



## Flux of life

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### ARTICLE INFO

#### Keywords:

autism  
brain imaging limitations  
cognition  
evolution  
non-linear trajectories  
plasticity  
resilience  
social start-up kits  
theory

### ABSTRACT

Developmental cognitive neuroscience is flourishing but there are new challenges and new questions to be asked. I argue that we need a bigger picture and an evolutionary framework. This brings some challenges, such as the need to rewrite the old story of nature and nurture, and the need to systematically investigate innate predispositions. While brain imaging has provided some splendid insights and new puzzles to solve, its limitations must not be ignored. Can they help us to find out more about the extent to which the infant brain already configures the adult brain? Can we find out why neurodevelopmental disorders often have severe consequences on cognition and behaviour, despite the mitigating force of brain plasticity? I wish to encourage researchers of the future to take risks by letting their imagination inspire theories to pursue hard questions. I end with a wish list of topics, from start-up kits to abstract reasoning, that I hope can be tackled afresh. However, collecting physiological and behavioural data is not enough. We need a deeper understanding of the mechanisms of cognitive development.

### 1. Introduction

The Flux congress in Berlin in 2018 was a good opportunity to take stock of where our field is moving. I was delighted to be able to wish Beatriz Luna, President of the Flux Society, a very happy sixth birthday. Flux means change, and so it would be wrong to fixate on the current state. Instead, the congress was an occasion to acknowledge that developmental science is moving, and like individual development, not necessarily in a linear fashion. The field of developmental cognitive neuroscience, as it grows, is like a growing tree and like the growing mind of a child: it turns, twists and twirls from uncertain beginnings towards ever more branching paths.

The essential similarities between a growing brain and a growing plant were revealed with the aid of the electron microscope by Peter R. Huttenlocher, in whose honour I gave a lecture. He traced the wondrous changes in the connections of neurons, documented their waxing and waning, and in particular, the pruning of synapses, and the increases in axonal growth and myelination (e.g. Huttenlocher and Dabholkar, 1997). In the words of neuroscientist and geneticist Kevin Mitchell “brains are not built, they’re grown.” Significantly, he adds, “and growing things is a messy, unpredictable business.”

### 2. Time to rewrite the old story of nature and nurture

Huttenlocher’s book “Neural plasticity” (Huttenlocher, 2002) had the subtitle: The effects of environment on the development of the

cerebral cortex. This was very much in line with the spirit of the time. Today the emphasis has shifted. Mitchell’s book “Innate” (Mitchell, 2018) has the subtitle: How the wiring of our brains shapes who we are. He argues persuasively that we need to give more prominence to internal, and importantly, purely random, factors that inexorably and unpredictably drive the tree-like branching of brain and mind.

Developmental science has lived forever with the tension between the opposing forces of nature and nurture, and everyone now agrees that both interact and each is as vital as the other. However, this somewhat facile agreement remains tied to correlational studies while weighing up as yet poorly understood ideas from epigenetics. A big theoretical picture has yet to emerge that takes account of what evolution over millennia has contributed to structure and function of our brain and mind, and what sheer learning and experience contributes to every individual’s brain and mind during their lifetime. Somehow, we have to relate changes in the brain that have happened and are happening at vastly different scales.

Evolutionary changes need to be studied in complex and painstaking experiments in which different species are compared. The changes that occur over the lifetime of an individual have to be tracked by longitudinal studies where results will only be known after some considerable time (Telzer et al., 2018; King et al., 2018). In either case the results are hard to interpret because of the sheer complexity and multitude of factors that are involved. Even if we limit ourselves to studying individual development, we cannot pretend to start with a tabula rasa, and we need to take account of the fact that individuals are

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<https://doi.org/10.1016/j.dcn.2019.100669>

Received 27 May 2019; Accepted 30 May 2019

Available online 01 June 2019

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deeply embedded in society and culture (e.g. Feldstein Ewing et al., 2018).

### 3. The need for theory and the bigger picture

How to sketch out a theory that provides a roadmap through this jungle of complexity? As Van den Bos and Eppinger (2016) suggest, we can start with heuristic models for specific domains. But heuristic models tend to remain piecemeal and are hard to relate to each other, while theories sketch out the bigger picture, to join up existing observations, to slot in previously ignored observations, and to predict entirely new ones. We need to agree on a framework, to create a common ground, where different theories can be planted. The different theories can then compete with each other. Some will give better explanations and predictions than others, but all theories carry the risk that they will be proved wrong. Some researchers shy away from this risk, but what is the alternative? Collecting masses of data hoping for results to emerge by themselves? First, this is no less risky than theorising and doing small but well targeted experiments. Second, a discovery only emerges if you have eyes to see it, and you can only see it if you have some expectation. So, we are back to theory – and back to getting things wrong. But we need to make mistakes in order to learn.

We should encourage young researchers to take risks and use their imagination to form abundant theories. There is nothing wrong with being imaginative and bold, as long as you then test your theory rigorously, by setting up detailed hypotheses. Admittedly, there is a knack to setting up hypotheses so that they lend themselves to decisive experiments. Munafo et al. (2017) give some good advice: Spell out what you are going to test. Be precise about the methods you intend to use for the experiment. Make sure that you will have adequate statistical power. If you follow this advice then you can avoid the traps that have thrown psychology into a replication crisis. Science is a slow business, and much of the work involved is hidden from view. There are no short cuts. We should always be suspicious of flashy results. Instead, reliability and replicability are key.

We should encourage young researchers to always try and see the big picture. Only by keeping in mind the big picture will it be possible to unite the many different strands of developmental cognitive neuroscience (see for example Crone and Ridderinkhof, 2011; Jernigan et al., 2016). This ambition is likely to lead to new questions about the relationship between the developing mind and brain and to new answers that will give us important new information.

### 4. Promises of brain imaging

One of the main strategic aims, when Sarah-Jayne Blakemore and I first talked about founding a journal as a home for the rapidly multiplying studies in the field, was to encourage research that used measures of brain structure or activity together with cognitive tasks. This, we hoped, would lead to a sea change. Up to the beginning of the 21<sup>st</sup> century, there had been only vague speculations, if any, about the relationship between developing mind and brain. I think the wealth of papers published in the journal *Developmental Cognitive Neuroscience*, and their increasing sophistication over the last ten years, has shown that our optimism was not misplaced. Actually, we might have expected far slower progress, because it was only since the 1990s that researchers could use Magnetic Resonance Imaging (MRI) scanning combined with efficient statistical analyses to measure brain activity. Furthermore, there was still doubt back then as to whether MRI scanners were sufficiently safe to be used with young children. Of course, MRI is not the only technology to look into the living brain. Electroencephalography (EEG) had been there for decades and Magnetoencephalography (MEG) was just being established. Gervain et al. (2011) discussed the use of functional Near Infrared Spectroscopy (fNIRS) with infants in the very first issue of the journal, when this technique was still hardly known. Now its use allows the study of individuals moving about in the real

world (Pinti et al., 2018).

We now know more about the *what* and *where*, but *how* is information processed in the brain? One promising approach to this question is to use computational models. Currently, only a limited number of models of cognitive abilities are available, mostly focussed on learning and decision making (van den Bos et al., 2016; Hauser et al., 2019). Differences in brain activation over time have been most successfully tracked over the period of adolescence (for an overview see Blakemore, 2018). This is a particularly flourishing part of the field as seen in numerous papers published in *Developmental Cognitive Neuroscience*. Some fundamental questions have been answered. As mentioned above, there is evidence for the existence of localised regions sensitive to processing particular types of information. There is evidence for plasticity of structure and function with specialised training, such as music (Habibi et al., 2016). There is also evidence for sensitive periods, although still mostly in animals (Byrne et al., 2017; Sugiyama, Prochiantz and Hensch, 2009).

### 5. And limitations

Other questions have proved rather more difficult to answer. For example: What actually is the road map for brain development? Which regions mature earlier and are pruned earlier, and which later? However, since Peter Huttenlocher's pioneering work, there are strong indications that bottom-up connections are myelinated before top-down connections, and this matches behavioural observations: babies' perceptual skills surpass their ability to perform voluntary actions. What are the limits of malleability as a result of learning? How can temporary changes be distinguished from long term changes due to external stimulation, such as education? What, if any, are the signs of the potential for learning a particular skill before learning even starts? When and how does the prefrontal-parietal control system exert itself? What are the cognitive symptoms in different genetic syndromes that involve abnormal brain development? What are the precursors of psychiatric disorders starting during adolescence or young adulthood? These questions are wide open and might prove fertile grounds for future research.

Did we expect too much from existing measures of brain activity? Probably yes. The usual measures are miniscule increases and decreases in the blood flow, correlated with neural activity, averaged over many trials, and over many participants. Let us remember that we are only indirectly generating information by subtracting activity observed between two task conditions that hopefully differ in just the one critical variable of interest. Looking at a single brain at a single point of a test trial produces too weak a signal and includes too much noise. Unfortunately, the interpretation and refining of the measures obtained by MRI, for example, by combining them with EEG or MEG measures does not make the interpretation any easier. Amazingly we still don't know for sure what it means for a brain region to be more active or less active, when comparing individuals with a different clinical diagnosis, or individuals at different stages of learning, or different levels of achievement. Also, being limited by the available technology, we do not know what changes in grey matter and white matter mean at the cellular level (Reynell and Harris, 2013; Easson and McIntosh, 2019).

### 6. Tantalising

There are many ways in which the application of brain imaging technology has changed our understanding of cognitive development. There are numerous new observations about where and how information is processed in the brain, and many of them have found a place in the journal *Developmental Cognitive Neuroscience*. But, most tantalising, to me at least, is a finding that has not yet received much comment: Multiple studies have confirmed that regions, which were known from adult neurology and neuropsychology to be associated with particular functions, seem to be associated with these functions

already in childhood. This applies for instance to language and speech (Marklund et al., 2019), face recognition (Nordt et al., 2018) and arithmetic skill (Peters and De Smedt, 2018). It is true even for social capacities, such as mentalising (Mahy et al., 2014).

It could have been otherwise. Indeed, how can it be that the future space for cognitive functions is already staked out, when these functions are not even there? It is almost uncanny to see how the infant brain pre-figures the adult brain (Dehaene-Lambertz & Spelke, 2015). It is an insight that gives pause for reflection: Are infant brains miniature adult brains after all? What are the implications for brain plasticity?

## 7. Challenges in the study of the developing mind and brain

There are teething problems in all emerging disciplines, and developmental cognitive neuroscience is no exception. One of the most well-known temptations is to interpret correlation as causation. Both, biological and psychological variables can be viewed as causes. For example, brain changes cause behavioural changes, as during puberty, where we can trace the effects of hormones. A good example of behavioural changes causing brain changes is learning to read (Caffarra et al., 2017; Liebig et al., 2017). Ellwood-Lowe et al. (2016) warn of the temptation to use reverse inference to explain findings that relate language and other cognitive variables to brain activity or to socio-economic status (SES). Catching changes in brain activity and in behaviour in children of different ages sounds straightforward. But it is not (Pfeifer et al., 2018). For instance, chronological age does not provide a secure basis for comparison since the course and speed of development of individual children is not directly pegged to the calendar.

Further, while development means change by definition, it is worth reminding ourselves that the changes are unlikely to be unidirectional (see Smith and Thelen, 2003, for a theoretical discussion of dynamic non-linear changes in cognitive development). An example of a possible set back is evident when considering the consequences of a change in social status when a child moves from primary to secondary school. Given Huttenlocher's discovery of pruning and the notion of sensitive periods, it is no surprise that younger children can sometimes outperform older children. Acquiring the distinct phonology of your mother tongue might be an example. Another example is a decrease in sensitivity to statistical probabilities after the age of 12 years, as shown by Janacek et al. (2012) using a serial reaction time task. Similarly, Rohlf et al. (2017) showed that 6-months old infants were superior to adults in implicit crossmodal learning using event-related potentials and sequences made up of auditory and visual elements.

One of the obstacles to progress in developmental psychology may well be the belief that tracking changes is an aim in itself, and is the same as tracking causal dependencies. However, the fact that B comes after A does not necessarily mean that there is a causal connection. It merely tells us about precedence. This key question – what is a necessary prerequisite for changes in development? – is nearly intractable, given the random variation that is part and parcel of the developmental process (Vogt, 2015). We simply cannot manipulate experimentally the conditions in human beings, as this would be profoundly unethical. Longitudinal studies whether of group averages or of individual trajectories have been an important tool in our field and their problems and solutions are discussed by King et al. (2018). Still, important though they are, they are unlikely to advance a causal understanding of development.

## 8. Finding ways around obstacles

There is another way. A great opportunity is offered by the study of disorders of development. Here it may be possible to trace a missing prerequisite at the cognitive level in the causal chain, as I myself tried to do in the case of autism and dyslexia (Frith, 2013a). In autism, a failure in automatic mentalising allowed a parsimonious explanation of

the characteristic difficulties in reciprocal social interaction and communication (Frith, Leslie & Morton, 1991). The difficulty in understanding false beliefs (Baron-Cohen, Leslie & Frith, 1985) was a novel prediction from this theory, as was the difficulty in understanding picture stories with social content, but not those with physical content (Baron-Cohen, Leslie & Frith, 1986). Mentalising failure also explained some puzzling observations; for instance, the absence of pretend play (Wing & Gould, 1979), and the difficulties in the fluent understanding of deception in autistic children (Sodian & Frith, 1992). In dyslexia, the assumption of a failure in phonological processing gave a parsimonious explanation of the difficulty in acquiring a phoneme-grapheme code, and predicted difficulties in speech processing tasks (e.g. Frith, 1999).

There are still unexploited opportunities to study development, failure and resilience of cognitive processes through the investigation of neurodevelopmental disorders. Research on so far identified genetic syndromes has produced rich data on structural brain abnormalities (e.g. Sethi et al., 2018), but we know far too little about the specific and general cognitive and behavioural consequences. It remains puzzling that, despite the evidence for brain plasticity and repair, these consequences can be so severe. Research on the consequences of early brain injury and prematurity have suggested that the brain is resilient and can partially reconfigure itself (Stiles et al., 2005). However, there are also findings that indicate that some early injuries and abnormalities continue to be associated with lasting cognitive impairments (Vargha-Khadem et al., 1997; Luu et al., 2009).

One of the more encouraging findings when tracking behaviour in children with neurodevelopmental disorders, is that behaviour improves with learning, even without targeted intervention or teaching. 'Compensatory learning' is an interesting phenomenon that has not yet been studied in much detail (but see Livingstone and Happé, 2017). Thus, despite missing cognitive prerequisites (*aka* start-up kits, see below), there are unusual and roundabout routes that may eventually reach a similar behavioural goal. This is not so much about reconfiguring the brain, as making use of redundancy in multiple possible pathways. This is strikingly demonstrated in the case of dyslexia, where skilled reading can be mastered through alternative strategies, which are served by alternative neural pathways (e.g. Barquero et al., 2014). This reinforces one of the foundational principles of cognitive psychology: behaviour is only what you see on the surface. The underlying processes are not only hidden, but diverse, and they can be revealed by an array of suitable tests.

## 9. A wish list for future research: from start-up kits to abstract reasoning

If we adopt an evolutionary framework, and we really should, then we need to ask questions about the nature of the long evolved and now innate start-up kits that underlie our cognitive capacities. Using a machine metaphor, I envisage start-up kits as the brain's factory settings, forged during the long process of evolution (Frith, 2013b). I imagine that certain stimuli that were once crucial for survival have acquired and now sustain the ability to trigger actions in the organism. A good example for an unlearned predisposition is the ability to detect animacy, using only self propulsion as cue, which has been demonstrated in newborn chicks as well as in newborn humans (Di Giorgio et al., 2016).

From the ability to detect animacy it may only a small step to the ability to detect agency and differentiate self from others. But additional cognitive mechanisms are needed to detect the nature of the agent. For instance, is it prey or predator? Ingroup or outgroup member? These are only some foundations of the social brain, and there are likely to be many more, filling a large programme of research. One thread to follow up is how start-up kits prioritise their own domains and make learning fast and efficient. How does this type of fast learning differ from other types of learning that are based on explicit teaching? How do the frontal-parietal control systems in the human brain manage to

control and override the triggers set by our ancient predispositions? How many start-up kits for social cognition might exist? What are their substrates are in the brain? We can only speculate at present.

Start-up kits for social capacities, such as agency detection, affiliation, mentalising, empathy, and in-group loyalty, seem to be remarkably independent of abstract reasoning abilities. Autism and psychopathy demonstrate that one or more of the basic social predispositions can be missing regardless of general intellectual ability. But what of abstract reasoning abilities? They are particularly interesting because they develop relatively late with a key role played by prefrontal cortex (Dumontheil, 2014). Presumably these abilities have an innate basis as well, otherwise, how could we explain their presence in all humans in all cultures, and their absence in cases of severe brain pathology. Perhaps, reasoning appeared as a by-product of least effort principles, such as using a straight line to reach a goal (Gergely and Csibra, 2003). Perhaps, reasoning appeared as a by-product of competition in verbal contests, since arguments, especially those that serve self-justification, are an effective means for winning over rivals (Mercier and Sperber, 2017).

Of all the human abilities, the origin of conscious reasoning and rational thinking, seems most obscure. It is likely that cultural teaching is critical for nurturing and shaping this ability. One obvious benefit of rational thinking is that it fosters self-control and inhibits impulsive responses that might have bad consequences. However, it does not always lead to the 'right' behaviour. Our conscious reasoning, once acquired, is able to provide us with excellent justifications for our prejudices and self-serving biases. Our unconscious predispositions, likes and dislikes, and 'visceral' feelings, can sometimes lead us towards better decisions. Can we learn to strike a balance between unconscious urges and conscious reason? This might mean that we always need to take account of broader social and environmental conditions as well as of intuitions. For example, resisting that marshmallow is not a good idea in a volatile environment (Kidd et al., 2013).

We need to be open to some really hard questions. For example, can we ever predict individual differences? Are average trajectories of the development of cognitive functions and brain structure even meaningful? Is there just too much noise in developing systems, an inherent chaotic complexity? Studies with genetically identical mice (Freund et al., 2013) and cloned fish (Bierbach et al., 2017) raised in an identical environment, suggest that individuality might be an inevitable and essentially unpredictable outcome of development. This would make it likely that the causes of developmental disorders, even if firmly rooted in genetic origins, are never exactly the same between one individual and another. If so, then it would be more profitable to study developmental processes retrospectively rather than prospectively, tracing forking paths from the end back to the beginning. However, this is not how we tend to formulate theories at present.

Only ten years have passed since the founding of our journal *Developmental Cognitive Neuroscience*, and it is still too early to judge the success or otherwise of the enterprise so far. However, ten years, roughly speaking, is a milestone in child development. It marks at once the end of childhood proper and the beginning of dramatic changes leading to adolescence. Flux is duly in flux. I wish the Journal and the Society all the best for an exciting future.

#### Conflict of interest statement

I have no conflict of interest to declare.

#### Acknowledgements

I am grateful to Sarah-Jayne Blakemore, Eveline Crone, Silvia Bunge, Ulman Lindenberger and Yana Fandakova for their helpful comments. I am also thankful to Chris Frith and Martin Frith for their constructive criticism of style and content.

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