH AS POVERTY

Exposure to stress and particularly exposure to chronic stress during gestation, infancy, childhood or adolescence has an impact on the brain, particularly on structures involved in cognition and mental health. Exposure to early stress is associated with alterations to the volume of the amygdala (Tottenham and Sheridan, 2010; Gee at al., 2013; VanTieghem and Tottenham, 2018), and a trophy of the hippocampus (Wei, Hao and Kaffman, 2014; Delpech et al., 2016; Dahmen et al., 2018) and the PFC (Cybele Raver, Blair and Willoughby, 2012; Hackman et al., 2015; Ursache et al., 2016; Haft and Hoeft, 2017). Stress alters dendritic growth and spine density as well as synaptic communication and circuits in brain regions that are maturing. These regions not only regulate the hypothalamicpituitary-adrenocortical response

to stress, but also control cognition, learning, EF abilities and emotional responses. Thus, short- and long-term effects of stress during development influence the course of brain development, the physiological response to stress and cause negative cognitive, emotional and behavioural responses both during development and throughout life. Early severe or prolonged stress programmes the brain so that the person stays in an anxious, hyper-vigilant state, always on the lookout for possible danger, easily and overly panicked potentially for the person's entire life (Glaser et al., 2006; Taylor et al., 2006; Van der Kolk, 2014; WG3-ch6).

Stressors associated with city life have a significant effect on brain development and EF abilities. Findings demonstrate the negative effects of poverty on brain development, particularly on the hippocampus (Wei, Hao and Kaffman, 2014; Delpech et al., 2016; Dahmen et al., 2018) and the PFC (Raver Blair and Willoughby, 2012; Hackman et al., 2015; Ursache et al., 2016; Haft and Hoeft, 2017), known to be sensitive to environmental stimuli. Children living in poverty are exposed to a greater number of stressful events like noise, family conflicts, food insecurity and housing instability, and are therefore more vulnerable.

We emphasize the importance of addressing the negative consequences of early stress and poverty in children. Important steps like early intervention should be taken at home, school or in other communities to improve responsive caregiving, achieve healthier brain development, and improve cognitive and emotional functions for success in school and in life (WG1-ch3, WG3-ch4).

2.8 .4

ACADEMIC STRESS

There are also school-specific types of stress that impact upon brain function and school performance. The issue of stress stemming from pressure to perform in an

... short- and longterm effects of stress during development influence the course of brain development, the physiological response to stress and cause negative cognitive, emotional and behavioural responses both during development and throughout life.

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... available evidence indicates that different indicators of poverty are associated with poorer performance in tasks that demand cognitive control and metacognitive processes, phonological processing, episodic memory and learning. academic context has been raised by UNICEF as one of the most pressing concerns cited by children in some countries (Liston, McEwen and Casey, 2009). Academic stress can be short term (e.g. exam stress), but this type of stress can also become chronic if experienced on a regular basis. Academic stress can have paradoxical effects on performance: in some cases, it can benefit performance, but it can also be detrimental (WG2-ch9).

2.8 .5

DEPRIVATION

Experiences of deprivation involve the absence of expected environmental stimulation for a developmental stage, as usually happens in contexts of poverty (Sheridan and McLaughlin, 2014). The neuroscientific evidence on poverty confirms that poverty measured in terms of family income, parental education and occupation, and community resources is associated with a diverse set of structural and functional changes in the nervous system (Noble et al., 2015; Farah, 2017). In particular, the aspects of the nervous system most commonly affected are related to executive functions, cognitive and emotional self-regulation, language, and learning (Noble et al., 2015; Farah, 2017; Stevens et al., 2020). At the behavioural level, the available evidence indicates that different indicators of poverty are associated with poorer performance in tasks that demand cognitive control and metacognitive processes (e.g. EF and theory of mind), phonological processing, episodic memory and learning. Without any type of intervention, these effects are observed at least through the first two decades of life. At the neural structural level, different indicators of family socio-economic status (SES) or poverty have been associated with changes in cortical thickness, surface and/or volume of several neural networks involving the hippocampus, amygdala, and prefrontal, parietal and occipital cortices, between one month and sixty-four years of age. At a neural functional level, low

SES or poverty has been associated with changes in the activation of occipital, temporal, parietal and frontal networks during tasks that demand emotional or cognitive control or that place demands on phonological processing during the two first decades of life (Johnson, Riis and Noble, 2016; Farah, 2017; Chan et al., 2018; WG2-ch7).

Evidence from cognitive neuroscience and other disciplines (i.e. education, developmental psychology, sociology and pediatric epidemiology) has allowed the identification of mediating and moderating factors of associations between SES/poverty, the development of self-regulation and EF and mental health (WG2-ch7). Among the most frequently identified factors are: perinatal exposure to infections, legal and illegal drugs, environmental toxins and/ or malnutrition; harsh, punitive or authoritarian parenting, less exposure to rich spoken language, and parents who are too busy and stressed to be the parents they would like to be; unsafe neighbourhoods, violence at

home, exposure to lead or mould, living near sites of high pollution (such as highways, industrial areas or toxic waste sites), food or housing insecurity, lack of access to healthy foods, lack of positive role models; less cognitive stimulation at home and in the childcare system; limited access to quality healthcare or education; lack of community resources such as green spaces, playgrounds or parks; cultural norms, values and expectations; and greater likelihood of exposure to different types of early adversity (e.g. Maholmes and King, 2012; Yoshikawa et al., 2012; Bradley, 2020; WG2-ch5).

Contemporary neuroscientific studies of mediators and moderators of the association between poverty and neural development are at a preliminary stage. The evidence to date has found that socio-economic status moderates the association between neural structures and functions; that neural structures and functions moderate the association between the socio-economic level and self-regulatory performance; that low early-life social class

The evidence to date has found that socio-economic status moderates the association between neural structures and functions ...

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Threats, negative life events, exposure to environmental hazards, family and community violence, family separations and moves, and job loss or instability, occur across the socioeconomic spectrum. leaves a biological residue manifested in stress hormone and pro-inflammatory signalling; and that different risk and protective factors mediate the association between socio-economic status and neural structure and function (Miller et al., 2006; Miller et al., 2009; Farah, 2017). This type of evidence has generated the hypothesis that the two pathways by which childhood poverty influences neural development during the first two decades of life are quality of parenting and the home environment and the regulation of the stress response (Ursache and Noble, 2016).

2.8 .6

THREATS

Threats, negative life events, exposure to environmental hazards, family and community violence, family separations and moves, and job loss or instability, occur across the socio-economic spectrum (Maholmes and King, 2012; Yoshikawa et al., 2012). The

neural systems associated with the regulation of such types of stressors include the hypothalamic pituitary adrenal axis, the sympathetic-adreno-medullar axis, the amygdala and the PFC, which together interact with the immune and cardiovascular systems. These systems work together to regulate the physiological and behavioural responses to stressors, contributing to the adaptative processes of each individual to their contextual circumstances. In the short term, the activation of these systems serves as an adaptive biological response against stressors. However, under continuous or chronic stress, they may be associated with physiological deregulation with the potential to affect emotional and cognitive performance, and physical and mental health including cardiovascular, respiratory and immunological health in the medium and long term (Felitti and Anda, 2010; McEwen and Gianaros, 2010; WG3-ch6).

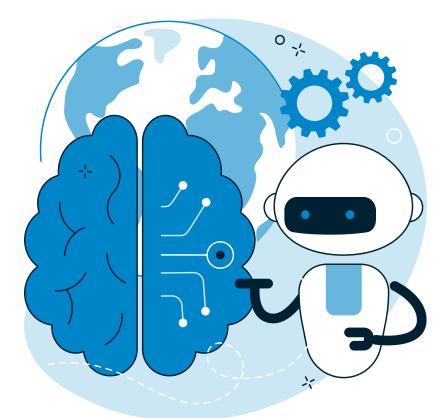
Recently, research has begun to study the modulation of epigenetic mechanisms (i.e.

In addition to the accumulation of potential risk factors, it is important to consider that each threat or deprivation can co-occur with other types of adversity and/or deprivation ... interactions between genetic and environmental factors) during early child development under different rearing and socio-economic conditions, where experiences can alter the expression of DNA. This evidence supports the hypothesis that besides the multiple mediation and moderation factors described for deprivation (see above), epigenetic changes may be involved at least partially in the long-term influences of early experiences (Gray et al., 2017; McDade et al., 2017; Frías-Lasserre, Villagra and Guerrero-Bosagna, 2018; Jiang et al., 2019; Torres-Berrío et al., 2019; Lang, Del Giudice and Schabus, 2020). In addition to the accumulation of potential risk factors, it is important to consider that each threat or deprivation can co-occur with other types of adversity and/or deprivation, such as being orphaned and consequent institutionalization, or exposure to domestic or community violence. In this sense, it is important to differentiate experiences due to lack of material resources from those characterized by the presence of threats to physical integrity (Sheridan and McLaughlin,

2014). The current consensus in developmental science is that the association between threats, deprivation and child development is modulated at least by the accumulation of risk factors, the co-occurrence of adversity, the susceptibility of each child to contextual factors, the timing of exposure to adversity, and mitigating or protective factors such as responsive, empathetic parenting (**Stevens et al.**, **2020**).



CHAPTER



2.9

Debunking neuromyths in education

Neuroimaging techniques can produce valuable insights for researchers seeking to understand the underlying processes by which learning occurs. However, they also frequently find their way into printed and broadcast media, where they feed public fascination with the brain and may be easily misinterpreted. Uninformed interpretation of images showing 'hot spots' can, for example, promote the idea of isolated functional units. Rather than a statistical map showing where activity has exceeded

Attempts to identify neuromyths amongst teachers suggest they are prevalent across diverse cultures. some arbitrary threshold, nonspecialists may see apparently well-defined and static islands on one side of a brain as suggesting localized, specific functions or modules that switch on and off. Considering brain function in terms of independent left and right hemispheres is one example of such misunderstanding. To categorize learners as leftbrained or right-brained takes the misunderstanding one stage further. This type of left-brain/ right-brain theory is a common example of a neuromyth – defined as a 'misconception generated by a misunderstanding, a misreading or a misquoting of facts scientifically established (by brain research) to make a case for use of brain research, in education and other contexts' (OECD, 2002, p. 111; WG2ch7).

Attempts to identify neuromyths amongst teachers suggest they are prevalent across diverse cultures (Howard-Jones, 2014). This may reflect the fact that neuroscience is rarely included in the training of teachers, who are therefore ill-prepared to be critical consumers of ideas and educational programs that claim a brain basis. Concern about neuromyths has contributed to the rationale for several attempts to introduce an understanding of neuroscience into initial teacher education and in-service professional development (Dubinsky et al., 2019; McMahon, Yeh and Etchells, 2019; Howard-Jones, Jay and Galeano, 2020).

Perhaps the most popular and influential myth is that students learn more effectively when they are taught in their preferred learning style. The implicit 'brain -based' assumption appears to be that, since different regions of the cortex have critical roles in visual, auditory and sensory processing, learners should receive information in visual or auditory or kinaesthetic form according to which bit of their brain works better (Politano and Paquin, 2000). The brain's interconnectivity makes such an assumption unsound, and although it is true that some learners learn

WORKING GROUP 3



better by either seeing images or listening to verbal instruction, reviews of educational literature and controlled laboratory studies fail to support such an approach (e.g. Coffield et al., 2004; Kratzig and Arbuthnott, 2006; Geake, 2008; Rogowsky, Calhoun and Tallal, 2020).

In recent years, the term 'neuromyth' has been criticized as tendentious (Gardner, 2020) while other researchers have questioned the extent to which teachers' beliefs in neuromyths has significant implications for classroom practice and students' learning. For myths that are closely related to practice (e.g. learning styles) such implications might appear self-evident, since few teachers would voluntarily implement an approach they believe to be ineffective. The implications of neuromyths about general brain function, such as the belief that we only use 10 per cent of our brain, are less clear. Krammer, Vogel and Grabner (2021) find no association of neuromyth belief on academic outcomes in a teacher training course, although this study does not assess teaching practice.

Horvath et al. (2018) explore whether belief in neuromyths predicted whether a teacher won an award and fail to find such evidence for most myths included in their study. The researchers do, however, find that underestimating brain plasticity (in relation to second-language learning and believing in critical periods after which children cannot learn certain things) appears to be a negative predictor of an award. A tendency to give greater weight to such biological constraints may contribute to a teacher's sense of powerlessness in relation to supporting their students. Belief that genes exert more influence than environment on cognitive ability has been found to be associated with an entity theory of intelligence which posits that our intelligence is set at birth and cannot be changed (Crosswaite and Asbury, 2019). These two neuromyths may be very detrimental since teachers who have knowledge about brain plasticity induce a growth mindset on motivation and academic achievement and are more prone to having a pedagogical stance

A tendency to give greater weight to such biological constraints may contribute to a teacher's sense of powerlessness in relation to supporting their students.

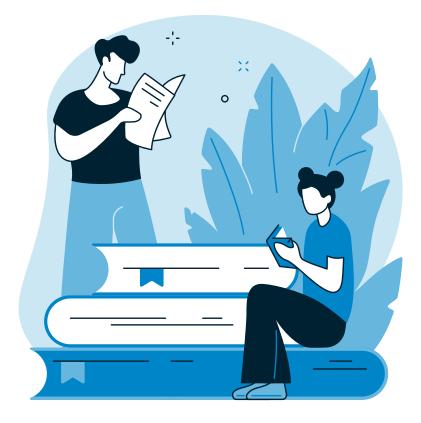
The fact that learning can change and reconfigure the brain, at all ages, in infants, children and even adults, is a fundamental theoretical discovery that has important implications for educational practices. adapted to student needs (Sarrasin et al., 2018; Canning et al., 2019). The fact that learning can change and reconfigure the brain, at all ages, in infants, children and even adults, is a fundamental theoretical discovery that has important implications for educational practices. Promoting to teachers, and also to students, this malleable representation of intelligence, of a brain sculpted by education and culture, which means that nothing is decided in advance, is an extremely powerful leverage for education.

When identifying neuromyths that should be addressed in teacher education, the potential relevance of each myth to classroom practice should be considered.



CHAPTER

2.10



Key findings

- Neuroscience, complementary to psychology, can inform education on how learning works and how learning is constrained by brain function and structure.

- Several physiological factors (e.g. nutrition, exercise, pollution and sleep) have effects on the brain and therefore on learning.

- Several social factors (e.g. stress, social interactions and cultural environment) have effects on the brain and therefore on learning.

- Human brain development is a complex, dynamic, continuous

and non-linear process that begins during the first weeks of gestation and lasts until early adulthood.

- Brain plasticity is very important during childhood and adolescence and plays a key role in cognitive development and learning.

- Subtle variations of the in utero environment can have long-term effects on cognitive abilities



2.11

Recommendations

- Include neuroscience in the training of teachers.

- Identify and popularize among teachers and parents the factors that have effects on the brain and on learning.

- Provide access in the school setting to adequate support for physiological needs that promote learning, such as pre- and posttraining sleep, nutrition and exercise. - Identify social factors that impair learning (trauma, poverty, deprivation, threat, academic stress) and provide psychological support in the school setting to mitigate their effects.

- Identify and debunk neuromyths in education.

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