The importance of tracing developmental trajectories for clinical child neuropsychology

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Children change. Despite the truism of the previous statement, the dynamics of developmental change are frequently absent from studies of child disorders. Why is this? We believe that the reason lies in the strong influence of *adult* neuropsychology, in which researchers and clinicians focus on brains that had originally developed normally and became consolidated by adulthood, prior to the brain insult. Since the adult brain is highly specialized, it is unsurprising that models of adult brain function focused on special-purpose, independently functioning modules, whose components could be damaged or left intact by a specific brain trauma: the metaphor of boxes in the brain to be crossed through when damaged. While the adult framework can be informative about the end-state of development, it is inappropriate for understanding developmental disorders or even typical development, because it ignores the dynamics of developmental change (Karmiloff-Smith, 1997, 1998). Indeed, the start-state of development is very different from the adult end-state. The normal infant cortex is initially highly inter-connected (Huttenlocher & Dabholkar, 1997; Neville, 2006), and it is only with time and with the processing of different kinds of inputs that the child brain becomes increasingly specialized and localized for function (Johnson, 2001). In other words, the brain does not start out with independently functioning modules; modules are emergent from a gradual and complex process of modularization (Karmiloff-Smith, 1992). This means that a tiny impairment early on in, say, the developing visual system might have cascading effects on the subsequent acquisition of, say, number or vocabulary. Such impairments may or may not be compensated for, depending on the severity and the specialization of the impairment in question. It also means that one cannot take a single snapshot of, say, middle childhood, describe the phenotype of a developmental disorder, and from that suggest an intervention program. This would not only be clinically imprecise for a given child, but likely to be inappropriate for the syndrome in general. In our view, to assist clinical diagnosis and subsequent intervention, it is crucial to ascertain how the current phenotype originated at the beginning of a developmental trajectory, as well as knowing

where it will lead to in the future of that developmental trajectory.

This chapter will therefore concentrate on the importance of tracing and tracking full developmental trajectories, as well as focusing on associations between domains and between syndromes, rather than the current focus on dissociations. For illustrative purposes, we will concentrate mainly on Autism Spectrum Disorder (ASD), Down syndrome (DS), Fragile X syndrome (FXS), and Williams syndrome (WS).

Prenatal learning

Foetal development starts very early, at the onset of zygote formation with the first neurons of the human forebrain present at a very early stage (Bystron et al., 2006). Moreover, for the cognitive neuroscientist, learning also starts very early. From about the 7th month of pregnancy onwards, the healthy foetus is actively processing various forms of auditory input (Hepper, 1995; Moore, 2002). Foetuses who heard a specific piece of music in the womb will discriminate that particular music from other pieces at birth. Newborns also recognise their mother's voice at birth, despite the fact that in the womb it was filtered through the amniotic fluid and sounds very different ex-utero. Yet, during intra-uterine life the foetus formed some abstract representation of mother's voice and is able to distinguish that from other female voices at birth (Kiselevsky et al., 2003). Furthermore, foetuses also learn the beginnings of the speech patterns of their mother tongue while in the womb. Research using acoustic spectroscopy has shown that, at 27 weeks, a foetus's cry already contains some features of his or her mother's speech, such as rhythms and voice characteristics. Also, DeCasper and colleagues showed that foetuses at 33 to 37 weeks gestation demonstrated memory of children's rhyme, while still in the womb, in response to mothers repeatedly reading a certain rhyme to their unborn baby (De Casper et al., 1994).

For the moment, we lack any knowledge about the learning capacities of the atypically developing foetus. However, for a truly full understanding of the

developmental trajectory of a child with a disorder, this is where we should in the future be grounding our field of enquiry. For the time being, we must begin with postnatal development.

Neuroconstructivism and postnatal learning

From the moment the child is born, s/he is bombarded with interesting stimuli: faces, voices, objects, etc. and, as a result of the repeated processing of these different stimuli, the infant brain becomes slowly but increasingly specialized (Johnson, 2001). Elsewhere we have argued that a middle way is needed between staunch Nativism, on the one hand, in which the infant brain is thought to be pre-specified for each of its modular abilities, and Behaviourism, on the other, in which a single general-purpose learning mechanism is invoked. Neuroconstructivism, an intermediate between Nativism and Behaviourism, holds that a small number of domain-relevant learning algorithms jump-start the infant brain (Elman et al., 1996). Initially, all algorithms attempt to process all inputs, but with time the one that is most domain-relevant (say, to rapid sequential processing) wins out in the competition between algorithms and *becomes* domain-specific over developmental time (Karmiloff-Smith, 1998). We speculate that this is the case for the typically developing infant. However, we do not know whether the atypically developing infant brain displays the same level of interconnectivity early on, and whether subsequent pruning leads to specialization and localization of function in children with developmental disorders. But theoretically we can already ask what the implications of early interconnectivity would be for the atypically developing brain.

Within the theoretical assumptions of Neuroconstructivism, the interconnectivity of early cortical development means that a tiny deficit could permeate all parts of cortex. But, given the interaction between different algorithms and different structures in the environmental input, some parts of the brain would be more seriously affected by the deficit than others. This could give rise, over developmental time, to a seemingly isolated

domain-specific impairment and the apparent preservation of other domains, i.e., scores "in the normal range". In other words, what seems in the end-state to be a domain-specific deficit may have originated in the start-state as a more domain-general deficit (Annaz & Karmiloff-Smith, 2005; Karmiloff-Smith, 1997, 1998; Karmiloff-Smith et al., 2004). We therefore strongly advocate the importance of investigating not only domains of weaknesses, but also domains in which individuals show proficiency, i.e., reach scores comparable to controls. Indeed, if changes to domain-relevant properties are initially widespread, and some properties are less relevant to a given domain, then that domain might exhibit lesser, more subtle impairments (Karmiloff-Smith, 1998; Karmiloff-Smith, Scerif & Ansari, 2003). Ideally, then, an explanation of developmental deficits consists in identifying how these initial domain relevancies have been altered in the disorder, and then how the subsequent process of emergent modularisation has been perturbed.

'Spared' versus 'impaired' processing?

In the literature on developmental disorders, one frequently encounters terms such as 'spared', 'intact', and 'preserved' when describing atypical development (e.g., Hoffman, Landau, & Pagani, 2003; Rouse, Donnelly, Hadwin, & Brown, 2004; Tager-Flusberg, Plesa-Skwerer, Faja, & Joseph, 2003). The notion of a selective deficit implies the impairment of a single process or domain together with the preservation (i.e., normal development and functioning across time) of others. When a brain has developed normally, resulting over time in specialised, localised functions, it is possible that after consolidation subsequent brain injury may produce selective damage(s) while other components continue to operate normally. Hence, it might be appropriate to consider them as 'spared/intact/preserved'. However, in the case of a developmental disorder of genetic origin, the use of such terms is questionable. They imply that the purported intact function has *developed normally* from infancy, through childhood to adulthood, with no interactions with other developing parts of the brain. Yet, as we mentioned above, the

infant brain starts out highly interconnected (Neville, 2006), so it is unlikely that one part of the brain can develop normally in total isolation, without being affected (even subtly) by other parts of the atypically developing brain. The use by clinicians of the 'intact/impaired' dichotomy in characterising developmental aspects of functioning has problematic implications for intervention (A = intact, no intervention required; B = impaired, intervention required). Such dichotomies, then, could actually hinder rather than enhance the study of the dynamics of atypical development. By contrast, if one considers development as a dynamic process of interactions and competition, it could be, for instance, that training in rapid sequential movements in the assumed "preserved" motor system could impact another non-motor domain which is impaired, rather than direct training in that non-motor domain.

Concrete examples from developmental cognitive neuroscience

Studies that have taken the Neuroconstructivist developmental approach to behavioural phenotypes have shown, for instance, that areas of purported relative strength at one stage of development (middle childhood or adolescence) were not necessarily stronger at earlier stages of development (Paterson, Brown, Gsoedl, Johnson, & Karmiloff-Smith, 1999). For example, Paterson and colleagues (1999) showed that infant cognitive profiles in WS and DS cannot be predicted from the adult end-state pattern of their cognitive functioning. One of the most compelling examples is vocabulary learning in toddlers with WS, which is very poor and as delayed as vocabulary acquisition in toddlers with DS. By contrast, when individuals with WS reach adolescence/adulthood, their language vastly outstrips that of their counterparts with DS. The same differences between the infant start state and the adult end state exist for number (Paterson et al., 1999; Paterson, Girelli, Butterworth & Karmiloff-Smith, 2006). Infants and toddlers with WS are sensitive to differences in small numbers, whereas those with DS perform even more poorly than younger MA infant controls. By contrast, in adulthood, scores for DS

in the number domain outstrip those for WS (Paterson et al., 2006). This highlights the importance at examining an entire developmental trajectory rather than a snapshot of development in childhood or adulthood.

Another example comes from studies of children with unusual genetic mutations. We have for several years been examining the cognitive phenotypes of children with deletions within the WS critical region but which are smaller than the typical WS deletion on chromosome 7 (Tassabehji et al., 1999; Karmiloff-Smith et al., 2003). Our aim is to delineate the functions of various genes in expressing the full WS phenotype. Here again developmental trajectories have played a crucial role. In the case of one partial deletion child, HR, we found on initial testing that she did not differ from normal controls on the Bayley Scales of Infant Development. We could have concluded that the genes deleted in her case played no role in the WS phenotype. However, as we began to trace her trajectory over developmental time, we saw that, although she had a milder phenotype, she none the less progressively approximated the WS phenotype and drew away from the typical trajectory. This was true at both the level of facial dysmorphology (Hammond et al., 2005) and that of her cognitive phenotype (Karmiloff-Smith et al., 2006). Figure 1 provides an illustration of this changing pattern.

- insert Figure 1 approx. here -

Another example from developmental cognitive neuroscience is provided by Scerif and colleagues (2005) who investigated visual search in toddlers with FXS and with WS. These researchers demonstrated how important it is to go beyond mere scores to examine patterns of errors. While both groups of atypically developing toddlers reached a similar overall level compared to MA controls, their pattern of errors was very different. Toddlers with WS made the highest number of erroneous touches on distractors. They were more affected than the other groups by the combination of larger display size and target–distractor similarity (conjointly increasing the perceptual load of

the search task). By contrast, the toddlers with FXS made more errors of perseverance to targets already visited. In other words, where performance scores did not distinguish between the two syndromes, their respective patterns of error did.

A third example comes from face processing in WS. There is no doubt that face processing is a relative strength in this syndrome, in that on some standardized tests individuals with WS achieve scores in the normal range (Bellugi et al., 1988; Udwin & Yule, 1991). However, it would be erroneous to maintain that face processing *develops* normally in this clinical group. Several behavioural and electrophysiological studies point to atypical development of face processing in WS compared to controls (Grice et al., 2003; Karmiloff-Smith et al., 2004). The general consensus (but see Tager-Flusberg et al., 2003, who continue to maintain that WS face processing is no different from healthy controls) is that the behavioural proficiency in WS face processing (and in ASD face processing) is underpinned by different cognitive processes (Annaz, 2006; Deruelle et al., 1999; Karmiloff-Smith, 1997, 1998; Karmiloff-Smith et al., 2004; Rossen et al., 1996). This was further corroborated by our ERP study comparing the brain processes of healthy controls versus adolescents/adults with WS when processing faces and cars (Grice, et al., 2003), as well as in another study of cerebral integration (Grice et al., 2001). The face processing findings highlighted the fact that although healthy controls processed both human and monkey faces in a relatively similar way, their brains treated cars very differently. By contrast, the brains of participants with WS displayed no differences between faces and cars. Moreover, unlike the healthy controls who showed a right hemisphere dominance for upright faces, the clinical group failed to display any difference in hemispheric activation (Karmiloff-Smith et al., 2004). This highlights two facts about the deviant trajectory of WS face processing, despite their behavioural proficiency. First, there is a lack of specialisation: individuals with WS show similar electrophysiological responses for both faces and cars, i.e., they have not progressively restricted the brain circuits responsible for face processing uniquely to face stimuli, but

process all manner of visual stimuli in a similar way. Second, there is a lack of localisation: healthy controls show stronger processing for faces in the right hemisphere, whereas the clinical population displayed equivalent bilateral activation. The lack of specialisation and localisation in WS face processing indicates that, despite enormous daily experience with faces, a face processing module fails to emerge over developmental time in this clinical population. In other words, their proficiency on some standardized tasks is achieved through different cognitive and brain processes than in normal development. It follows that clinicans need to be cautious when they encounter scores in the normal range, given that these may camouflage different cognitive and brain processes from healthy controls.

The sensitivity of standardised tests is, as we saw above, open to discussion, raising the risk that scores in the normal range may be achieved by atypical brain and cognitive processes. It also raises questions about what is being matched when researchers do group or individual MA matching. Annaz (2006) illustrated these problems by testing children with WS and those with high-functioning autism (HFA) on the Benton Face Recognition Task (Benton, Hamsher, Varney, & Spreen, 1983). Figure 2 illustrates how both groups score within normal range on this face-processing task. However, to examine whether both groups were processing faces like their typically developing counterparts, Annaz carried out an in-depth examination of their face recognition skills. She found that both clinical groups performed significantly more poorly on face-specific tasks in which configural processing was manipulated, suggesting that the Benton task can be solved by featural processing and does not require the configural processing used by normal controls.

------Figure 2 approx. here--------

We have illustrated in the case of face processing just how crucial it to differentiate ‘normal’ scores at the behavioural level from underlying cognitive and brain processes. It is also obvious that the choice of a matched control group has theoretical

implications. If one matches on IQ, it implies that intelligence affects the domain in question, say, language. If one matches, say, WS with DS, this is not theory neutral because a match on their overall IQ camouflages the fact that in one case the score is brought down by the spatial component and in the other case by the verbal component. These differences will clearly affect all subsequent measures. So, what is the best way to gain a deeper understanding of developmental disorders? We believe that it is by building task-specific, full developmental trajectories.

The need for developmental trajectories

Of course, the most informative way of gaining an insight into how developmental changes occur over time in clinical groups (or, in fact, typically developing children also) is to conduct longitudinal studies. However, these studies are highly time-consuming and may put parents, children and teachers under unnecessary pressure. Drop-out rates are indeed high in longitudinal studies. An alternative to the longitudinal method is to build ***developmental trajectories*** by means of a cross-sectional design. This approach has been successfully used in recent studies (Annaz, 2006; Karmiloff-Smith et. al., 2004; Thomas, et al. 2001). The developmental trajectories approach seeks to build a task-specific typical developmental trajectory by first measuring performance across a wide range of ages in the normal population. Then, given an individual with a disorder, one can next establish whether his/her performance fits *anywhere* on the typical trajectory. Unlike the use of matched controls, this comparison is theory neutral. Secondly, one can assess whether the individual fits on the trajectory at the position predicted by their CA or MA. Additionally, one can use a variety of other predictors (e.g., Language Age, Non-Verbal Reasoning Age, etc.) and assess whether the individual fits on the normal trajectory according to *any* aspect of their cognitive profile. Indeed, one will often discover that predictors differ between healthy controls and the clinical group. So, for instance, whereas language predicts scores in

numerical cognition in WS, it is spatial scores that predict numerical outcome in the typical group (Ansari et al, 2005; Ansari & Karmiloff-Smith, 2002).

Tracing developing trajectories is not only possible for the normal population. Given a group of individuals with a certain disorder, with a wide age range, it is also possible to construct atypical task-specific developmental trajectories for a particular disorder and contrast this against the typically developing group. So, rather than comparing scores at a single point in development, the trajectories approach offers a more direct way of addressing the question "Does the target behaviour ***develop normally or atypically*** in the disorder?" Such an approach also makes it possible to reconsider the notions of delay versus deviance.

An illustration comes from a cross-syndrome study (WS, DS, and ASD) by Annaz (2006). She and her colleagues investigated the development of featural and configural face recognition using the Jane faces task that had been extensively tested on the normal population (Mondloch et al., 2003). In the low-functioning ASD group, atypical U-shaped performance was observed on the inverted featural face trials: younger children with autism displayed better performance on inverted trials, followed by a decrease in accuracy at around 9 years of age (Figure 3). Yet for the whole developmental period, accuracy on upright featural trials continued to increase. However, performance on the configural trials did not significantly increase with CA or when assessed against other predictors (such as language). Had the research used the traditional MA-matched individual or group comparisons, these effects would actually have been masked.

Figure 3 about here

The use of the trajectories approach made it possible to go beyond describing behaviour as delayed. In other words, it becomes possible to provide more in-depth descriptors in terms of a **delayed onset**, which implies a normal rate (not statistically different from

normal trajectory); a **delayed rate** of developmental trajectory, which implies normal onset but slower rate of increase in performance; a **delayed rate and onset**; or, finally, **zero rate** (gradient not significantly different across time) (Annaz,2006). It is also possible to examine intra- and inter-group variability using the trajectories approach.

Use of developmental trajectories is not only necessary at behavioural level but it also needs to be complemented at the neuroanatomical level (Shaw et al., 2006). Shaw and colleagues used a longitudinal design to examine the relationship between cortical development and cognitive variation. They found a marked developmental shift from a predominantly negative correlation between intelligence and cortical thickness in early childhood to a positive correlation in late childhood and beyond. This study indicates that the neuroanatomical expression of intelligence in children is dynamic. Many other studies also indicate that IQ levels are not static but change with brain development and are impacted by environmental factors. Indeed, environmental factors may play a more important role than research often grants it (Mareschal et al., 2005). A child must always be considered within the environment he/she lives, because as soon as parents are told that their child has a developmental disorder, their behaviour changes subtly. They may unwittingly impede their child from freely exploring the environment and/or they may make the child avoid making mistakes, whereas the natural process of learning actually involves erroneous overgeneralisations and so forth.

Concluding thoughts

No approach to developmental disorders is without its inherent problems. And, Neuroconstructivism is no exception. For example, Thomas (2005) highlights two unanswered problems associated with the theoretical assumptions of Neuroconstructivism. First, a clearer picture is needed of the initial domain-relevancies that pre-date a particular domain, and of the nature of the process that eventually delivers domain-specific functional structures. The second difficulty is related to methodological

issues of building developmental trajectories from infancy through to adulthood. It cannot be assumed that the same task is treated in the same way across developmental time, i.e., using the same brain and cognitive mechanisms at very different ages. Clearly these questions need to be at the heart of new research within the developmental trajectories approach.

In our view, the notions of ***interactivity***, ***competition, compensation, specialization, localization and modularization*** will be key in characterising in more depth how atypical development proceeds at the cognitive level, notions that have significant implications on the formation and functioning of mechanisms over developmental time (Karmiloff-Smith, 1992, 1998; Scerif & Karmiloff-Smith, 2005; Karmiloff-Smith & Thomas, 2003; Thomas 2003, 2005), and as yet these mechanisms have in the main been neglected in developmental cognitive neuroscience. We reiterate the importance of examining more closely 'scores in the normal range'. It is also important to recall that phenotypical outcomes at the cognitive level could stem from much lower-level deficits. Indeed, a very small difference in developmental timing, gene expression, neuronal formation, migration and density, and many other genetic and biochemical factors can impact on development over time and result in much greater deficits in the phenotypic outcome. This is why we contend that the task-specific developmental trajectories approach, starting wherever possible at the very outset of infant development, constitutes a first but important step towards gaining a deeper understanding of both the dissociations and associations across different syndromes.

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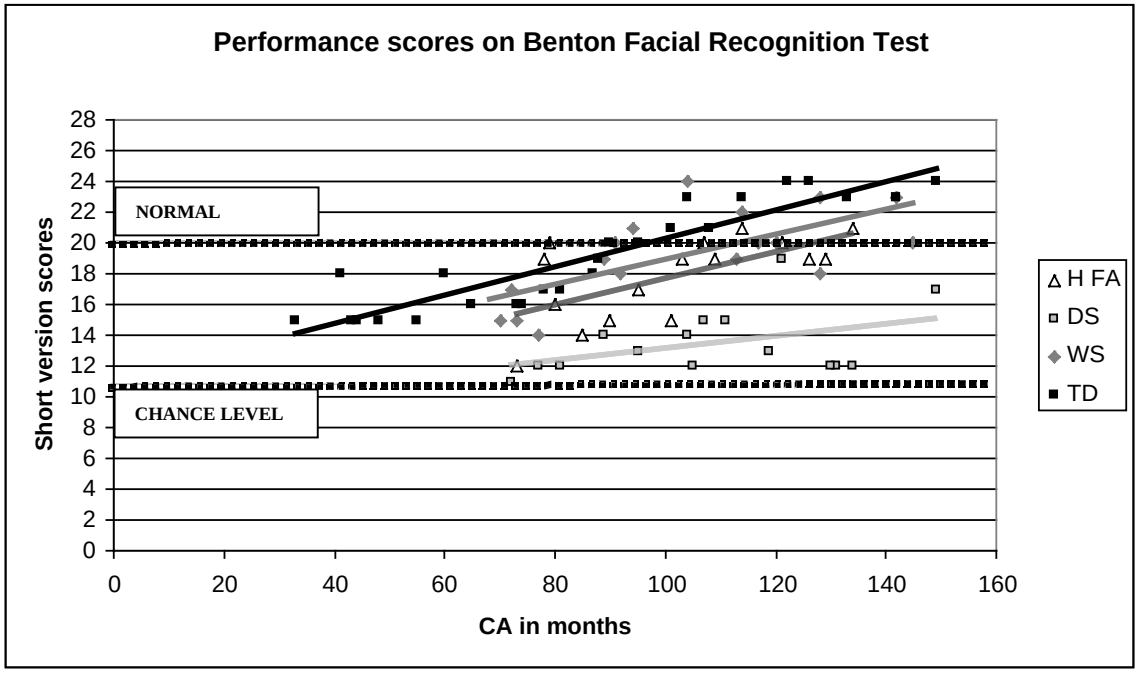
Figure 1

Figure 2


Performance scores on Benton Facial Recognition Test
Short version scores
CA in months
NORMAL
CHANCE LEVEL
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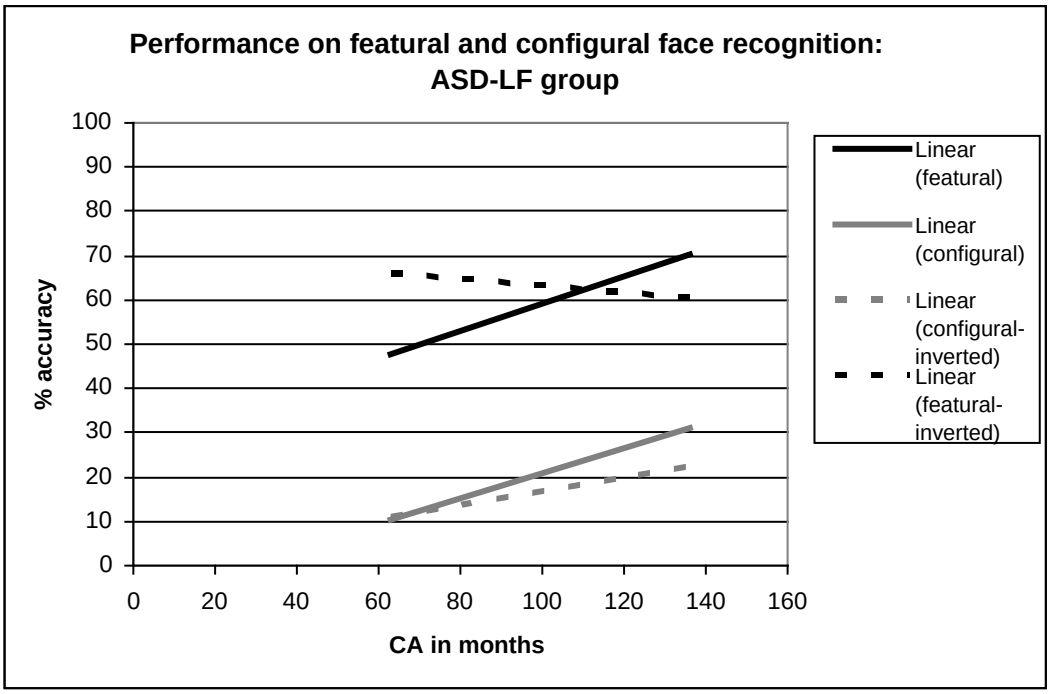
160

Figure 3


Performance on featural and configural face recognition:
ASD-LF group
% accuracy
100
90
80
70
60
50
40
30
20
10
0
0
20
40
60
80
100
120
140
160
CA in months
Linear (featural)
Linear (configural)
Linear (configural-inverted)
Linear (featural-inverted)