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Neural basis of cognitive training and development

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This paper gives a brief overview of phases in brain development and discusses the hypothesis that mechanisms of working memory development are partly the same as those of working memory training. Brain development could be related to different, but overlapping phases: (i) structural maturation, with a relatively high reliance of preprogrammed processes; (ii) interactive specialization, which is a reorganization of the functional networks, partly in response to the environmental demands; (iii) training or skill learning, which is a qualitative change, such as strengthened connectivity of existent networks. The mechanisms of this skill learning could be similar to those neural processes observed during controlled studies of working memory training, where strengthened connectivity between frontal and parietal regions is suggested to play a central role. Education and formal schooling could be one important factor driving the training and skill-learning phase of executive functions, including improvement of working memory.

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A central aim in developmental and educational cognitive neuroscience is to understand the mechanisms of brain development, their relation to cognitive abilities and the genetic and environmental factors driving them. This paper will review studies of cognitive development and training. In particular, the development and training of working memory will be related to the hypothesis that partly the same neural mechanisms underlie both training and development.

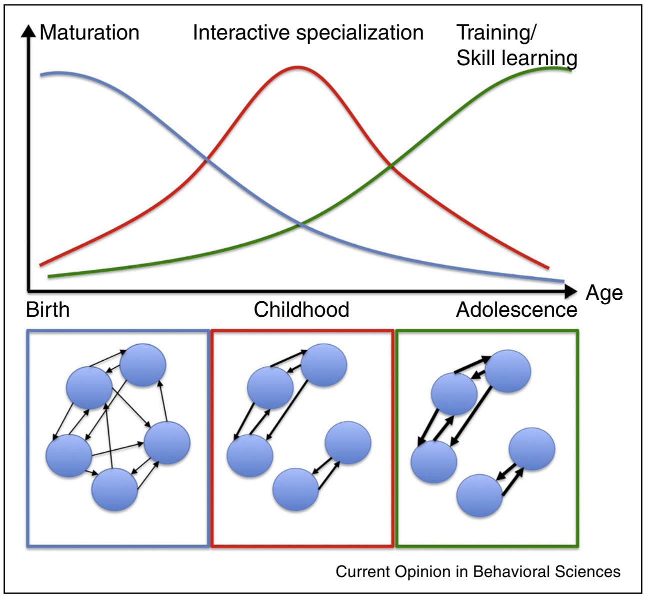
In a simplified account of child development one can identify three main views, or theories, on what is driving brain and cognitive development: (i) structural maturation, a largely genetically preprogrammed set of processes; (ii) interactive specialization [1•], which is a reorganization of the functional networks partly in response to the environmental demands; (iii) training or skill learning, which is a qualitative change, such as strengthened functional connectivity of existent networks [2]. These three views are not mutually exclusive, but are more likely overlapping phases during development (Figure 1a). The exact timing of these phases is likely to differ for different cognitive and academic abilities. Specialization for face processing, for example, should occur before specialization to perceive letters or numbers. Differences in the environment for each individual will also lead to differences in timing.

It should also be emphasized that the phases do not correspond to a distinction between nature versus nurture; maturation can only occur in a nourishing environment and genetics play a role in determining response to training [3]. Gene by environment interactions is important in all phases of development, but that does not mean that separate sources of brain development can be identified.

One example of these phases is the development of language. During the maturational phase, connectivity between cortical regions are established. These axons are then myelinated, which is necessary for quick signal transduction involved in distinguishing rapid frequency shifts in language, and later for the rapid perception of text during reading. The interactive specialization involves a left hemispheric word form area that gradually acquires specialization through exposure to text [4,5] and through its interaction with other language related cortical regions. During the interactive specialization, the functional network thus changes qualitatively [6] (Figure 1b). But after the basic network for processing text is established, there remains years of practice before a child can attain adult proficiency, a skill learning phase that is associated with quantitative changes, for example of white matter microstructure [7,8], influenced by genetic variability between individuals [9,10].

In mathematics, it has been assumed that there would be a number form area, corresponding to the word form area [11•]. Intracranial electrophysiological recordings were first used to identify an area in the inferior temporal gyrus that responded more to numerals than to letters or false fonts [12]. Recently this area was also identified in both hemispheres with fMRI [13]. This number form area is must gradually achieve its specialization through interactive specialization, although this process has not been documented in developmental studies yet.

Figure 1



(a) A schematic drawing of hypothetical phases of development. The *y*-axis represents the rate of change, for example how much myelination changes from one year to the next. The blue, red and green curves represent the factors driving these changes. Age in years is not specified, as the absolute timing will depend on each specific function. The maturational phase is hypothesized to be mainly driven by genetically determined signals. During the interactive specialization, the networks are rearranged to respond to novel environmental stimulation. In the training/skill learning phase these networks are gradually strengthened. **(b)** Hypothetical changes of networks during development. Circles represent cortical areas or subcortical regions, and the lines the axonal connections. Thicker connections represent stronger connectivity, that is the functional impact of activity in one region upon another. The underlying neuronal mechanisms could be either changes in myelination and axonal thickness or changes in number or size of synapses.

The role of the environment is obvious for behavior that is evolutionary new, such as reading text and understanding symbolic arithmetics. But similar phases might also be distinguished for development of cognitive functions such as working memory, inhibition and reasoning [2].

One indication of separate phases in cognitive development comes from an analysis of 9000 youths aged 8–21. This analysis focused on variability in reaction times within an individual who performed a large number of cognitive tasks, and how this variability differed between individuals at different ages [14]. The variability followed a u-shape, with an initial decrease until mid adolescence followed by an increase during the later teenage years. The authors interpreted the initial decrease as the end of a maturational phase and the later increase in variability was taken as indication of task specific skill learning in the cognitive domain.

The role of environmental stimulation and cognitive training for development of executive functions

Formal, school based education is a cognitively demanding activity, which could be one important, factor influencing the development of executive functions.

A recent analysis of more than 1000 individuals from the Lothian Birth Cohort sought to further characterize the effect of education on cognition. Comparison of different statistical models suggested that the effect of education on IQ is driven via individual cognitive abilities, rather than a direct and diffuse effect on 'g' [15].

The effect of education specifically on working memory capacity was estimated in 1727 children between 6 and 7 years, who participated in repeated testing over a year [16]. Over the school year, capacity increased with about 0.6 standard deviations. The amount of time spent in the classrooms significantly affected the development of working memory capacity, above and beyond the effect of chronological age. This is a strong indication that environmental factors play an important role for development of working memory.

Other activities that that might affect cognitive development is practice of musical instruments [17]. A longitudinal study found that practicing a musical instrument was associated with higher WM capacity, and that development was proportional to the amount of practiced hours [18]. On the other hand, a large twin study investigated the association between musical practice and IQ, here estimated with a single test of reasoning. Although there was a statistically significant association between the two measures across all individuals ($r = 0.1$) it disappeared when controlling for genetic and shared environmental influences, indicating that a highly practiced twin did not have higher IQ than the untrained co-twin [19]. Although these are only a few studies, together they could suggest that the effects of both schooling and musical practice were larger for working memory than for IQ. The environmental stimulation might thus affect some specific cognitive functions, such as working memory, but not more diffuse constructs, such a IQ, consistent with the findings from the Lothian Birth Cohort [15].

The effect of education on cognitive abilities is consistent with the malleability of cognitive functions, in particular the contention that working memory capacity can be increased by training [20]. The effect of working memory training has been summarized in several recent meta-analyses [21–25]. Although the total number of participants is still too low to allow powerful analyses of subgroups, meta-analyses are surprisingly consistent in showing increases in non-trained capacity by around 0.6 standard deviations. Another meta-analysis showed significant transfer effect for training of 'executive control' [26].

In line with the suggestion that education effects single cognitive abilities more than general constructs such as IQ [15], one study found effects of working memory training on non-trained measures of working memory, but not for IQ [27].

Both schooling and cognitive training could thus be examples of skill learning, or training phase, for cognitive functions. An interesting question is whether similar neuronal processes underlie cognitive training over weeks and environmental effects of months or years. Here one particular mechanism will be considered: increased functional connectivity between frontal and parietal regions.

Neural mechanisms of connectivity

Long-range connections between cortical areas do not grow out after birth, but existing connections can be changed in at least two ways. The effect of activity in one neuron on another can be modulated by outgrowth of new synapses, dendrites or boutons [28]. These processes are activity dependent, via the well-studied processes of long-term potentiation. The consequence is a stronger functional connectivity between two neurons.

Secondly, the myelin around the axons connecting two areas can be increased, which increases conduction speed and thus the function of the neural network. Axons can also be lost. A study in macaque monkeys suggested that 70% of axons at birth are lost during the first few months [29]. In is unknown to what extent axons are lost during later childhood and adolescents in humans.

A recent study uncovered a potential third cellular mechanisms that could be important for relating training or practice to changes in white matter. In mice, stimulation of cortical neurons led to maturation of precursor cells into mature oligodendrocytes [30••]. Four weeks later, this led to thicker myelin sheet around the stimulated axons. Generation of new oligodendrocytes might thus be a mechanism behind MRI detected changes in white matter associated with training and development.

However, a study in humans, using the integration of nuclear bomb test-derived ^{14}C, showed that although myelin is exchanged at a high rate, the maturation of precursor cells is substantially lower in humans, at least in the part of corpus callosum that was analyzed [31••]. The data suggested an annual rate of 0.3% renewal of oligodendrocytes in the human corpus callosum, which is probably too low to explain changes in white matter during development and training as measured with MRI.

Changes in connectivity during development

Functional connectivity can be estimated by analysis of resting state data. There is a gradual change in connectivity through ages that correlates with chronological age [32]. Some recent studies have attempted to directly relate the connectivity to cognition. Fronto-striatal connectivity has been associated with improvement in inhibitory ability [33]. In a longitudinal study, connectivity was measured in the same individuals at age 10 and 13 [34]. The connectivity was analyzed in terms of default mode network (DMN) and a central executive network (CEN). There was an increased integration within each of the networks, including increased connectivity between prefrontal and parietal cortex of the CEN network, but segregation between networks. Integration within the CEN was associated with IQ. A MEG study of children aged 8 to 11 years, found that working memory capacity was associated with the strength of connectivity between a fronto-parietal network and visual areas in inferior temporal cortex [35]. These results are consistent with previously described trends of integration and desegregation in cross-sectional studies [36], and schematically illustrated in Figure 1b.

Changes in white matter could be one factor behind the changes in functional connectivity. A longitudinal study of youths aged 6–20, showed that fractional anisotropy (FA) was linked both to current WM capacity, but was also predictive of future development of capacity [37•]. These results were further explored in a region-of-interest based analysis using probabilistic tractography. This confirmed that both striato-frontal and fronto-parietal connections correlated with WM capacity, but also predicted future capacity [38].

Changes in connectivity with cognitive training

Changes in functional connectivity during rest, in particular between frontal and parietal regions, is not only associated with cognitive development, but also cognitive training [39], including working memory training [40–42].

Instead of analyzing resting state connectivity, Kundu *et al.* [43•] used EEG to measure how an impulse from transcranial magnetic stimulation (TMS) over the parietal cortex was propagated over the cortex. They found that after working memory training, the impulse led to increased signals in the frontal and temporal lobe, demonstrating that training led to an increase in functional connectivity, specifically during task performance.

Astle *et al.* [44•] used magnetic encephalography (MEG) to analyze resting state connectivity before and after 5 weeks of WM training in 13 children aged 8–11, and in 14 children in an active control group. A group x time interaction was found for connectivity between the right-hemisphere frontoparietal network and left lateral occipital cortex, with increased connectivity for the training group. In a second analysis, the gain in WM score was used as a covariate. This gain was associated with increased connectivity in bilateral frontoparietal networks that comprised bilateral superior parietal cortex and frontal eye-fields. Both analyzes used the lower beta-band (13–20 Hz).

Conclusions

The hypothesis that development and training share similar neuronal processes predict that if a mechanism shows a significant effect for how much individuals improve by training, it would be a significant predictor also for how fast individuals develop during childhood. This could be tested for a range of different processes, for examples genetic variants that predict how much an individual improves by training. A number of such variants have been identified and the relation to development could be tested [3,45–47].

There are similarities between the neural effects of cognitive training and cognitive development, at least regarding the skill learning/expertize phase of development (Figure 1c). Strengthening of fronto-parietal connectivity seems to be an important aspect of both these processes. Cognitive training could provide a controlled way to experimentally study the effect of environment on brain development.

Future research will be needed to further characterize the phase of interactive specialization for cognitive functions and to understand the considerable inter-individual differences in rate of development and response to training. Studying the neural basis of cognitive training could be a way to understand general principles of brain plasticity relating to development of cognitive functions.

Conflict of interest

Nothing declared.

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