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349

Gavin Price

Numerical Magnitude Representation in Developmental Dyscalculia

Behavioural and Brain Imaging Studies

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ABSTRACT

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Diss.

Developmental dyscalculia (DD) is a behavioural learning disorder affecting the successful acquisition of arithmetic skills. The root causes of this disorder, however, are poorly understood. This thesis investigates the theory that dyscalculia is caused by a core deficit in the representation and processing of numerical magnitude information by comparing behavioural and functional magnetic resonance imaging (fMRI) profiles during symbolic and nonsymbolic numerical comparison. Dyscalculic and typically developing (TD) children are compared on both the behavioural and neural distance effects. The behavioural results reveal that DD children show stronger effects of distance on comparison accuracy than the TD group in both symbolic and nonsymbolic comparison. fMRI results reveal that during nonsymbolic numerical comparison the TD group show increased activation in the right intraparietal sulcus for small distance comparisons relative to large distance comparisons. The DD group, on the other hand show no such distance related modulation of brain activity in this region. As the IPS is thought to house a domain specific representation of numerical magnitude these results suggest a core deficit in the representation of numerical magnitude in DD. Brain activation during symbolic comparison, on the other hand, did not reveal parietal differences between groups, but rather a set of regions which may relate to the visual recognition and processing of Arabic digits.

A high rate of comorbidity exists between dyscalculia and dyslexia, and the causes of this comorbidity are poorly understood. Therefore this thesis also investigates whether the mental representation of numerical magnitude in children with comorbid dyscalculia and dyslexia (CM) shows more in common with that of children with either pure dyscalculia or pure dyslexia (DL) using behavioural evidence from symbolic and nonsymbolic numerical comparison tasks. The results reveal that while the DD group show stronger accuracy distance effects during both symbolic and nonsymbolic comparison, the CM group show a stronger accuracy distance effect during symbolic number comparison only. These results suggest that while the DD group has an impaired representation of numerical magnitude, the CM group has an intact representation but a specific deficit in accessing that representation through visual symbols, a deficit which is not shared with either the DD or DL groups.

Keywords: dyscalculia, fMRI, distance effect, comorbidity, number comparison, number sense

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CONTENTS

1 INTRODUCTION

Numbers are one of the most pervasive stimulus categories in our natural environment. Almost every walk of life requires the use of numerical information, from telling the time, through the use of money to complex computational procedures. Numbers are an integral foundation of modern society.

There are, however, a large number people who struggle to learn arithmetic, and even struggle with the most basic numerical processes, such as judging the larger of two numbers. This mathematical learning disorder is called developmental dyscalculia (DD), and is as common as dyslexia, yet comparatively understudied. Despite having equivalent intelligence, socio-economic background and schooling environment as their typically developing peers, approximately 3-6% (Shalev, Auerbach, Manor, & Gross-Tsur, 2000) of individuals fail to develop the numerical skills necessary to carry out even the most basic numerical operations with the same ease as the rest of us.

Although impairments of numerical processing resulting from acquired brain damage have been studied for over a hundred years, the last ten years have seen a dramatic increase in the number of research studies investigating the neuro-anatomical networks which support numerical cognition in the healthy brain. Despite the dramatic advances in our understanding yielded by the growing body of numerical cognition research, developmental dyscalculia has remained relatively understudied, and its causes remain poorly understood.

Recent theoretical advances in the understanding of numerical cognition in healthy adults have identified key neural substrates for the representation and processing of numerical magnitude information. These developments have prompted some researchers to suggest that a developmental impairment of this neural circuitry may underlie DD (Butterworth, 1999; Dehaene, 1997). According to this view, impaired neural representation of numerical magnitudes undermines the foundation on which school level arithmetic learning is based.

In order to develop effective interventions for DD, its root causes need to be clearly understood. Research into these causes has been hindered by highly variable selection criteria and terminology across studies, reducing the coherent impact of multiple sets of results. Furthermore, there has been a general tendency for studies to focus on higher level arithmetic abilities rather than fundamental numerical processing (Ansari & Karmiloff-Smith, 2002).

This thesis investigates the integrity of the mental representation of numerical magnitude in children with DD, by comparing brain activations during numerical comparison with those of Typically Developing (TD) children.

A high rate of comorbidity exists between dyscalculia and dyslexia, yet, as with the root causes of DD, the source of this high comorbidity rate is as yet unclear. Therefore, this thesis also investigates the integrity of the mental representation of numerical magnitude in children with comorbid dyscalculia and dyslexia, in order to shed light on the source of arithmetic impairments in comorbid children.

This thesis will begin by briefly reviewing the historical context of research into domain specific impairments of numerical processing, and will then proceed to outline the behavioural characteristics of DD. This will be followed by a review of domain general and domain specific theories of DD, including a review of recent neuroimaging research into the neural substrates of numerical cognition in healthy adults, typically developing and atypically developing children. The current state of knowledge regarding comorbidity between DD and Dyslexia will be briefly discussed.

Behavioural and functional magnetic resonance imaging (fMRI) evidence will then be presented from a numerical comparison paradigm that investigates both symbolic and non-symbolic numerical comparison. Each results section will close with a brief discussion specific to the empirical questions answered by that data set, and the thesis will close with a general discussion, including outlines for future directions of research in this field, as well as possible implications for focused interventions.

2 DEVELOPMENTAL DYSCALCULIA

> *A structural disorder of mathematical abilities that has its origin in a genetic or congenital disorder of those parts of the brain that are the direct anatomico-physiological substrate of the maturation of the mathematical abilities adequate to age, without a simultaneous disorder of general mental functions (Kosc, 1970)*

The ubiquity of numerical information in everyday life means that the ability to process that information is taken for granted by many people. In comparison to the widespread awareness of other developmental disorders such as dyslexia and ADHD, developmental dyscalculia (DD) remains relatively unknown. When one contrasts the large body of research into dyslexia to the small, but growing research body into dyscalculia, it is clear that the latter has been somewhat neglected. It has even been suggested that impairments in mathematical abilities are more "socially acceptable" than equivalent deficits in reading, writing or spelling (Cohn, 1968). Over the last fifty years, the ratio of reading disability studies to dyscalculia studies has declined from 100:1 to 14:1 (Gersten, Clarke, & Mazzocco, 2007), but despite the increase in dyscalculia research, studies investigating reading disabilities are still far more numerous.

Temple (1992) defines mathematical disability as "a disorder of numerical competence and arithmetical skill which is manifest in children of normal intelligence who do not have acquired neurological injuries", and the vague nature of this definition is indicative of the level to which the causes and manifestations of DD are currently understood. Despite the paucity of research into origins and treatment of DD, poor numeracy is no less of an obstacle to successful education and employment than poor literacy (Bynner & Parsons, 1997), and furthermore, epidemiological studies have estimated that DD is as widespread in the general population as dyslexia with prevalence estimates in the range of 3.5-6.5% (Badian, 1983; Gross-Tsur, Manor, & Shalev, 1996; Kosc, 1974; Lewis, Hitch, & Walker, 1994).

3 HISTORICAL PERSPECTIVE

The history of research into mathematical learning disabilities has its roots in neuropsychological case studies reported in the early part of the 20th century. One of the first studies reporting a case of calculation deficits in the absence of any aphasia was a report by Lewandowsky & Stadelmann (1908) who observed a patient with posterior left hemisphere lesions resulting in an isolated impairment of written and mental calculation. Prior to that time it had been widely thought that impairments of arithmetic occurred only as a consequence of aphasia. Furthermore, Lewandowsky and Stadelmann's report was a sign of things to come, in that it examined the calculation deficit in its component parts, rather than viewing arithmetic as a unitary construct. This is an issue which remains an important focus even in modern day research (Gersten et al., 2007).

The first suggestion of an anatomically specific calculation centre in the brain, specifically the left angular gyrus came from Peritz (1918), and subsequently, Henschen (1919, 1925) first used the term "Akalkulia" or acalculia, to describe a disorder arising from damage to a distinct and autonomous cortical network responsible for the arithmetic processing.

The varied loci of brain lesions that lead to the calculation deficits observed by Henschen, illustrates the difficulty in assigning "calculation" per se to a single brain region, but the major impact of his work was to reveal that calculation deficits could occur in the context of intact language abilities. Despite this apparent dissociation, some patients did exhibit impairment in both language and calculation, and subsequently, Berger (1926) demonstrated that acalculia could present as a specific cognitive deficit, but could also be part of a larger clinical spectrum, including disturbances in memory and language. Berger proposed a classification system whereby calculation impairments in isolation would be termed "*Primary Acalculia*" and the calculation deficits concomitant with other disorders, "*Secondary Acalculia*" (Berger, 1926). Later, Hecaen, Angelergues, & Houilliers (1961) extended the conceptual division of calculation impairments by attributing problems in performing calculations to three neurobehavioral impairments: agraphia or alexia for numbers, spatial dyscalculia, and anarithmetia (pure deficit of calculation).

Moving on from studies of acquired numerical processing impairments, in 1970 a seminal paper published by Kosc (1970) attempted to summate existing research on mathematical learning disabilities and apply a structured classification system. Furthermore, Kosc promoted a definition that stated DD could not be accompanied by impairments of general intelligence and still be considered as a specific mathematical learning disorder. Subsequently, Kosc was the first to coin the term "Developmental Dyscalculia" (Kosc, 1974), and also importantly highlighted what he called "pseudodyscalculia" which could arise from external factors such as poor teaching. It was not until 1980 that mathematical disabilities were recognised in diagnostic manuals of the psychiatric profession (*DSM-III*, American Psychiatric Association, 1980), using a definition that stemmed from the earlier work of Kosc (1970), relying on discrepancy between mathematics performance and general intelligence.

Recent years have seen a rapid growth in research interest in DD. However, there still exists no agreement on the existence of a domain specific core deficit that underlies the disorder, which could guide diagnosis and intervention. Instead, a range of differing terminologies and diagnostic criteria used across studies has made it difficult to combine disparate findings in order to discern a coherent research body.

4 TERMINOLOGY AND DIAGNOSIS

4.1 Terminology

One of the reasons for the lack of unified progress in understanding dyscalculia is the wide range of terminologies that have been used to describe the disorder. Examples of different terms include "Mathematics Disorder" in the DSM-IV (American Psychiatric Association, 1994), "Developmental Dyscalculia" (Gross-Tsur et al., 1996; Kosc, 1970; Shalev & Gross-Tsur, 1993, 2001), "Arithmetic Learning Disabilities" (Koontz & Berch, 1996) "Specific Arithmetic Learning Difficulties" (Lewis et al., 1994; McLean & Hitch, 1999), "Mathematics Disabilities" (Geary, 1993; Geary, Hamson, & Hoard, 2000; Geary, Hoard, & Hamson, 1999), and "Arithmetic Deficits" or "Mathematics Difficulties" (Jordan, Kaplan, & Hanich, 2002).

While the terms mathematics, arithmetic, math, arithmetical are essentially used interchangeably across the literature, and denote the same area of study, there is an essential difference between the terms disability and difficulty (Mazzocco, 2007). While 'Disability' reflects an inherent inability to acquire the necessary skills within a given learning domain, and suggests a biologically based disorder, the term 'difficulty' has been explicitly defined as referring to poor achievement stemming from any one of a number of causes, with no presumed biological basis (Hanich, Jordan, Kaplan, & Dick, 2001a; Jordan, Kaplan, Oláh, & Locuniak, 2006). Mathematical difficulties is a term that encompasses not only a broader range of causes, but also a much wider range of performance than is typically denoted by the term 'disability', the former including performance in the below average to low average range on standardised arithmetic tests (Gersten, Jordan, & Flojo, 2005). "Mathematical Difficulties" are often operationalised as those scores which fall below approximately the 35th percentile on standardized scores, that is, the lowest 35% of performers, a cut off which sits high above the estimated prevalence rate for developmental dyscalculia (Mazzocco, 2007).

The contrast between these definitional terms means that the research field has, in broad terms, employed two different population samples (those with Dyscalculia and those with mathematical difficulties) yet the findings from one are frequently generalised to the other. This may in part explain the apparent difficulties in isolating the causes of DD, when much of the influential behavioural research has in fact focused on the more heterogeneous group of those with 'mathematical difficulties'.

In the present work, the term developmental dyscalculia (DD) will be used to refer to a specific impairment of school level arithmetic ability diagnosed with a selection criteria of at least the lower 10th percentile, or 1.5 standard deviations below the control mean on standardised arithmetic tests, or equivalent, in the absence of other learning disorders or neurologically based developmental abnormalities. When reviewing studies which use less strict selection criteria, their populations will be referred to as having arithmetic difficulties (AD) but it should be noted that these populations are likely to include children with DD. These terms will be used even when the original study employs alternative labels, so as to maintain consistency and allow easier comparison of separate research findings.

4.2 Diagnosis

Clinical diagnosis of DD usually occurs on the basis of a discrepancy criteria, whereby a child's score on a standardised test of arithmetic is compared to non-arithmetical intelligence measures, or by a 2 year difference in chronological school grade and level of arithmetic achievement (Shalev & Gross-Tsur, 2001).

There are many reasons, however, why a child's performance may fall below the expected level in a given subject. Motivation, teaching method, learning environment may all vary in such a way as to reduce the child's performance in a given subject, and hence assessment by a qualified clinician is necessary to establish the presence of a learning disorder (Brody & Mills, 1997). Attentional difficulties (Lindsay, Tomazic, Levine, & Accardo, 2001), mathematics anxiety (Faust, Ashcraft, & Fleck, 1996), mainstreaming in classrooms, whereby children of different abilities are not separated but rather taught together in the same class, inadequate teaching methods and untested curricula (Miller & Mercer, 1997) are some examples of non-neurobiological factors which can adversely affect mathematical performance in children, yet should not qualify a child as Dyscalculic. Thus it remains important that at the clinical level diagnosis is highly tailored to the individual, in that it takes account of individual circumstances and extraneous factors which may negatively influence learning, and is conducted by trained specialists capable of assessing the multiple potential sources of mathematical deficits.

Discrepancy scores as a criterion for diagnosing DD run the risk of failing to identify some cases. While it is important to rule out concomitant deficits in general IQ and other cognitive domains, it is also possible that the underlying cognitive deficit that leads to DD may impair performance on other standardised tests such as measures of spatial IQ for example (Mazzocco, 2007). Naturally it is hard to determine the direction of causality when two impairments are evident in separate tests, such as arithmetic and spatial IQ. It is easy to assume that the deficit in the standardised test measuring the more domain general cognitive system (IQ in this case) is the one influencing the impairment of the more domain specific system (arithmetic in this case). However, it may also be the case that the standardized tests commonly used to assess basic processes such as spatial IQ, are not as pure a measure as is generally assumed, and that impairments in more domain specific systems such as a "Number Module" (Butterworth, 1999) or "Number Sense" (Dehaene, 1997) may impair performance.

In the absence of more advanced diagnostic tools, operational criteria for research studies are typically discrepancy criteria, or simple cut off scores on standardised arithmetic tests. An overview of some of the criteria that have been used is given in Table 1, which shows the study, the test used to assess arithmetic ability, the selection criteria, and any additional exclusionary criteria in order for a participant to be categorised as dyscalculic.

Although DD research is in its relative infancy, and thus such discrepancy and cut off criteria may be the most appropriate until a deeper understanding of the disorder is achieved, as that understanding progresses a greater uniformity of selection criteria which use more focused and in depth diagnostic tools will be important in building a coherent research body.

TABLE 1 Examples of Selection Criteria for AD and DD studies.

Study	Terminology	Test	Criteria	Exclusions
(B Butterworth, 2003)	Dyscalculia	Item-timed tests of enumeration and number comparison	Bottom 2 stanines (lowest 11% of scores)	
Geary et al., (1999)	Mathematical disabilities	Woodcock Johnson Mathematics Reasoning	Bottom 30th Percentile	IQ < 80
Geary et al., (2000)	Mathematical disabilities	Woodcock Johnson Mathematics Reasoning	Bottom 35th Percentile	
Jordan et al., (2002) Jordan et al., (2003a, b)	Mathematics difficulties	Woodcock Johnson Broad Mathematics Composite	Bottom 35th Percentile	
Koontz &Berch (1996)	Arithmetic learning disabilities	Iowa Tests of Basic Skills	Bottom 25th Percentile	Below 30th percentile on reading or below normal IQ
Landerl et al., (2004)	Developmental Dyscalculia	Item-timed arithmetic and teacher's classification	3 Standard Deviations below the mean	50th + Percentile IQ
McLean & Hitch (1999)	Specific arithmetic learning difficulties	Graded Arithmetic-Mathematics Tests	Bottom 25th Percentile	Mid-50% on Primary Reading Test
Shalev et al., (1997)	Developmental Dyscalculia	Standardised arithmetic Battery	2 grades below chronological age group average	IQ < 80
Temple & Sherwood (2002)	Number fact disorder	WOND numerical operations	12 months below chronological age group average	

5 BEHAVIOURAL CHARACTERISTICS

Mathematical proficiency requires mastery of numerous skills, from counting and enumeration all the way to higher level reasoning, which may be employed to different degrees depending on the mathematical problem being solved. Children with DD may have deficits in one or more of the elementary skills necessary for arithmetical performance, or may even have impairments in understanding and carrying out the actual principles and procedures of mathematics (Geary et al., 2000; Hanich et al., 2001). The nature of these abilities and their impairments may have varying development trajectories, and furthermore may differ between adults and children (Mazzocco, 2007).

In addition to the wide range of requisite skills, the abilities required to maintain arithmetic proficiency change over time, both in the range of necessary abilities and the skill with which those abilities are performed. Mathematics becomes increasingly complicated as school progresses, and thus the nature of behavioural deficits may vary over time. An important question is whether deficits observed at a later stage of schooling are the result of a difficulty with a new concept or skill, or can they be traced back to an underlying core deficit that is stable across development, and which interrupts the structured acquisition of more advanced mathematical abilities.

In other words, DD may emerge at different stages of development, and this may be the result of different cognitive deficits interacting with the changing skill set required for successful arithmetic performance. Indeed, it has been observed that out of a sample of 3rd grade DD children, 65% met the diagnosis criteria in kindergarten, but 20% only began to meet the criteria during second grade (Mazzocco & Myers, 2003). Since it is unclear whether those 20% would have been diagnosed earlier had more sensitive criteria been used, this finding highlights the need for developmentally appropriate diagnostic criteria.

In order to better understand the behavioural characteristics and core deficits underlying DD, it is important for researchers not only to characterise the nature of mathematical deficits that occur in children, but also the developmental trajectories of those impairments. Such developmental research, however, remains sorely underrepresented in the field. An in depth characterisation of the behavioural deficits which occur in DD is a necessary starting point for the investigation into whether DD is rooted in a domain specific core deficit.

5.1 Arithmetic

Despite the relatively recent growth of the dyscalculia research field, and the problems faced therein, there is a general agreement on some of the primary behavioural manifestations of the disorder.

The most consistently observed deficit in DD and AD is the learning and retrieval of arithmetic facts from semantic memory. This lack of automaticity in arithmetic fact retrieval is also associated with the perseverant use of immature problem-solving and counting strategies (Geary, 1993; Geary, Bow-Thomas, & Yao, 1992; Geary, Brown, & Samaranayake, 1991; Geary et al., 2000; Geary, Hoard, Byrd-Craven, & Catherine DeSoto, 2004; Hanich, Jordan, Kaplan, & Dick, 2001b; Jordan & Hanich, 2003; Jordan, Hanich, & Kaplan, 2003; Jordan & Montani, 1997; Landerl, Bevan, & Butterworth, 2004; Russell & Ginsburg, 1984). As an indication of the severity of this deficit, typically developing children have been found to recall an average of three times as many arithmetic facts as DD children (Hasselbring et al., 1988).

Pellegrino & Goldman (1987) observed that the best indicator of DD was an impairment of the efficient retrieval of arithmetic solutions from memory. The authors suggested that those children who were unable to recall the answers to simple arithmetic problems fluently were forced to resort to finger counting in order to compute the solution. Consequently these children were unable to follow and assimilate the more complex procedural knowledge being taught. Thus, a deficit in arithmetic fact retrieval may have knock on effects for other aspects of arithmetic ability which may be unrelated in terms of underlying processes.

Furthermore, when DD children do recall arithmetic facts from memory, their answers are error prone and show reaction time and error patterns different from typically developing children (Barrouiliet, Fayol, & Lathuliere, 1997; Fayol, Barrouillet, & Marinthe, 1998; Geary, 1990; Rasanen & Ahonen, 1995). These findings have been incorporated into many attempts to develop focused interventions for DD, however, deficits in arithmetic fact retrieval tend to persist throughout elementary school even in the event of focused intervention (Jordan & Montani, 1997; Ostad, 1997, 1999).

A second group of commonly observed deficits are difficulties executing calculation procedures, and the use of immature problem-solving strategies (Butterworth, 1999; Geary, 1993). Geary and colleagues (Geary et al., 2000; Geary et al., 1999) observed that in the first and second grades, children with AD frequently used less efficient strategies than controls for solving calculations, such as counting all rather than counting min (whereby counting starts with the higher number in the equation and proceeds until the solution is reached). Furthermore, while typically developing children progressed from finger counting to verbal counting and fact retrieval from first to second grade, AD children did not show the same developmental trajectory. A cross sectional study by Geary et al., (2004) revealed that while typically developing children progress from finger counting through verbal counting to fact retrieval from 1st to 5th grade, much fewer children with mathematical learning disabilities showed the same developmental trajectory. This pattern of results shows that atypical development of calculation procedures is present only in some of the sample studied, and perhaps this inconsistency is due to the liberal selection criteria used by Geary and colleagues (see Table 1). Thus it emphasises the need to employ strict selection criteria when defining atypical populations for research, in order to allow a more specific focus on subtypes of developmental learning disorders.

Although DD and AD children have been observed to show impairments in both arithmetic fact retrieval and procedural knowledge, it has been suggested that in fact these deficits are dissociable (Temple, 1991; Temple & Sherwood, 2002) and hence may stem from separate causal pathways. However, such dissociations have primarily been evidenced using case rather than group studies, and hence are difficult to generalise. Furthermore, contradictory evidence has revealed no dissociation between arithmetic fact ability and procedural ability in children with numerical processing difficulties (Ashcraft, Yamashita, & Aram, 1992). Similarly, Russell & Ginsburg (1984) found that children with "mathematical difficulties" showed problems with both written calculation problems and arithmetic fact retrieval.

In light of the extant literature, it has been suggested that while procedural problems are likely to improve with experience, retrieval problems are more persistent, because retrieval deficits stem from impairments in semantic long term memory, whereas procedural deficits reflect a lack of conceptual understanding which may be more easily remediated through focused educational intervention (Geary, 1993). However, other authors suggest that both procedural and retrieval deficits may arise from memory impairments, with procedures being simply easier to remember than large numbers of arithmetical facts, which are meaningless without an understanding of cardinality (the numerical value of a set of objects) (Landerl et al., 2004).

Thus, deficits in arithmetic fact knowledge and arithmetic procedural knowledge are common in children with AD and DD, but not universal. Again, the lack of uniformity of these findings may be related to the range of selection criteria employed across studies meaning that populations with heterogeneous impairments of arithmetic are compared to those with more process pure learning disorders.

In addition to impairments of arithmetic fact retrieval and procedural knowledge, some studies investigating children with arithmetic difficulties (not pure DD) have found a lack of understanding of some counting principles in children with arithmetic difficulties, such as counting each object only once and understanding that items can be counted in any order (Geary et al., 1992; Geary et al., 2000; Geary et al., 1999). Although DD children show considerable improvement in counting ability from first to second grade (Geary, 1994), when monitored longitudinally from the age of 10-11 for 3 years, children with AD showed little improvement, and those diagnosed with DD in fifth grade maintained that diagnosis into eighth grade (Shalev, Manor, Auerbach, & Gross-Tsur, 1998). Thus, in children with AD and/or DD counting abilities and understanding of the principles that govern counting appears to be negatively affected to different degrees, but at present there does not seem to be a uniform pattern of impairment across studies. Not all children with mathematical learning difficulties show counting impairments, but in those who do, the deficits tend to persist throughout development.

Studies attempting to characterise arithmetic deficits in DD have yielded a complex set of results. It can be concluded that in general, DD children show marked deficits in arithmetic fact retrieval and delayed development of arithmetic procedures. However, the studies reviewed above essentially provide a characterisation of the range of deficits observed in DD and AD children. What is as yet unknown is whether these impairments are underscored by a core deficit in a cognitive system specialised for the representation and processing of numerical information, or whether they are a by product of impairments in other cognitive domains such as memory or language.

The wide range of arithmetic impairments reviewed here do not provide a coherent characterisation of DD, instead they suggest a distinct lack of uniformity in the behavioural manifestations of the disorder at the arithmetic level. It is possible, however, that this variation is the consequence of an interplay between an underlying core deficit and compensatory mechanisms which vary between individuals. Thus, a core deficit in the mental representation of numerical quantity may impair the development of arithmetic skills, but the exact nature of that impairment varies between individuals depending on their ability to employ other cognitive processes to compensate the core deficit.

Therefore, this thesis investigates the representation and processing of numerical quantity at the most basic level, in order to investigate the existence of a core deficit in DD.

5.2 Basic Processes

Although developmental dyscalculia is a disorder manifest in deficient school level arithmetic, with a range of possible impairments (see above), some researchers have suggested that the root cause of the failure to acquire arithmetic skills is a core deficit in the basic representation and processing of numerical quantity or 'numerosity' (Butterworth, 1999; Dehaene, 1997). In order to investigate this idea, several researchers have investigated very basic numerical processing abilities in children with arithmetic difficulties, as well as in children with more severe DD.

One of the first studies of this nature by Koontz & Berch (1996), employed a task in which children had to decide whether two stimuli were physically identical (e.g. 2 – 2 or A – A), and in a second task had to say whether two stimuli represented the same numerosity (e.g. 2 ●●, 2 – 2, or ●● ●●). The results of this study showed that typically developing children showed interference from numerical information when judging whether two stimuli were physically identical, while those with arithmetic difficulties (AD) did not. In other words, when the stimuli were numerically identical (e.g. 2 ●●), the typically developing children were slower to say no when asked if they were physically identical than when the numerical values did not match (e.g. 2 ●●●). The AD group on the other hand, showed no such interference and answered with the same speed whether the numerical values were the same or different. This suggests that the AD group did not activate the numerical semantic information of the stimuli automatically, while the control children did. On the other hand, when making judgements about the numerosity of stimuli, AD children showed interference from irrelevant physical characteristics, while the typically developing children did not, suggesting that the AD children were attending more to the superficial elements of the stimuli and perhaps having trouble accessing the underlying numerical semantic information.

The idea that DD is associated with a failure to activate internal representations of numerical magnitude has subsequently been explored by Rubinsten & Henik (2005), who investigated the automatic activation of numerical semantic information in a group of adults with developmental dyscalculia using a numerical stroop paradigm. In this task subjects had to select which of two Arabic digits was physically larger (e.g. 3 – 5). Trials were either congruent (larger physical size and larger numerosity), incongruent (larger physical size and smaller numerosity), or neutral (different physical size and same numerosity). This study employed the same design to test the interference of numerical information on judgements of digits size, height and greyness, so in no task was numerosity a task relevant dimension. The results of this study showed that while DD subjects showed interference from numerical information during incongruent trials, they showed no facilitation of processing during congruent trials. It has been suggested that facilitation reflects automaticity while interference reflects attentional processing (Posner, Nissen, & Ogden, 1978). Thus, Rubinsten & Henik (2005) interpret their results as indicating a lack of automatic association of Arabic numerals with their numerical, semantic referents. Whether this lack of association is due to a deficit in the actual construction of those associations, or whether it is due to an impairment of the semantic representation of numerical itself is an open question, and one this thesis seeks to address.

The integrity of the mental representation of numerical magnitude is frequently investigated using numerical comparison paradigms, and several studies have shown impaired processing of numerical magnitude during number comparison in DD. Butterworth (1999) reported the case of Charles, an adult man who suffered with DD his entire life, and at the age of 31 still relied of finger counting to solve simple calculations. During tests of number comparison Charles was forced to rely on counting, leading him to be four times slower than controls and to show a reverse distance effect (numbers that were closer together were faster to compare than those far apart). The distance effect refers to a robust psychophysical effect during numerical comparison first observed by Moyer & Landauer (1967), whereby numbers which are separated by a small numerical distance take longer to compare and elicit more errors than numbers which are separated by a large numerical distance (e.g. comparing 3 vs 5 takes longer to compare and elicits more errors than 3 vs 9).

Geary et al., (1999) observed that children with AD showed marginally lower accuracy than controls during number comparison, particularly so during visual presentation of stimuli compared to auditory presentation. This study used a cut off point of the 30^{th} percentile to define mathematical difficulties, and therefore it is possible that had a more stringent criterion been used, more pronounced group differences would have been observed. An interesting point is that the group classification scheme in the study by Geary et al., (1999) study was based on tests of arithmetic reasoning, which has been suggested to relate specifically to right hemisphere function (Langdon & Warrington, 1997), suggesting that the numerical comparison impairments seen in this study could relate to underlying dysfunction of right hemisphere numerical processing mechanisms.

In recent years there has been a growing emphasis on investigating numerical processing impairments in children with pure dyscalculia rather than less severe arithmetic difficulties. Landerl et al., (2004) conducted the first in depth investigation of basic numerical abilities in children with strictly defined DD (3 standard deviations below the control average on standardised arithmetic tests). The study found that DD children were slower than controls on tasks of number naming, even when general naming speed was controlled. Other studies have also observed slowed naming speed specific to numerical stimuli in DD (van der Sluis, de Jong, & Leij, 2004), suggesting that even the most basic processing of numerical information is impaired in DD. During number comparison, Landerl and colleagues found that DD children were slower than controls when comparing numerosity but not when comparing digit size. DD children were also slower than controls at verbal counting, and marginally slower at dot counting.

This pattern of results provides strong evidence for a cognitive deficit specific to the processing of numerical magnitude in children with DD. The key factor is that in this study the selection criteria was stringent, resulting in a high probability that the atypical group consisted of individuals with genuine learning disorders as opposed to less severe mathematical difficulties and thus, while arithmetical difficulties may stem from a wide variety of sources, developmental dyscalculia appears to be related to a domain specific impairment of the processing and representation of numerical magnitude.

Numerical magnitudes can be externally represented in multiple formats, such as Arabic numerals, number words and non-symbolic arrays (such as dots or squares). This raises the question of whether numerical magnitude processing deficits observed in DD are format specific, or whether they persist across formats. Although different studies have looked at different number formats independently, to my knowledge, only one study to date (Rousselle & Nöel, 2007) has compared numerical magnitude processing across formats in DD children within the same study.

Rousselle & Nöel (2007) demonstrated that DD children were slower and less accurate than controls during symbolic number comparison. During nonsymbolic comparison, however, the authors found no group differences in reaction time or accuracy after controlling for general processing speed and general error rate respectively. The authors suggest that these results reflect an impairment of the ability to access numerical magnitude representations through the use of numerical symbols (Arabic digits) and that this deficit underlies impaired arithmetic performance in DD. However, the DD group in this study comprised children with pure DD as well as those with comorbid reading disabilities, and the effect of collapsing these groups is difficult to assess given the current state of knowledge in the field, as the comorbid dyslexia present in some participants may differentially effect the processing of one format versus another. Therefore, this thesis is the first work to directly compare the effect of presentation format on basic numerical magnitude processing in pure DD.

Another task which is thought to tap the mental representation of numerical magnitude is approximate calculation, whereby participants are asked to choose between the more plausible of two incorrect answers to calculation problem. In contrast to exact calculation, approximate calculation is thought to require access to the mental representations of numerical magnitude (Dehaene, Spelke, Pinel, Stanescu, & Tsivkin, 1999). Children with mathematical difficulties have also been shown to perform worse than controls in approximate calculation, further suggesting an impairment in the ability to access and process mental representations of numerical magnitude in DD (Hanich et al., 2001a; Jordan & Hanich, 2003).

In summary, children with DD appear to show a range of behavioural deficits in school level arithmetic, but importantly, they also show impairments in tasks of basic numerical processing such as number comparison as well as reduced automatic activation of mental representations of numerical magnitude. These findings suggest that the observed arithmetic impairments may stem from the inability to develop typical representations of numerical magnitude and access these in the context of a numerical task, such as performing an arithmetic calculation. Some debate still exists, however, regarding whether the observed behavioural impairments in basic numerical processing stem from a deficit in accessing numerical magnitude representations through Arabic digits, or whether the representation itself in impaired. By comparing numerical comparison performance using both symbolic and nonsymbolic stimuli in children with pure DD, this thesis will address this open question.

6 THE ROOTS OF DEVELOPMENTAL DYSCALCULIA

Although the behavioural manifestations of DD at the arithmetic level are widely agreed upon, and descriptions of impairments in basic numerical magnitude processing are becoming more widespread, there still exists some debate as to the root causes of theses impairments. A broad distinction can be drawn, between causal theories of DD, which focus on domain general causes such as memory or language impairments, and those which focus on domain specific core deficits of numerical processing. Domain general theories have thus far been based primarily in behavioural research, while domain specific theories have stemmed from a growing body of neuropsychological and neuroimaging evidence. Theories from both these approaches to understanding the origins of DD will be discussed in turn.

6.1 Impairments of Domain General Cognitive Systems

One approach to understanding the causes of DD has been to investigate impairments in those domain general cognitive skills which contribute to successful arithmetic performance, such as general IQ, memory (Geary, 1993) and verbal and non-verbal information processing mechanisms identified through neuropsychological test batteries (Rourke, 1989a, 1993; Rourke & Strang, 1978, 1983).

In accordance with clinical definitions of DD which emphasise the impairment of arithmetical abilities in the context of normal general intelligence (e.g. DSM-IV), several studies have revealed no systematic differences in IQ between DD children and their typically developing peers (Gross-Tsur et al., 1996; Landerl et al., 2004; Shalev et al., 2001) and thus, having ruled out low IQ as a cause of DD, research has focused on alternative cognitive domains.

6.1.1 Memory

One hypothesis suggests that impairments of memory systems underlie arithmetic fact retrieval deficits in DD. Impairments in working memory may lead to a failure to construct a reliable network of arithmetic facts to be stored in long term memory, thus impairing fluent mathematical performance (Geary, 1993; Geary, 1994; Geary et al., 1991; Geary & Hoard, 2005).

This theory follows the logic that in order to store the solutions to common arithmetic problems in long term memory, both the problem and the solution must be simultaneously active in short term working memory. Thus, if the problem cannot be maintained in working memory until the solution is calculated, the connection between problem and solution is not stored and the arithmetic 'fact' not learned. Furthermore, if working memory is responsible for the allocation of attentional resources during arithmetical problem solving, impaired working memory may result in incorrect solutions being derived and thus erroneous associations being stored in long term memory.

A further impact of impaired working memory for arithmetic processing would be that in the event of a failure to solve an arithmetic problem, children with poor working memory would not be able to resort to back up strategies that place high demand on the working memory system. Instead they would have to rely on immature, inefficient but less demanding strategies such as finger counting rather than verbal counting, 'counting all' rather than 'counting min' (Geary et al., 2004; Nöel, Seron, & Trovarelli, 2004). However, finger counting can be both a cause and a consequence of poor memory for arithmetic facts, as finger counting leads to delays and errors in working memory (Butterworth & Reigosa, 2007).

As with general IQ, the contribution of working memory to successful arithmetic performance is essential (Andersson, 2006; DeStefano & LeFevre, 2004), and many studies have shown an association between children's working memory performance and mathematical performance (Bull, 1999; Bull & Scerif, 2001; Gathercole & Pickering, 2000). Several studies have reported evidence showing that DD children show impairments of various working memory components including the phonological loop (Hitch & McAuley, 1991; Koontz & Berch, 1996; McLean & Hitch, 1999), visuo-spatial sketch pad (McLean & Hitch, 1999), and central executive tapped by forward and backward digit-span (Geary et al., 1991; Geary et al., 1999; Passolunghi & Siegel, 2004).

However, other studies have not supported the existence of working memory differences between DD children and their typically developing peers. A recent, well controlled study in which DD children were selected on the basis of a stringent classification criteria (Landerl et al., 2004) found no differences between DD children and controls in either backward or forward digit span. Furthermore, a comparison of DD children and controls on a range of working memory measures (Temple & Sherwood, 2002) failed to reveal any significant differences between groups on any measure, including forward and backward digit span, corsi blocks, and word span. Furthermore, this study found no correlation between any of the measures of working memory and mathematical performance, further suggesting no causal link between working memory and DD.

In the absence of a clear and consistent impairment in working memory in DD, some authors have suggested that DD children exhibit an impairment of working memory specific to numerical information. Siegel & Ryan (1989) found DD children to be poorer than controls on working memory tasks requiring counting and remembering digits, but not on tasks that did not involve numerical information, suggesting there may be dissociable memory systems for numerical and non-numerical information. Furthermore, phonological working memory was found to be intact in DD (McLean & Hitch, 1999), although DD children did show a trend towards poorer digit span than controls, thus leading the authors to suggest that a deficit of working memory specific to numerical information may exist. However this study also found evidence of poorer spatial working memory and some aspects of central executive function in DD, so it cannot be argued that the working memory deficits were purely specific to numerical information.

Research investigating working memory impairments in DD has not produced a consistent set of results, and thus impaired working memory is unlikely to represent a core deficit in DD. However, an alternative explanation may be that the failings of the working memory system with regards to numerical information results from a degraded representation of numerical magnitude itself, and thus domain general systems such as working memory are unable to process that information with the same degree of efficiency as non-numerical information. In other words, poor representations of numerical magnitude may result in greater demands on working memory during mathematical tasks, revealing that working memory is associated with DD as a consequence of impaired representations of numerical magnitude.

A further limitation of the argument that impaired working memory underlies arithmetic fact retrieval deficits in DD is that it depends on a functional dependency between working memory and semantic long term memory, in that it assumes arithmetic facts must be successfully held in working memory in order to be transferred to long term memory stores. Yet, there is a wide body of research demonstrating the neural and functional independence of these systems (McCarthy & Warrington, 1990). In other words, it is not necessarily the case that an impairment of working memory would lead to deficits in storage and retrieval of arithmetic facts from long term semantic memory.

Geary and colleagues (Geary et al., 2000; Geary & Hoard, 2001) also suggest that an impairment of semantic long term memory itself may be responsible not only for difficulties in learning and retrieving arithmetic facts, but also for the comorbid reading difficulties frequently found to co-occur with DD. However, there is little evidence for a deficit in non-numerical semantic memory in DD children. Furthermore, Cappelletti, Butterworth, & Kopelman (2001) show in a neuropsychological study that number knowledge is dissociable from verbal semantic knowledge, suggesting that memory of arithmetic facts may be mediated by a separate semantic memory store than that for general semantic memory. In support of this dissociation, neural activation patterns associated with numerical and non-numerical semantic memory have been found to be spatially separable (Thioux, Seron, & Pesenti, 1999), suggesting that a general impairment of long term memory is unlikely to be the root cause of DD.

Thus, the studies reviewed above do not provide a consistent body of evidence to support the hypothesis that impairments in either semantic long term memory or working memory are responsible for the fact retrieval and procedural deficits observed in DD. Thus, while impairments of either working memory or long term memory would undoubtedly impact negatively on mathematical performance, they do not seem to represent a core deficit in DD.

6.1.2 Cerebral Asymmetry and the "Nonverbal Learning Disabilities Syndrome"

Another influential domain general approach to understanding mathematical learning disabilities is the "Nonverbal Learning Disabilities Syndrome" (NLD). Rourke and colleagues have pioneered a research program aimed at revealing subtypes of dyscalculia, the characteristics of which are determined by whether the atypical brain development affects the left or right cerebral hemisphere of the individual (Rourke, 1975, 1993; Rourke & Conway, 1997; Rourke, Dietrich, & Young, 1973; Rourke & Finlayson, 1978; Rourke & Fisk, 1988; Rourke & Strang, 1978). The NLD approach contends that differential patterns of mathematical disabilities observed in children can be explained by the relative contributions and impairments of left hemisphere language systems versus right hemisphere visuo-spatial processing systems.

Rourke & Conway (1997) argue that the left hemisphere subserves the processing of numerical symbols, retrieval of arithmetic facts from semantic memory and simple calculation, while the right hemisphere supports adaptive reasoning and spatial manipulations necessary for arithmetic problem solving. These authors suggest that in contrast to acquired brain damage, which typically affects a focal region and impairs the functioning of an already developed cognitive process, such as calculation per se, developmental impairments of brain function are likely to be more subtle and perhaps more widespread. The impact of a developmental brain level impairment is the interruption of a structuring process during which increasingly more sophisticated abilities are built upon those foundations already established through the learning process. Thus, according to this argument, developmental disorders of mathematical processing are more likely to reflect low level functional impairments to broad domain general systems, rather than the domain specific incapacitation that occurs following acquired brain damage in adulthood. In other words, developmental disorders disrupt a sequence of building certain cognitive abilities, rather than cause the loss of a single existing function (B. P. Rourke & Conway, 1997).

The early work of Rourke and colleagues (Rourke et al., 1973; Rourke & Telegdy, 1971; Rourke, Young, & Flewelling, 1971) revealed that patterns of discrepancy between Verbal IQ and Performance IQ predicted patterns of performance on the Wide Ranging Achievement Test WRAT (Jastak & Jastak, 1965), suggesting that a distinction may be drawn between children with verbal impairments versus those with visuo-spatial impairments. Their subsequent work investigated whether children with different patterns of learning disability would show distinct patterns of performance on a range of neuropsychological tests which tap verbal and visuo-spatial processing (Rourke, 1993).

In the first of these studies, Rourke & Finlayson (1978) compared children with AD, children with RD and children with comorbid AD/RD. It is important to note that RD and AD groups in fact had equivalent arithmetic performance, despite showing very different overall profiles. The classification of RD children was therefore based on the fact that reading performance was impaired to a greater degree than their arithmetic performance. Furthermore, both AD and RD groups showed significantly better performance on the WRAT arithmetic subtest than the AD/RD group, thus the group distinctions are not especially well delineated.

Despite the performance overlap in the arithmetic domain, this study found that the AD/RD and RD groups showed significantly better visuo-spatial and visual perceptual ability than the AD group while the AD group showed significantly better performance on tests of verbal and auditory perception. Contrasts of verbal and performance IQ measures revealed that while the AD/RD and RD groups had superior performance IQ relative to verbal IQ, the AD group showed the opposite pattern. The authors interpreted these findings as reflecting the different cerebral sources of impairment between groups. AD/RD and RD groups showed impairments only on those tasks thought to be subserved by left hemisphere language processes, while the AD group was impaired only on those tasks thought to be underpinned by right hemisphere visuo-spatial processing mechanisms. Thus, despite the equivalent arithmetic performances of the RD and AD groups, the authors suggest that the source and nature of those impairments stem from verbal deficits in the AD/RD group, and visuo-spatial deficits in the AD group.

Rourke & Strang (1978) attempted to confirm the cerebral asymmetry hypothesis by testing the same three groups as Rourke & Finlayson (1978) on a range of motor, psychomotor and tactile-perceptual tasks known to tap left or right hemisphere functional systems, including tests of finger agnosia, finger tapping and grip strength. The results of this study showed that the AD group was impaired relative to the RD and AD/RD groups on several visuo-spatial tests (maze and groove peg board tests), and that interestingly, this difference was particularly pronounced when using the left hand, suggesting a broad neurodevelopmental impairment within the right cerebral hemisphere in the AD group.

Further research by Strang & Rourke (1983) compared the RD and AD groups on the Halstead Category Test (Reiton & Davison, 1974), a complex measure of nonverbal reasoning and concept formation (Rourke & Conway, 1997). Based on Piagetian theory (Piaget, 1954) that the visual and tactile perceptual abilities found to be deficient in the AD group are necessary in order to learn effectively from early sensori-motor experiences, Strang and Rourke (1983) hypothesised that the AD group would be impaired relative to the RD group on the Halstead Category Test. Indeed this was found to be the case, with AD children making significantly more errors than the RD group. While this result does reveal some form of developmental impairment in nonverbal ability in the AD group, there is no evidence to suggest that performance on the Halstead Category Test is right lateralised, and thus this study can be taken as evidence only for the cognitive aspects of Rourke and colleague's "NLD" (Rourke, 1987, 1989b, 1993; Rourke & Conway, 1997) theory, and not for the neuroanatomical hypotheses.

Rourke (1993) points out, the pattern of symptoms exhibited by the AD group is somewhat analogous to those that make up the so called "Gerstmann's Syndrome" (Gerstmann, 1940), namely, deficient arithmetic in the context of normal reading and spelling, visual-spatial orientation difficulties, general psychomotor coordination problems including dysgraphia, and impaired tactile discrimination including finger agnosia. However, while Rourke's research suggest a generalised right hemisphere dysfunction as the root cause of the symptom pattern, Gerstmann's Syndrome is typically associated with damage or dysfunction of the left hemisphere, in particular the left angular gyrus (Benson & Geschwind, 1970; Rusconi, Walsh, & Butterworth, 2005). There is no clear reason for this contradiction, but the existence of Gerstmann's Syndrome as a syndrome is debatable in itself (see below).

While Rourke and colleagues have produced considerable evidence in favour of the cerebral asymmetry hypothesis, the "NLD" cannot account for the evidence reviewed above showing that children with AD and DD show impairments in specific tasks of basic numerical processing. The NLD theory cannot account for the fact that DD children are impaired in the processing of numerical information more than any other stimulus category. There is no explanation within this theory of why a visuo-spatial processing deficit would cause specific impairments in numerical processing. It is highly plausible that developmental impairments in the right hemisphere may be widespread and subtle, and it is known that numerical processing regions and spatial attention areas of the brain lie in close proximity within the superior parietal lobe (Hubbard, Piazza, Pinel, & Dehaene, 2005). Thus, it is possible that developmental abnormalities in these regions may impair both numerical and visuo-spatial abilities, but that is not to say that the numerical impairments are *caused* by the visuo-spatial deficits.

Studies supporting the domain general approach have often used participant samples with a relatively broad range of ability, for example the bottom 30th percentile (e.g. Geary et al., 1999) on standardised arithmetic tests, and thus are likely to contain participants with both AD and DD. It is possible that domain general factors may influence less severe arithmetic difficulties, while dyscalculia as a bona fide learning disorder may be related to a domain specific core deficit.

6.2 Impairments of a Domain Specific Number Module

While it is clear that impairments in a number of cognitive domains can adversely affect mathematical performance, and lead to arithmetic *difficulties*, the theories reviewed above cannot fully account for the incidence and nature of numerical processing deficits in developmental dyscalculia. An alternative approach is to ask, which mechanism or mechanisms, specialised for the processing of numerical information may be impaired in DD?

Several theoretical models have emerged which propose the existence of a domain specific cognitive module for the representation of numerical magnitude. However, some lend themselves to the study of dyscalculia more than others.

McCloskey and colleagues (McCloskey, 1992; McCloskey, Caramazza, & Basili, 1985; McCloskey, Sokol, & Goodman, 1986) have proposed a functional model of numerical processing based principally upon evidence from neuropsychological studies of patients with acquired brain damage.

This model distinguishes mechanisms of number production from number comprehension, and within those mechanisms, distinguishes the processing of Arabic numbers versus verbal numbers (number words). The comprehension system translates either Arabic numbers or verbal numbers into abstract internal representations of number which specify the quantity and the associated power of ten. Calculations are then performed on these representations and the output then translated into verbal or Arabic numbers by the number production module. A further distinction between lexical and syntactic processing of numbers is suggested. This model also proposes stored representations of arithmetic facts which may be individually impaired, rather than impairments occurring on the basis of the type of arithmetic operation. Such a dissociation between subcomponents of arithmetic processing has been reported in multiple cases in the literature (e.g. Temple, 1989).

McCloskey and colleagues' model is principally a model which seeks to explain, at the cognitive level, the numerical processing mechanisms present in the adult brain. The model does not elucidate how such processes may emerge over the course of development within the brain, and hence is of limited utility as a foundation from which to explore the roots of DD.

Though also not explicitly developmental, a more useful model for generating hypotheses regarding the underlying causes of DD because of its specific cognitive and neuroanatomical descriptions, is the "Triple Code Model" (Dehaene, 1992; Dehaene & Cohen, 1995, 1997; Dehaene, Piazza, Pinel,

& Cohen, 2003). The 'Triple Code Model' proposes three separate systems by which numerical information may be represented and processed. These three systems or 'Codes' are 1) the Verbal Code, in which numbers are represented syntactically, phonologically and lexically, as with any other linguistic system, 2) a Visual Code, in which numbers are encoded as strings of Arabic digits and 3) an Analogue magnitude representation, a system which represents numerical quantities as nonverbal semantic size and distance relations between numbers.

According to the Triple Code model, simple calculations are processed by the verbal system and stored as verbal representations, and hence can be retrieved from verbal memory when the solution to a given simple arithmetic problem is required. This verbal code represents the system by which rote learning of arithmetic facts occurs, and is in essence independent of the quantity representations to which verbal numbers often refer.

Anatomically, the verbal code is suggested to be subserved by the left lateralised perisylvian language network extending into the left inferior parietal lobe. The visual system, on the other hand, is supported by bilateral inferior temporal regions for the asemantic processing of visual symbols, and superior parietal visual attention mechanisms for orienting visual attention along a mental number line, while the analogue magnitude system is suggested to be housed along the horizontal section of the intraparietal sulcus (HIPS) (Dehaene et al., 2003).

Several researchers have suggested that the impairment of a domain specific mechanism that supports the representation and processing of numerical magnitudes, such as that outlined in the triple code model, may represent a core deficit in DD (Butterworth, 1999; Dehaene, 1997). While the specific conceptualisation of how numerosity representations are characterised in this system vary between theorists, most agree that this 'number module'(Butterworth, 1999, 2005) or 'number sense' Dehaene (1997) is located at the neuroanatomical level in the posterior parietal lobes, specifically the intraparietal sulcus.

These theories support the existence of an innate domain specific system by drawing on from evidence of infant and animal numerical capabilities as well as neuroimaging studies of typically developing children and adults. These supporting bodies of evidence will be briefly reviewed in turn, following a brief commentary on the experimental paradigms typically used to investigate the representation of numerical magnitude.

6.3 Numerical Comparison and the Distance Effect

Developmental dyscalculia is manifested at the behavioural level as a deficit in arithmetical ability. However, the search for an underlying core deficit should focus on basic cognitive mechanisms potentially present at birth or at least infancy if it is to succeed in identifying a core deficit that would compromise the development of and not just performance of already developed arithmetical skills.

The measurable quantity or 'numerosity' of a set of objects is an important piece of information which guides human and animal interaction with the environment in many circumstances, and one that must be recognized and represented before any form of numerical processing can be carried out (Dehaene, 1992). 'Quantification' is the process by which the numerosity of a set of object is ascertained, and three parts to quantification have been suggested; counting, subitizing and estimation (Klahr, 1973; Klahr & Wallace, 1973).

Counting involves the serial enumeration of a set of objects. It comprises a set of logical principles and can be achieved using a number of strategies which are thought to become more efficient over the course of development (Gelman & Gallistel, 1978). Counting can be achieved through verbal and nonverbal strategies (Gelman & Gallistel, 1978; Whalen, Gallistel, & Gelman, 1999) and has been shown in neuroimaging studies to activate classical language areas (Hinton, Harrington, Binder, Durgerian, & Rao, 2004) and intraparietal areas associated with numerical representation and processing (Piazza, Mechelli, Butterworth, & Price, 2002).

The process of 'subitizing' refers to the rapid recognition of small sets of objects, usually up to 4, without counting (Kaufman, Lord, Reese, & Volkmann, 1949), and considerable debate currently exists as to whether counting and subitizing reflect different cognitive processes or are differentiated simply by a continuum of difficulty (S. Dehaene, 1992; Piazza et al., 2002). Finally, estimation refers to the process of approximate enumeration (Klahr, 1973) carried out when a set of objects is too large to subitize or count within the allotted time span.

Numerical estimation performance is thought be reflect the way numerical magnitudes are represented in the brain and the most common way to tap those representations is through numerical comparison tasks. Numerical comparison refers to the comparison of either two numbers (Arabic or Verbal) or two sets of objects with respect to their relative numerosity (typically participants select the item or array with the larger numerosity). This task elicits what is now well known as the 'distance effect' that was first observed by Moyer & Landauer (1967). The distance effect refers to a monotonic increase in both reaction time and error rates as the numerical distance between the two comparators decreases. Thus comparing the numerosities of 5 vs 9 would be produce less errors and be performed faster than comparing 8 vs 9. The distance effect is a highly replicable effect (Ansari, Dhital, & Siong, 2006; Fias, Lammertyn, Reynvoet, Dupont, & Orban, 2003a; Moyer & Landauer, 1967; Piazza, Izard, Pinel, Le Bihan, & Dehaene, 2004; Pinel, Dehaene, Riviere, & LeBihan, 2001). Furthermore the distance effect has been shown to correlate with brain activation in the intraparietal sulcus in both children and adults (Ansari, Garcia, Lucas, Hamon, & Dhital, 2005; Pinel et al., 2001).

According to Dehaene & Cohen (1995) the internal representation of numbers is organised along a mental number line which is housed in the IPS

(Dehaene et al., 2003). The closer two numbers are on this number line the more they overlap in terms of representational space, thus making it harder to distinguish one from the other. It is this representational overlap which is thought to give rise to the numerical distance effect. The size of the distance effect decreases over the course of development (Duncan & McFarland, 1980; Sekuler & Mierkiewicz, 1977) suggesting that the mental representations of numerical magnitudes become more distinct and less overlapping.

The importance of numerical comparison is not limited to simple elucidation of the nature of numerical representation. A new finding relates the distance effect to higher level mathematical performance. In a recent study, it was found that the size of the distance effect was negatively correlated with mathematics scores as measured by the Mathematics Fluency and Calculation subtests of Woodcock Johnson III Tests of Achievement (Holloway & Ansari, in press). These data suggest that higher mathematics achievement is related to a smaller distance effect. In essence, these data reveal an important link between reaction times associated with very low-level numerical magnitude processing and school level arithmetic performance. Furthermore, (Delazer, Karner, Zamarian, Donnemiller, & Benke, 2006) present the case of a patient with posterior cortical accuracy extending into the right parietal lobe who showed both impaired arithmetic performance and an increased distance effect during numerical comparison. Thus, a gradually increasing collection of studies suggests a tripartite relationship between the parietal cortex, numerical distance effect, and arithmetic performance.

It should be noted that in an untimed paradigm, in which participants are not required to provide a solution within a certain time frame, different strategies may be used to solve the problem (e.g. counting). However, when a time limit is imposed it reduces the possibility that alternative strategies which do not require access to numerical semantics are used.

Thus, not only do numerical comparison tasks tap underlying numerical magnitude representations, but those representations are evidently related to the development of more sophisticated arithmetic abilities. A numerical comparison task which contains a within task manipulation of distance, therefore, represents an ideal paradigm with which to probe the representation and manipulation of numerical magnitudes in developmental dyscalculia.

6.3.1 Infant and Animal Numerical Processing Abilities.

6.3.1.1 Infants and Children

If DD is caused by the disruption of an innate domain cognitive system for representing and processing numerical magnitude, then evidence of that system should be present in infants and typically developing children.

Research suggests that human infants have both an exact representation of small numerosities, affording them some basic computational ability, as well as a more approximate understanding of larger numerosities, allowing them to discriminate between sets of objects based on number. The earliest studies of infant number processing found that 4 month old infants could discriminate between sets of dots (Starkey & Cooper, 1980) and sets of objects (Strauss & Curtis, 1981) made up of numerosities less than 3, but could not discriminate between sets numbering more than 3. This finding was later replicated with neonates (Antell & Keating, 1983) providing a strong suggestion that infants have some representation of discrete quantities, albeit those lower than 3.

Multiple studies have subsequently confirmed the ability of infants to detect changes in the numerosity of sets of objects (Starkey, Spelke, & Gelman, 1990; van Loosbroek & Smitsman, 1990). Furthermore, infants are aware of changes in the numerosity of a set, even when those changes take place behind a screen, suggesting that as well as a basic representation of small numerosities, infants have an arithmetic expectancy regarding numerical transformations of the number of objects in a set. (Wynn, 1992, 1998).

However, the exact nature of numerical abilities in infants has been challenged by researchers whose studies show that infants respond not to numerosity per se, but rather to changes in non-numerical dimensions, such as surface area and contour length which vary systematically with numerosity (Clearfield & Mix, 1999, 2000; Feigenson, Carey, & Spelke, 2002). Even children as old as three years old have been shown to rely on non-numerical visual cues in order to discriminate between sets of objects (Rousselle, Palmers, & Nöel, 2004). Evidence on this matter is mixed however, as several studies have shown that infants still respond to changes in number even when non-numerical continuous variables are strictly controlled, typically when larger numerosities are tested (Brannon, 2002; Lipton & Spelke, 2003; Wynn, Bloom, & Chiang, 2002; Xu, 2003; Xu & Spelke, 2000).

The extent to which this numerical discrimination mechanism, present in infants in children, operates on numerosity versus continuous physical variables is an important issue in understanding how the domain specific numerical mechanisms present in adults develop. Brannon (2002) used a preferential looking paradigm to show that 9 month old infants were sensitive to changes of size but not number of squares, while 11 month old infants could detect both. This finding suggests there may be an ontogenetic relationship between visual discrimination mechanisms and the development of a domain specific numerical processing system. In other words, the numerosity of a set of objects may be an emergent property of the visual characteristics of the set, and hence numerical representations develop early in infancy but are not present at birth.

The majority of infant research has thus far been cross sectional, and thus the nature of the processes by which infant abilities develop into adult end states, or in the case of developmental disorders do not, remains open. However, it is apparent that some level of numerical processing ability exists before any formal exposure to arithmetic learning, and even before learning can take place in the home, suggesting a phylogenetically specified cognitive mechanism for representing and processing numerical quantity. Furthermore, infant numerical discrimination abilities are sensitive to the effects of numerical distance and size (e.g. Xu, 2003), suggesting that the innate numerical magnitude representation shared by typically developing adults, children and infants can be identified by its susceptibility to changes in numerical distance. This supports the use of a numerical comparison paradigm with distance manipulations as a method of assessing the integrity of that representation.

6.3.1.2 Animal Numerical Cognition

The idea that the human brain should be endowed with an innate representation of numerical magnitude rests on the assumption that such a representation would have evolutionary value. Evidence of numerical representation and processing abilities in animals support this idea.

The first reliable studies showing animal numerical abilities came from Koehler (Koehler, 1941, 1951), who showed that birds could recognise numerosities of sets both in match-to-sample paradigms and when they had to select a pre-trained numbers of items in sequential order. Subsequent research observed numerical discrimination abilities in rats (Church & Meck, 1984; Mechner, 1958; Mechner & Guevrekian, 1962; Meck & Church, 1983), orangutans (Shumaker, Palkovich, Beck, Guagnano, & Morowitz, 2001), monkeys (Brannon & Terrace, 1998; Washburn & Rumbaugh, 1991) and pigeons (Emmerton, Lohmann, & Niemann, 1997).

An obvious criticism of evidence which shows numerical processing abilities in animals is that such ability is purely a result of training. A pioneering study by Brannon & Terrace (1998) addressed this concern by showing that monkeys are able to transfer their trained numerical knowledge to novel numerosities. In this study monkeys were trained to select sets with numerosities 1 – 4 in ascending order, and were subsequently shown to be able to order sets with numerosities 5 – 9 without any training, suggesting a true understanding of the ordinal relationship between numerosities. Furthermore, the monkeys' performance accuracy increased as the numerical distance between the numbers to be ordered increased. In other words, the monkeys' performance showed a classical distance effect, indicative of a mental representation of numerical magnitude that shares at least some properties and perhaps a phylogenetic basis with that of humans.

As well as numerical discrimination and ordering, research has also revealed computational abilities in animals. Studies modelled on the arithmetic expectancy tasks used in human infant research (Wynn, 1992, 1996) have found that non-human primates also recognise when the outcome of a numerical transformation on a set of objects is incorrect (Hauser, MacNeilage, & Ware, 1996; Santos, Sulkowski, Spaepen, & Hauser, 2002; Uller, Hauser, & Carey, 2001). Furthermore the one-by-one addition performance of chimpanzees was found to match those of human children (Beran & Beran, 2004).

Further support for the existence of numerical processing abilities in animals independent of training comes from field studies showing that when female lions hear the voices of another group of lions, they decide whether or not to react aggressively or retreat by comparing the number of voices in the other group with the number of their own (McComb, Packer, & Pusey, 1994). Furthermore, groups of Chimpanzees will only enter into a violent contest if they outnumber the opposing group by a factor of 1.5 (M. L. Wilson, Hauser, & Wrangham, 2001). These findings suggest that numerosity is an important environmental stimulus category even for animals, and in the absence of training they are biologically equipped to represent and process numerical information. The question is, however, whether these abilities in animals are underpinned by the same neural mechanisms as those observed in humans.

An emerging body of single cell recording research has shown that neurons in the monkey brain respond selectively to numerical information. Nieder, Freedman, & Miller (2002) showed that when monkeys were made to judge whether two successive displays contained the same number of items, neurons in the lateral prefrontal cortex were maximally activated by the number of items rather than the appearance of the objects. Nieder & Miller (2004) showed that in the parietal cortex, number selective neurons were most common in the fundus of the intraparietal sulcus, in areas homologous to the human intraparietal sulcus. Furthermore, the responses of these neurons were related to the numerical distance between the presented and preferred numerosities. Specifically, the greater the distance between the presented and preferred numerosity the lower the firing rate of these 'number neurons'. In other words, the firing rate of number specific neurons exhibits a distance effect. This is very important as it shows that the highly replicable behavioural distance effect (see above), which is thought to represent the mental representation of numerical magnitude at the brain level, is present even at the single cell level. This further reinforces the distance effect as a key indicator of the integrity of numerical magnitude representation and suggests that the effect reflects neuronal response properties.

A significant body of research, therefore, shows that at least some level of numerical processing ability present in human adults is shared with human infants and even non-human animals. This ability appears to depend appears to be supported by neurons in the intraparietal sulcus and the prefrontal cortex. Interestingly, the tuning curves of the response functions for the neurons, tested in the work of Nieder and colleagues, overlap remarkably with the behavioural accuracy response distributions in many of the behavioural animal studies (e.g. Mechner, 1958; Mechner & Guevrekian, 1962) suggesting a tight coupling between neuronal activity and cognitive function.

These results suggest the existence of a phylogenetically specified neural mechanism for the representation and processing of numerical magnitude that is subject to the numerical distance effect. That this mechanism exists in animals, children and adults makes it a prime candidate for a system whose impairment may represent a core deficit in developmental dyscalculia. In order to better understand the nature of this mechanism it is important to understand the neural correlates of its function in human adults and children.

Studies of neuropsychological patients with focal lesions resulting in specific behavioural deficits have provided many insights into the neural underpinnings of numerical cognition. This has been supported more recently by a growing body of neuroimaging research. These two sources of evidence will now be discussed in turn.

6.3.2 Neuropsychological Case Studies

Historically, neuropsychological case studies have tended to focus on impairments of sub-domains of arithmetic ability, such as selective deficits of multiplication or subtraction and division. Recent neuropsychological case studies show that some aspects of arithmetic, such as multiplication, thought to rely on verbal systems can be successfully performed despite impaired performance on tasks thought to rely on understanding of numerical quantities, such as subtraction, division and the understanding of number meanings (Dehaene & Cohen, 1997; Delazer, Karner, Zamarian, Donnemiller, & Benke, 2006; van Harskamp & Cipolotti, 2001).

In contrast, other case studies have shown that multiplication may be impaired while other arithmetic operations such as division and subtraction, thought to rely on domain specific numerical systems, remain intact (Delazer et al., 2004; Hittmair-Delazer, Semenza, & Denes, 1994; van Harskamp & Cipolotti, 2001) These findings suggest distinct neural substrates for arithmetical operations compared to more basic numerical magnitude representation as well as showing that while arithmetic facts may be stored in memory as verbal routines, calculation can still be impaired in the context of spared language, suggesting that arithmetic performance depends upon more than just verbal memory. Together these sets of results support the distinctions within the "Triple Code" model between neural circuits which underlie verbal representations of arithmetic facts, and those which underlie the representation of numerical magnitude information, and suggest that these circuits may be independently impaired.

Neuropsychological evidence suggests that, in the adult brain at least, arithmetic procedures may be differentially impaired following brain damage. However, interpreting this evidence in terms of developmental learning disorders is difficult as the cognitive modules shown to be impaired in these studies are the product of lifelong learning. Arithmetic is a composite process drawing on linguistic skills, memory and executive function, and thus it is important to ask whether basic numerical magnitude processing abilities can show an isolated impairment following brain damage.

To date, only a few neuropsychological case studies have investigated the understanding of numerical quantities independent of formal calculation procedures, that is, those processes, such as number comparison and numerical estimation, thought to depend upon a domain specific number sense (Dehaene, 1997). In studies that have compared basic quantity processing with conceptual arithmetic knowledge (Delazer & Benke, 1997; Delazer et al., 2004) dissociations have been observed between intact quantity processing and impaired conceptual knowledge, but not the reverse, suggesting that the quantity processing system is a more fundamental foundation upon which more sophisticated arithmetic knowledge is built.

Dissociations have also been observed between exact and approximate numerical abilities which are thought to tap arithmetic fact memory and numerical magnitude representation respectively (Dehaene et al., 1999). In the first such case study Warrington (1982) reported the case of a patient who, following damage to the left parietal and occipital lobes, was unable to solve even the most basic calculation problems. However, he was able to clearly define arithmetic operations, as well as being able to give approximate solutions to simple and complex calculations (e.g. when asked "5 + 7" he replied "about 13") suggesting that the underlying representation of numerical magnitude was intact. Subsequent studies have also revealed a relationship between damage to the left parietal lobe and impaired exact calculation in the context of intact approximate numerical abilities (Dehaene & Cohen, 1991; Lemer, Dehaene, Spelke, & Cohen, 2003). These findings support the idea that arithmetic depends on both an exact verbal system for representing and processing discrete numbers and an approximate system for representing and processing numerical magnitude, and that these processes can be differentially impaired following brain damage.

A recent case study explored basic numerical processes in a patient with a cerebral lesion restricted to the left IPS (Ashkenazi, Henik, Ifergane, & Shelef, 2008) and observed an interesting set of results. The patient (AD) showed impairments in calculation but not number comprehension and production, as well as impaired performance in magnitude comparison from dots to digits and from dots to dots and in dot counting and subitizing. Interestingly, AD also showed a larger distance effect than controls, an effect observed when comparing children to adults (Ansari et al., 2006) as well as a lack of a facilitation effect during congruent trials of a numerical stroop task, an effect observed in adults with developmental dyscalculia (Rubinsten & Henik, 2005).

These results suggest that not only can basic numerical magnitude processing be impaired following damage to the IPS, but that impairments in that domain relate to a stronger distance effect. In combination with the results of Ansari et al (2006), these findings suggest that a stronger distance effect may reflect impairment or lack of development of the mental representation of numerical magnitude.

An obvious and serious problem with making inferences about cognitive architecture from brain damaged patients is that brain lesions rarely respect the confines of functionally defined cortical areas. Often several processes are impaired, making it difficult to make specific interpretations from the resulting impairment patterns. Furthermore, patients are frequently able, consciously or not, to employ alternative, compensatory cognitive mechanisms in order to carry out tasks, thus further confounding any interpretations of error patterns.

Despite the limitations of the neuropsychological approach, the results reviewed above do suggest that a selective impairment of the mental representation of numerical magnitude is possible, and that it is most likely that it arises from damage to the intraparietal sulcus. Whether this cognitive module can be so selectively impaired as a consequence of atypical brain development in dyscalculia, however, remains an open question. The current thesis seeks to address this question with both behavioural and neuroimaging evidence.

While neuropsychological case studies may be highly valuable in elucidating the separability of cognitive systems, in terms of localising those systems to neural loci it is unfortunately approximate. Modern advances in neuroimaging, however, have provided a powerful complimentary tool for investigating the neural bases of numerical processing mechanisms.

6.3.3 Neuroimaging of Numerical Comparison in Adults and Children

6.3.3.1 Adults

Domain specific theories of developmental dyscalculia suggest that a core deficit in the representation of numerosity may impair the structured development of mathematical learning, in that more sophisticated school level knowledge would lack the necessary semantic foundations on which to be built. Several researchers have suggested that the neuroanatomical location of this core deficit may be the posterior parietal lobe (Butterworth, 1999; Dehaene, 1997). The advent of greater spatial resolution and more sophisticated paradigms and analysis methods in fMRI has afforded researchers the possibility to construct more detailed descriptions of how cognitive representations such as those outlined in the triple code model (Dehaene & Cohen, 1995; Dehaene et al., 2003) may be instantiated at the neuroanatomical level and subsequently, allowed a greater degree of neuroanatomical specificity in hypotheses of a brain based core deficit in DD.

In a seminal meta analysis Dehaene et al (2003) outlined three neural circuits suggested to support different aspects of numerical cognition. The left angular gyrus (AG) tends to be more active in verbal tasks such as multiplication and “exact addition” (Chochon, Cohen, van de Moortele, & Dehaene, 1999; Dehaene et al., 1999; Lee, 2000), the posterior parietal lobe is active in tasks requiring the shifting of spatial attention (Dehaene et al., 1999; Lee, 2000; Pinel et al., 2001), while the intraparietal sulcus (IPS) is involved in number specific tasks such as number comparison, numerical estimation and approximation, and subtraction (Chochon et al., 1999; Dehaene et al., 1999; Lee, 2000).

Thus, if DD is caused by a deficit in the development of numerical magnitude representation, then the most likely neural substrate for that impairment is in the IPS. However, before one can investigate the atypical development of that representation, it is important to understand its neural correlates in typically developing children and adults.

As discussed above, numerical comparison and estimation serve as ideal tasks for probing the representation and processing of numerical magnitude, and a growing body of neuroimaging research has employed these tasks with the aim of elucidating the neural substrates of this potentially domain specific cognitive mechanism.

An early PET study of numerical comparison (Dehaene, 1996) revealed that parietal regions are involved in comparing both Arabic digits and number words. Furthermore, an effect of numerical distance was observed over the right parieto-occipital-temporal region, showing greater difference amplitudes for close distances than for far. Subsequent neuroimaging studies of number comparison have consistently reported activation of the IPS in both cerebral hemispheres. Activation of the IPS has been reported for number comparison but not digit naming (Chochon et al., 1999), for comparison of two-digit numbers in both Arabic and written form to a reference number (Pinel et al., 2001), for comparison of verbal numerals to a reference number (Thioux, Pesenti, De Volder, & Seron, 2002) and for number comparison relative to judging the orientation of digits (Pesenti, Thioux, Seron, & De Volder, 2000). These results provide strong evidence of the key role of the IPS in representing and processing numerical magnitude.

As well as investigating number comparison using Arabic digits and number words, studies have probed the domain specificity of numerical processing in the IPS using nonsymbolic stimuli (i.e. collections of objects). Castelli, Glaser, & Butterworth (2006) observed that the bilateral IPS was more active for comparing the numbers of blue versus green squares relative to comparing the amount of blue versus green hue in a single large square, indicating that the IPS responds specifically to numerosity rather than a simple more than/less than magnitude system.

Venkatraman, Ansari, & Chee (2005) used nonsymbolic stimuli (dot patterns) in an addition paradigm, comparing exact and approximate additions in both symbolic and nonsymbolic formats. The results of this study showed that while nonsymbolic addition activated the IPS bilaterally, symbolic addition predominantly activated the left IPS, suggesting some level of shared representation but perhaps some subtle format related hemispheric differences. Piazza, Giacomini, Le Bihan, & Dehaene (2003) showed that bilateral posterior parietal regions are more active for counting sets of four to seven objects compared with subitizing sets of less than four, and that activation in the IPS showed a linear increase in relation to the number of items being counted.

These results show that the IPS is active during the processing of numerical magnitude regardless of the visual format in which stimuli are presented. However, a question which arises then, is whether the IPS is involved specifically in the *processing* of numerical magnitude, rather than housing the representation thought to be tapped by numerical comparison tasks and the distance effect (see above). Some researchers have argued that the observed IPS activations during numerical processing stem from more domain general processes such as response selection mechanisms, rather than from activation of the representation of numerical magnitude (Göbel, Johansen-Berg, Behrens, & Rushworth, 2004; Göbel & Rushworth, 2004).

In order to address this concern, several studies investigating nonsymbolic number processing have employed a technique known as functional magnetic resonance adaptation (fMRA). In an adaptation paradigm, stimuli are presented sequentially, and during this presentation one stimulus attribute is held constant, while others vary. For example, a series of sets of dots may be presented, each with 35 dots, but the individual shapes of the dots may change, as might the overall surface area covered by the set, as well as density of stimuli within the surface area. Thus, numerosity would be considered the *invariant dimension* in this example.

Repeated presentation of this stimulus dimension leads to a decrease, or *habituation,* of the brain activation in areas whose activation initially increased in response to the stimuli. Finally, a *deviant* stimulus is presented in which the previously invariant stimulus dimension is altered (e.g. a series of sets containing 35 dots followed by a set with 55 dots). This deviant stimulus leads to a recovery, or *dishabituation,* of function in those areas which are responsible for the processing of the invariant stimulus dimension. Typically participants are asked to attend to a neutral element in the display such as a fixation cross. Thus the paradigm involves no response selection and no task dependant attention (for a detailed description of this method see Grill-Spector, Henson, & Martin, 2006)

Using an fMRA paradigm which used sets of 16 or 32 dots as habituation stimuli, Piazza et al (2004) showed that the anterior IPS bilaterally responds to changes in numerosity but not in individual item shape, and that the greater the change in numerosity when the deviant stimuli was presented, the great the activation recovery in the IPS. Piazza, Pinel, Le Bihan, & Dehaene (2007) showed that the IPS bilaterally recovers in response to numerosity changes, even when the deviant stimulus is in a different notation (digit deviant in dot habituation and vice versa). In this study the left IPS showed greater sensitivity to notation changes when digit deviants were presented amongst dot habituation series, again suggesting there may be hemispheric asymmetries in the processing of numerical stimuli. Critically, these studies reveal that the IPS is sensitive to changes in numerosity even when no explicit processing of the stimuli is required, strengthening the idea that this region houses a representation of numerical magnitude.

fMRA has also been used to explore the neuronal populations responsive to numerosity comparison using Arabic digits and number words. Naccache & Dehaene (2001) observed bilateral IPS activation recovery for numerosity changes using both Arabic digits and number words. Cohen Kadosh, Cohen Kadosh, Kaas, Henik, & Goebel (2007) employed a passive viewing fMRA paradigm using Arabic digits and number words. The authors observed dishabituation in the left IPS in response to changes in numerosity for both Arabic digits and number words, and dishabituation only for Arabic digits in the right IPS. This result suggests that while the bilateral IPS responds to changes in numerosity, there may be a specialised role for the left IPS in processing verbal number words.

In addition to showing the IPS as simply being active during numerical processing, numerical comparison paradigms have revealed neural correlates of the behavioural distance effect, a key indicator of access to numerical semantic information. Pinel et al. (1999) employed an event-related fMRI paradigm to show that when comparing Arabic digits or number words, smaller numerical distances between comparators correlates with increased activation in the bilateral IPS. This finding has since been replicated in multiple studies (Cohen Kadosh et al., 2005; Kaufmann et al., 2005).

Furthermore, fMRA studies have shown that the greater the distance between the deviant and the habituated numerosity, the greater the degree of signal recovery in the IPS (Piazza et al., 2004; Piazza et al., 2007). This finding is in line with computational models of numerosity representation (Dehaene & Changeux, 1993), and supports the idea that the mental representation of numerical magnitude is sensitive to the effects of numerical distance at the brain level. These findings lend further support to the hypothesis that the IPS is crucially involved in the representation and processing of numerical magnitude and that this cognitive system is highly domain specific. Furthermore, the distance related activation changes in the IPS observed in humans parallel the distance related response tuning curves of parietal neurons in monkeys (see above), suggesting that the nature of the numerical magnitude representation in the IPS is phylogenetically specified, and hence represents a plausible candidate for core deficit in DD which may be present from birth.

A second line of argument against the domain specificity of numerical representation in the IPS, however, comes from findings showing common activation in the IPS for magnitude judgements involving stimuli that are not explicitly numerical, such as, letters, shapes, line length, angle width, character size and luminance (Fias, Lammertyn, Reynvoet, Dupont, & Orban, 2003b; Fulbright, Manson, Skudlarski, Lacadie, & Gore, 2003; Pinel, Piazza, Le Bihan, & Dehaene, 2004). These findings have led to suggestions that observed activations in the IPS reflect the operation of a domain general magnitude system (Fulbright et al., 2003; Walsh, 2003) rather than a domain specific representation of numerical magnitude. However, in the Pinel et al., (2004) study, the regions activated by different dimensions of magnitude were found to be overlapping but distinct, with numerical magnitude being linked to anterior regions of the IPS. Furthermore, Ansari et al (2006) used an fMRA paradigm to show that the IPS responds to changes in number but not surface area. Thus, the evidence suggests that while the parietal lobe may process domain general magnitude, it appears to also contain a domain specific numerical system, possibly located in more anterior regions of the IPS.

6.3.3.2 Children

The above studies show that in typically developing adults, the IPS supports the representation and processing of numerical magnitude, and that the behavioural effects of changes in numerical distance are mirrored in the neural responses of the IPS. However, neuroimaging studies of healthy adults alone cannot address the question of whether such a neural mechanism supports the development of numerical abilities, or whether this is caused by a lifetime of learning and experience of numerical processing. Recently several researchers have started to explore the neural substrates of numerical cognition in children in order to investigate whether the numerical processing abilities present so early in development at the behavioural level (see above) are tied at the neuroanatomical level to the same systems supporting those processes in adults.

Calculation tasks consistently activate parietal regions in adults (see above) and several studies have revealed an interesting pattern of similarities and differences in children's brain activation. Kawashima et al (2004) compared brain activation between children and adults during simple addition, subtraction and multiplication. The results revealed that while the adults show IPS activity during all three tasks, children only showed activation in the right IPS during subtraction. Furthermore, subtraction was also the only task to reveal right IPS activation in adults, the other two showing left lateralised IPS activity. Subtraction and division are thought to require greater access to numerical semantic information than addition and multiplication which can be solved using stored arithmetic facts. Thus, these results point to an ontogenetic specialisation of the left IPS for calculation, but suggest a shared right IPS mechanism present in childhood for more basic numerical processing.

Another study looked at differences between children and adults in the neural circuitry underlying calculation (Rivera, Reiss, Eckert, & Menon, 2005). This study found that children recruit more frontal areas including superior, middle and inferior frontal gyri compared to adults during addition and subtraction. Adults on the other hand, recruit more posterior areas including lateral occipital cortex, mid-temporal areas, the left supramarginal gyrus, and the left IPS. These findings suggest that the involvement of the parietal cortex in calculation may be the product of ontogenetic specialisation, perhaps by means of mapping Arabic digit symbols onto nonsymbolic representations of numerosity held in the parietal cortex from infancy.

The results above suggest that in children, the IPS perhaps does not play as strong a role in supporting calculation as it does in adults. The question arises then, whether this difference is related to differences in the calculation procedures used by children and adults, or to the development of representation of numerical magnitude in the IPS.

In order to address this question it is necessary to investigate the neural correlates of numerical processing in the absence of calculation. In fact, the first study to investigate the neural correlates of numerical processing in children used symbolic and nonsymbolic number comparison in an ERP paradigm (Temple & Posner, 1998). This study observed similar behavioural and electrophysiological effects of numerical distance for both children and adults, centred over posterior parietal electrodes. However, the limited spatial resolution of ERP makes more specific anatomical inferences impossible.

More recently, Ansari et al (2005) used fMRI to examine the neural correlates of the distance effect during symbolic number comparison in children and adults and found that while distance modulated a frontal and parietal network in adults, in children distance modulated a primarily frontal and sub-cortical network. However, the children did show an effect of distance in the right superior parietal lobe, further suggesting that the numerical processing specialisation of the parietal cortex may emerge earlier in the right hemisphere than the left.

Extending the results of the above studies, which lacked a direct statistical contrast between children and adults, Ansari & Dhital (2006) investigated age related changes in brain activation during numerical comparison of nonsymbolic stimuli and employed a direct statistical comparison between adults and children. The authors observed that while children showed a classic distance effect (increased activation for smaller distances) in the left IPS, adults showed the same effect in the IPS of both hemispheres. Furthermore, the left IPS region showed a group x distance interaction driven by a stronger effect of distance in the adults than the children. This was the first study to reveal an ontogenetic development of IPS activity during nonsymbolic number comparison, and shows that the neural distance effect increases with age. This pattern is interesting in the context of behavioural evidence showing an age related decrease in the distance effect (Duncan & McFarland, 1980; Sekuler & Mierkiewicz, 1977), suggesting that stronger parietal activation during numerical comparison may reflect greater integrity and efficiency within the numerical magnitude system.

fMRA has also been used to explore age related changes in nonsymbolic number comparison. Cantlon, Brannon, Carter, & Pelphrey (2006) showed that in adults, the bilateral IPS responds to changes in the number of objects in a set of dots. In 4 year old children, however, the response was right lateralized. This study provides further evidence of a possible developmental shift from right IPS dominance to more bilateral processing of numerical information. This shift may be linked to the increasing role of language in the child's understanding and processing of numerical information. However, the studies above have produced conflicting evidence regarding the hemispheric lateralisation of number processing in the IPS, and thus it is difficult to speculate as to the different roles of the left and right IPS during the development of numerical processing abilities.

Neuroimaging studies of numerical processing in children reveal several key points. Firstly, the IPS is involved in numerical processing in children, albeit to a lesser extent than in the adult brain. Secondly, changes in numerical distance during number comparison modulate activity in the IPS of children, again, albeit to a lesser extent than for adults. Finally, some studies suggest a right IPS specialisation for the representation of abstract numerical magnitude and a left IPS specialisation for symbolic or verbally based number processing, although other studies present evidence contrary to this dichotomy. Thus the question of hemispheric asymmetry requires further focused investigation.

If the numerical representations housed in the IPS are weaker in typically developing children than adults, then it may be that those representations are in turn weaker in children with mathematical learning disorders than in typically developing children, effectively creating a developmental hierarchy of the strength of numerical representations in the brain. The current thesis investigates this question by comparing brain activation during symbolic and nonsymbolic comparison in children with developmental dyscalculia and typically developing controls. This is the first work to investigate this issue using both symbolic and nonsymbolic stimuli. Although a very small number have studies have recently begun to probe the neural correlates of numerical representation in DD children, the results have proved inconclusive, and the integrity of the representation of numerical magnitude at the brain level in DD remains an open question.

6.3.3.3 Neuroimaging of Number Processing in Atypical Populations

In contrast to research on mathematical disabilities, studies examining the neural correlates of dyslexia have been fairly widespread, and have thus been able to identify key differences in brain activation between dyslexics and normal readers, especially in the left occipito-temporal area (e.g. Shaywitz et al., 2002) These findings have been highly relevant in informing theories of developmental dyslexia based on deficits in phonological decoding for example (Lyytinen, Erskine, Aro, & Richardson, 2006). In view of this highly significant progress in the field of dyslexia research, it is likely that the study of mathematical learning disabilities would benefit from similar neuroimaging contributions.

The first body of neuroimaging studies which investigated atypical numerical processing looked at populations with numerical and visuo-spatial impairments occurring in the context of genetic developmental syndromes, such as Turner Syndrome (TS) and Fragile X syndrome (fraX).

Using both functional and structural neuroimaging methods, Molko et al (2003) compared Turner Syndrome patients to typically developing controls during calculation. While the control subjects showed increased activation in the bilateral IPS as the difficulty of exact calculations increased, the TS subjects did not show the same modulation. Subsequent morphometric analysis revealed abnormal structural organization of the right hemisphere IPS in TS subjects. The behavioural results of this study showed that TS subjects performed disproportionately worse when the difficulty of exact calculations increased relative to controls. In addition the IPS, i.e. the brain area associated with supporting the increased level of quantity processing in controls, does not respond to increased demand in TS subjects, a pattern also observed in females with fragile X syndrome in calculation verification tasks (Rivera, Menon, White, Glaser, & Reiss, 2002).

Taken together these findings suggest that atypical development of parietal brain regions, and in particular the right IPS, may undermine the development of arithmetic abilities. These findings are additionally important as they link atypical development of the IPS, the presumed locus of the representation of numerical magnitude to atypical development of arithmetic abilities, not just basic magnitude processing skills, thus suggesting a potential causal link between atypical development of numerical magnitude representations and developmental dyscalculia.

Molko et al (2004) further supported this finding with Voxel Based Morphometry (VBM) evidence showing that TS subjects showed decreased grey matter volume in the left superior temporal sulcus and right IPS. Similarly, Isaacs, Edmonds, Lucas, & Gadian (2001) found that adolescents of very low birth weight who showed deficits in numerical operations had reduced grey matter volume in the left hemisphere IPS. Again, the causes for hemispheric asymmetries between studies are unclear.

An important caveat in the interpretation of anatomical studies of atypically performing groups is that the observed structural changes may be either a cause or an effect of impaired performance in the cognitive domain with which that brain region is associated, so causal inferences should be treated with caution. Furthermore, groups of atypically developing individuals, with different genetic disorders, have been compared as though they shared a single deficit in numerical processing. Although the consequences are unknown, the fact that these groups present these mathematical impairments as part of broader genetic syndromes should not be forgotten when generalizing the results of these studies to pure DD.

Few studies have investigated the neural correlates of numerical processing in children with developmental dyscalculia rather than wider genetic syndromes. Kucian et al (2006) conducted an fMRI experiment with developmental dyscalculics in the 3rd and 6th Grades, defined by discrepancy between scores on a battery of mathematical and reading tests and general IQ, and two groups of age matched controls. The experiment included approximate and exact calculation conditions and a magnitude comparison task, comparing small sets of different objects (e.g. strawberries vs. nuts). The results of the fMRI showed similar activation patterns, albeit generally weaker and more diffuse, for DD and control groups in all conditions. There was no effect of age on activation pattern.

The main difference between groups in this study was found using region of interest analysis in the IPS. In this region DD subjects showed significantly weaker activation in response to approximate calculation in the left IPS, and a non-significant trend in the same direction in the right IPS. During the numerical comparison task, a region of interest analysis revealed significantly weaker activation during numerical comparison for DD children in the left IPS and a trend toward the same pattern in the right IPS. Thus, this study revealed essentially similar networks for all tasks between groups, albeit with weaker activations in the DD group. However, these results were not supported by whole brain statistical analysis, and thus do not represent strong evidence in favour of brain level differences in the IPS between DD and control children. The failure to observe group differences at the whole brain level may be because the magnitude comparison task used stimuli comprised of set of different objects (e.g. nuts vs strawberries) and there was no assessment of the effect of numerical distance on brain activation. Therefore it may be that the task was simply too coarse to elucidate subtle group differences.

A recent ERP study sought to investigate the neural correlates of the distance effect in DD children using symbolic number comparison (Soltesz, Szucs, Dekany, Markus, & Csepe, 2007). This study observed no significant differences in the distance effect at an early time window, but at a later time window, the control group showed a non-significant distance over right parietal areas, while the DD group showed no such signs. Although non-significant, these qualitative differences suggest the possibility of a right parietal dysfunction in DD. The only concrete support for the role of developmental abnormalities of the right IPS in DD comes from a recent VBM study, which revealed reduced grey matter volume in the right IPS in DD children relative to controls (Rotzer et al., 2007).

Thus, neuroimaging studies investigating numerical processing in pure DD have thus far hinted at potential defects in the right IPS during number comparison, but have yet to provide robust evidence of such an impairment.

Transcranial Magnetic Stimulation (TMS) studies have shown that temporary lesions of the right IPS disrupts automatic processing of numerical magnitude during a numerical stroop task (Cohen Kadosh, Cohen Kadosh, Schuhmann et al., 2007), mirroring a result shown in behavioural studies of adult dyscalculics (Rubinsten & Henik, 2005). Furthermore, TMS of the left IPS has been shown to slow both symbolic and nonsymbolic numerical comparison (Cappelletti, Barth, Fregni, Spelke, & Pascual-Leone, 2007; Dormal, Andres, & Pesenti, 2008). These findings support the crucial role of the IPS in numerical representation, but again show that the issue of hemispheric lateralisation requires further focused research in order to be understood.

Neuroimaging of basic number processing in atypically developing populations has so far provided variable results. Different experimental designs and populations with highly variable cognitive profiles outside the number domain have made it difficult to apply a uniform interpretation of the findings. However some consistent findings have emerged, in that almost all of these populations, when the task is well controlled, show some abnormal functional or structural modulation of parietal region, making a developmental impairment of this region a strong candidate for a core deficit in DD. The current thesis is the first work to address this open question by comparing the neural distance effect during symbolic and nonsymbolic comparison between children with pure DD and typically developing controls. In this way the integrity of the underlying representation of numerical magnitude can be probed at both the brain and behavioural levels.

7 COMORBIDITY – MATHEMATICS AND READING

A notable characteristic of developmental dyscalculia is the high rate of comorbidity with dyslexia. Recent estimates suggest between 50% and 75% of children with mathematical difficulties also have reading difficulties (Barbaresi, Katusic, Colligan, Weaver, & Jacobsen, 2005). The question of comorbidity is important as comorbid and pure DD may represent two subtypes of arithmetical learning disorder, with inherently different causes, behavioural outcomes, and developmental trajectories, and thus may require very different methods of intervention (Fletcher, 2005), and yet the cognitive sources of this comorbidity are not understood.

It is possible that comorbidity between the two disorders results from a mutual dependence on language mechanisms shared between reading and certain aspects of mathematics (Geary & Hoard, 2001). The current best understanding of the root cause of dyslexia is a disruption of phonological processing skills that support language acquisition (Lyytinen, Erskine, Aro et al., 2006). A disruption in phonological skills may lead to deficits in processes such as counting which are required in order to learn arithmetic facts (Geary & Hoard, 2001). In other words, the reading deficit in dyslexia and comorbid dyslexia and dyscalculia may be the same, while the arithmetical deficits in pure dyscalculia and comorbid dyscalculia and dyslexia are inherently different since one stems from difficulties with the verbal elements of arithmetic, while the other stems from difficulties in representing numerical quantity information (Fletcher, 2005).

However, this line of argument would suggest that all dyslexic children should show deficient arithmetic retrieval, but this is not the case and so it is unlikely that impaired phonological awareness alone accounts for the high rate of comorbidity between dyscalculia and dyslexia.

Another possibility is that the arithmetic deficits in the comorbid group stem from a cognitive deficit prevalent in dyslexia, but separate from phonological processing; a deficit of retrieving semantic information through symbolic visual stimuli, typically measured by tasks such as rapid naming (Lyytinen, Erskine, Tolvanen et al., 2006). Some authors have suggested that such a retrieval deficit represents a core deficit in dyslexia which is separate to core deficit in phonological awareness (e.g. Manis, Seidenberg, & Doi, 1999; Wolf & Bowers, 1999). Dyslexic children frequently show deficits in rapid naming (e.g. Willburger, Fussenegger, Moll, Wood, & Landerl, 2008) and data from a major longitudinal study of dyslexia (the Jyväskylä Longitudinal Study) has shown that at many children at risk for dyslexia show retrieval deficits, indexed by tasks such as rapid naming (Lyytinen, Erskine, Tolvanen et al., 2006).

Rapid naming (or semantic retrieval) has been suggested to require visual discrimination and feature detection, integration of visual features with stored orthographic representations, access and retrieval of phonological labels and activation and integration of semantic and conceptual information (Wolf & Bowers, 1999). Thus, it is possible that an impairment of rapid naming could negatively affect arithmetic performance, particularly in the domain of fluent arithmetic fact retrieval, but also in comparing the relative magnitude of visually presented numbers through an impaired access to the underlying semantic information.

This 'retrieval deficit' may be analogous to the 'access deficit' suggested by some to underlie arithmetic deficits in both pure and comorbid dyscalculia (Rousselle & Nöel, 2007). The access deficit hypothesis suggests that DD children have an impaired ability to access numerical magnitude representations through the use of symbolic stimuli, but that the representations themselves are intact. In combination with the retrieval hypothesis, such a deficit would potentially explain the high rate of comorbidity. However, before focusing on an independent core deficit in comorbid children, it is necessary to first investigate whether the arithmetic deficits in comorbid children stem from the same core deficit as those in dyscalculic children, i.e. a core deficit in the representation and processing of numerical magnitude.

The typical research approach to this issue has thus far been to contrast children with isolated deficits in arithmetic (AD) to those with comorbid arithmetic and reading disorders (AD/RD) on a range of tasks in order to ascertain whether the groups can be divided on the basis of performance on arithmetical tasks that rely on language skills and those that do not.

Geary et al (2000) used such a comparison in a longitudinal study across 1st and 2nd grades that compared children with AD only, RD only, AD/RD and typically developing (TD) controls. The two AD groups performed worse than RD and TD groups in tests of counting knowledge and addition, and furthermore the AD/RD group performed worse than the AD only group on addition. No group differences were observed for number comprehension and the mazes spatial task. In addition, RD and AD/RD groups performed worse than the other groups on articulation speed of familiar words. The results of this study suggest that arithmetic deficits in the AD/RD group are not caused by the phonological processing deficits which underlie dyslexia but instead occur independently. The two groups with arithmetic difficulties showed generally similar performance on numerical tasks. However, this study used a cut off criteria of the lowest 35th percentile for selecting children with arithmetic difficulties, and thus it is difficult to speculate as to the source of the arithmetic impairments in either group, let alone whether or not those sources were shared.

A longitudinal study by Jordan et al (2003), that also used an arithmetic difficulties group selection criteria of the 35th percentile, compared AD children with AD/RD children across 2nd and 3rd grade and found that AD only children were superior in tests of problem solving, such as arithmetic story problems and arithmetic principles. The two groups performed equally poorly in tests of basic calculation, such as timed fact retrieval and estimation. At the end of third grade, both group relied heavily on finger counting to solve arithmetic problems, however, the AD only group did so more accurately, suggesting the use of more mature counting procedures. These results may suggest that, while both groups share some basic impairment in numerical processing, the AD only group are able to employ linguistic skills to compensate to some extent during verbally based tasks, while the comorbid group are not. However, this study included no tasks of nonsymbolic numerical processing and thus it is impossible to say whether or not the atypically developing participants had any cognitive deficits beyond the processing of symbolic Arabic digits.

Children with comorbid AD/RD typically show poorer performance on arithmetic tests than children with isolated AD or RD. One explanation for this is that children with isolated AD can use their intact linguistic skills to compensate their impaired numerical representations, while children with AD/RD cannot (Jordan, 2007).

In support of this theory Jordan et al (2002) showed that AD only children improve in mathematical skill more quickly than AD/RD children, while in reading skill, the growth rate of RD only and AD/RD children are equivalent. Furthermore, AD/RD children have been found to be significantly more impaired on tests of arithmetic than children with dyscalculia alone, and that the observed differences were related to performance level rather than category, and thus there were no qualitative differences between AD only and AD/RD (Shalev, Manor, & Gross-Tsur, 1997). However, this study also used the liberal selection criteria of 35th percentile and did not test basic numerical processing skills with nonsymbolic stimuli. Thus, although it is entirely feasible that the AD only group were able to compensate their impaired arithmetic with language skills more so than the comorbid group, the root causes of the arithmetic disorders in each group are not elucidated by this study.

Rourke (1993) has suggested that different patterns of impairment between AD and AD/RD children reflect different hemispheric lateralisation of developmental impairments of brain function (see Cerebral Asymmetry Hypothesis above). Thus, a combined deficit of reading and arithmetic would reflect shared developmental impairments resulting from atypical development of left hemisphere language systems, while pure dyscalculia would reflect abnormalities in the development of right hemisphere visuo-spatial mechanisms. However, behavioural and neuroimaging research has not supported such a dichotomous hemispheric asymmetry in the processing of arithmetic and numerical stimuli, and this hypothesis does not explain why only some children with developmental reading disorders show comorbid arithmetic deficits.

Landerl et al (2004) conducted the first in depth study of basic numerical abilities in both dyscalculic and comorbid children using a stricter criterion for selecting children with dyscalculia rather than arithmetic difficulties (3 standard deviations below the mean on standardised tests of arithmetic). This study found that DD and DD/RD groups did not differ on a series of basic number processing tasks, including number naming, number reading and writing, number comparison, counting and dot enumeration. Both of the DD groups performed worse than non-DD groups on these tasks, but there were no group differences on a range of general cognitive measures.

These results suggest that arithmetic impairments in DD/RD and pure DD are both underscored by more basic impairments in numerical processing. However, this study did not investigate the numerical distance effect using nonsymbolic numerical comparison, and thus it is difficult to conclude whether the basic numerical processing impairments were driven by an impaired representation of numerical magnitude in both groups, as the majority of tasks required some form of Arabic digit processing. Therefore the CM group could have an intact representation of numerical magnitude but a deficit in accessing that representation through visual symbols, while the DD group could simply have an underdeveloped representation, and yet performance on the range of tasks used in this study could be similar for both groups.

The first study to investigate basic numerical processing skills using both symbolic and nonsymbolic stimuli with strictly defined dyscalculic and comorbid children was conducted by Rousselle & Nöel (2007), and gave rise to the 'access deficit' hypothesis. One of the main findings of this study was that children with dyscalculia performed worse than typically developing controls on symbolic numerical tasks but not nonsymbolic tasks, leading the authors to suggest that DD is caused by a deficit in accessing numerical semantic information through the use of Arabic digits (visual symbols). This study collapsed pure dyscalculic and comorbid children into one group on the basis that they did not differ on overall performance on any of the tasks. However, the groups were not compared in terms of their symbolic and nonsymbolic distance effects before being collapsed, and as the distance effect is a reliable and robust measure of the integrity of numerical magnitude representation, this leaves open the possibility that the groups may in fact have differed in terms of their core deficits.

The above studies, although largely revealing similar performance on range of basic numerical tasks between comorbid children and DD children, have typically employed liberal selection threshold for atypical groups, or have not investigated nonsymbolic numerical processing in addition to symbolic processing and arithmetic. Furthermore, no study to date has compared CM and DD children on numerical comparison using both symbolic and nonsymbolic stimuli and employing a comparison of the effects of distance. This leaves open the possibility that although CM and DD children show similar behavioural profiles on relatively basic numerical tasks, those similarities are driven by factors other than an impaired representation of numerical magnitude which may be revealed using more subtle within task manipulations. The distance effect during numerical comparison (as discussed above) represents an ideal paradigm for investigating the integrity of numerical magnitude representations.

Thus, in order to begin to understand the sources of comorbidity between dyscalculia and dyslexia, this thesis investigates whether arithmetic deficits in comorbid and dyscalculic children are underscored by a shared impairment of the representation of numerical magnitude, by examining the distance effect in dyscalculic, dyslexic, and comorbid children during both symbolic and nonsymbolic numerical comparison. This is the first work to compare both symbolic and nonsymbolic distance effects between children with pure DD and comorbid DL and DD.

8 SUMMARY

The evidence reviewed above suggests that, although DD is typical recognised by impairments in school level arithmetic abilities such as arithmetic fact retrieval, conceptual, and procedural arithmetic knowledge, these impairments may be caused by underlying impairments in the representation and processing of numerical magnitude. A growing body of evidence shows that DD children have difficulties comparing the relative numerosity of two numbers, and that this impairment may be related to developmental abnormalities in the intraparietal sulcus. Patterns of behaviour and brain activity in typically developing adults and children suggest that the numerical comparison task, and in particular the effect of manipulating the distance between the two numbers being compared, provides a key insight into the integrity of brain level representations of numerical magnitude. Thus, given the current state of knowledge of the field, the most plausible candidate for a core deficit in DD is an impairment of the representation of numerical magnitude housed within bilateral regions of the intraparietal sulcus. The present work will investigate this hypothesis using symbolic and nonsymbolic numerical comparison tasks.

Furthermore, a high rate of comorbidity exists between dyscalculia and dyslexia. Behavioural evidence regarding the source of arithmetic impairments is thus far inconclusive as to whether arithmetic deficits in comorbid children are caused by an impaired representation of numerical magnitude, or a deficit in accessing that representation through the use of visual symbols (Arabic digits). Thus, this thesis addresses one side of the debate by investigating whether the quality of numerical representations among comorbid children is more closely aligned with the representations of numerical magnitude measured in dyscalculic children or dyslexic and typically developing children.

9 AIMS AND STRUCTURE

9.1 Aims

Aim 1: To investigate the integrity of numerical magnitude representation in children with developmental dyscalculia

Aim 2: To investigate the integrity of numerical magnitude representation in children with comorbid dyscalculia and dyslexia.

9.2 Structure

In order to address the above aims, the following structure will be adopted in this thesis: Behavioural results comparing performance on numerical comparison tasks between dyscalculic (DD), dyslexic (DL), comorbid (CM) and typically developing (TD) groups will be presented first for nonsymbolic stimuli and then for symbolic stimuli. Within each section main effects of group on reaction time and accuracy will be addressed first, followed by the effects of numerical distance on comparison performance.

Following the behavioural results, the fMRI results will be presented, first for nonsymbolic stimuli, secondly for symbolic stimuli. Within these sections, activation profiles for numerical comparison versus rest will be presented first, followed by an examination of the regions that are modulated by the distance between the number pairs presented.

10 GENERAL METHODS

10.1 Participant Recruitment

10.1.1 Recruitment Procedure

45 children were recruited as participants through either a database of families participating in the 'Jyväskylä Longitudinal Study', direct recruitment from local schools in the Jyväskylä area, or through a screening process for a separate project within our lab 'NeuroDys'. All children were invited to participate in initial behavioural screening sessions in order to assess mathematical ability, nonword reading ability and IQ. Results of the behavioural screening sessions were used to assign participants to experimental groups: dyscalculic (DD), dyslexic (DL), comorbid (CM) or typically developing (TD) children.

10.1.2 Selection Criteria and Standardised Tests

Mathematical ability was assessed using the RMAT test of arithmetic achievement (Räsänen, 2004). The RMAT is a standardized 10 minute test consisting of 56 arithmetic items. Items include single and multi-digit addition, subtraction, multiplication and division, decimal conversions, fraction calculations and simple algebra. The RMAT test was adapted from the WRAT test, and has been shown to have a high internal validity and external reliability (Räsänen, 2004). Developmental dyscalculia was defined on the basis of a standardized math scores at least 1.5 standard deviations below the control mean. As discussed above (see TABLE 1), a range of criteria have been used to operationalise dyscalculia, and the criterion used here is stricter than those the majority of behavioural studies carried out to date (for an exception see (Landerl et al., 2004). Furthermore, in order to be classified in the DD group, participants had to be free from diagnosis of comorbid developmental disorders such as developmental dyslexia or ADHD. Dyslexia was operationally defined as a deficit in phonological decoding (Ramus, 2003; Vellutino, Fletcher, Snowling, & Scanlon, 2004) and therefore a test of pseudoword reading (Kairaluoma, Aro, & Rasanen, 2005) was used to rule out children with comorbid developmental dyslexia. Two pseudoword lists contained 26 items each from 4 to 9 letters. The time to read the list from start to finish was recorded by the experimenter. The two lists were tested at intervals 1 hour apart, at the start and the end of the behavioural screening session. The mean reading speed of these two lists was contrasted to the results of a reference group of 64 children of same age. In the reference sample the correlation between the reading speed of the pseudoword list and a standardised test of reading (*A standardised reading test for grade levels 1–6* (Häyrinen, Serenius-Sirve, & Korkman, 1999) was .832 ($p < .001$) (Kairaluoma et al., 2005).

For the purposes of this study, participants were classified as dyslexic if either their nonword reading speed or nonword reading error rate fell 1.5 standard deviations below the control mean, while having a verbal IQ within the normal range (i.e. above 80). Comorbidity was defined as meeting the criteria for both dyscalculia and dyslexia while having IQ scores above 80. IQ scores were obtained for WISC-III Similarities and Block design subtests as measures of verbal and non-verbal IQ respectively (Wechsler, 1991). IQ scores were unavailable for one control participant, however standardised maths and reading scores for that participant were well above average. **Table 2** summarises the classification criteria for each participant group. One subject (Control) was excluded from further analysis on the basis of extremely long RTs and poor accuracy (at least 4 standard deviations away from control mean in accuracy and speed in each condition), hence we were unable to be sure that the child had understood the purpose of the task.

TABLE 2 Classification Criteria for Each Experimental Group (dyslexia classification was on the basis of nonword reading errors OR speed).

		Screening Measure				
		Arithmetic	**Nonword Reading Speed**	**Nonword Reading Errors**	**WISC-III Block Design**	**WISC-III Similarities**
Group	**Control**	> -1.5sd	> -1.5sd	> -1.5sd	> 80	> 80
	Dyscalculic	< -1.5sd	> -1.5sd	> -1.5sd	> 80	> 80
	Dyslexic	> -1.5sd	< -1.5sd	< -1.5sd	> 80	> 80
	Comorbid	< -1.5sd	< -1.5sd	< -1.5sd	> 80	> 80

10.2 Data Collection

10.2.1 Experimental Procedure

Prior to experimental testing, participants took part in a practice scan session using a mock scanner. During the practice session children were familiarized with the tasks and with the procedural aspects of participating in an fMRI study. It was ensured that each subject understood the goal of the task, and had perfect accuracy during an untimed practice session using a subset of the trials presented during formal experimentation.

During the session data were collected for four different trial types, two numerical comparison tasks (symbolic and nonsymbolic) and two line comparison tasks (not reported here). Data were collected from 3 runs per condition, resulting in a total of 12 runs. For each run the stimulus presentation began with 9 seconds of fixation on a white dot in the centre of the screen. Four trial blocks of 15s each were then presented, separated by 18s fixation. Each block contained 6 trials of 2.5s each. Trial time was comprised by 1200ms stimulus presentation and 1300ms fixation, during which responses were still recorded although responses were typically made during the 1200ms stimulus presentation. After the final block of trials a block of rest was presented for 15 seconds before the run terminated. Thus, the total duration of each run was 2.5 minutes. The task stimuli were created using Adobe PhotoShop software and presented using E-Prime 1.1 Software (Psychological Software Tools, Pittsburgh, PA). All stimuli were presented in white color on a black background measuring 600x800 pixels. Stimuli were presented equidistant from a fixation dot that appeared between individual trials. There were 24 trials per run, and 3 runs per condition. Thus there were 144 trials in the experiment, 72 trials for symbolic comparison and 72 for nonsymbolic comparison. Once split into small and large conditions there were 36 trials per condition.

Participants were instructed to choose, as quickly and as accurately as possible, which of the two arrays of squares contained the greater number of squares in the Nonsymbolic condition, and which of the two Arabic digits represented the greater numerosity in the Symbolic condition. These instructions were repeated at the beginning of each run to ensure subjects focused on selecting the array with the greater numerosity, rather than any other variable. Subjects were asked to make the appropriate responses as quickly and accurately as possible by depressing a response button that corresponded to the correct side of the screen. All responses were made with the right index and middle fingers. Index finger was pressed if the correct response was the left hand array, while the middle finger response was used if the correct response was the right hand array.

10.2.2 Tasks

10.2.2.1 Nonsymbolic Number Comparison

Participants were instructed to choose, as quickly and as accurately as possible, which of two arrays of white squares contained the larger number of items. Set sizes of 1-9 items were presented simultaneously on either side of a centrally positioned fixation dot (FIGURE 1 gives an example of the experimental paradigm and stimulus pairs). Set pairs were divided into two conditions according to the numerical distance between the two digits being compared. Pairs with a distance of 1-3 were assigned to the 'Small Distance' condition, while pairs with a distance of 5-8 were assigned to the 'Large Distance' condition. To control for the possible confound of continuous variables, the density, individual square size, and total area of each array was systematically varied across trials. Specifically, in each run, 2 of each 6 pairings, the larger numerosity had a larger overall area than the smaller numerosity. In another 2 pairs, the smaller numerosity had a larger overall area. In the final 2 pairings, the numerosities occupied equal amounts of the display. Density was varied in each of these 3 subgroups of 2 stimuli. One of the two stimuli in each group associated larger density with the larger numerosity and one of the stimuli associated smaller density with the larger numerosity. Additionally, individual square sizes were varied over all stimuli in such a way that the individual squares within an array differed from one another. These variations ensured that numerosity could not be reliably predicted from variables continuous with it.

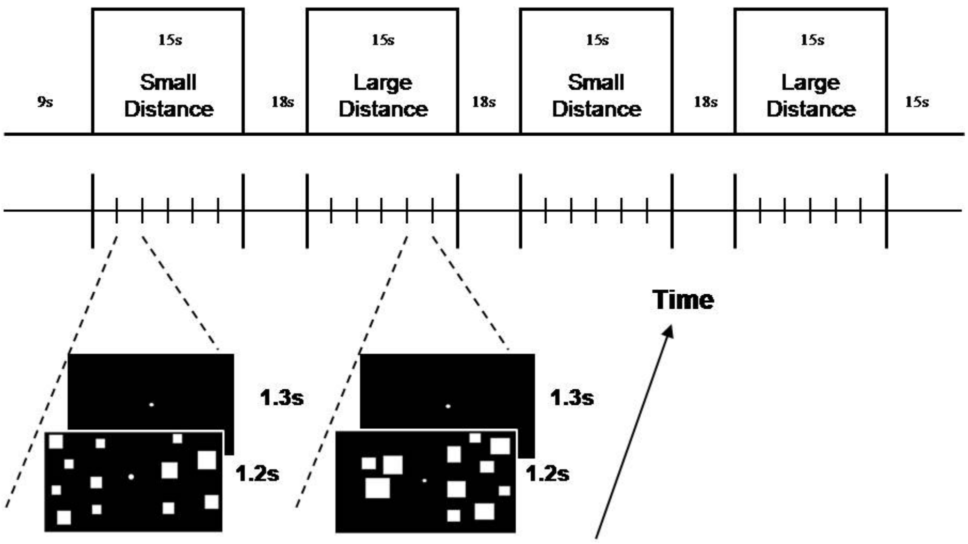


FIGURE 1 Nonsymbolic Number Comparison Stimulus Timing and Paradigm Structure.

10.2.2.2 Symbolic Number Comparison

Participants were instructed to choose, as quickly and as accurately as possible ,which of two simultaneously presented Arabic Digits represented the larger numerosity. Digits 1-9 items were presented simultaneously on either side of a centrally positioned fixation dot (FIGURE 2 gives an example of the experimental paradigm and stimulus pairs). Digit pairs were divided into two conditions according to the numerical distance between the two digits being compared. Pairs with a numerical distance of 1-3 were assigned to the 'Small Distance' condition, while pairs with a numerical distance of 5-8 were assigned to the 'Large Distance' condition. The task stimuli were created using Adobe PhotoShop software and presented using E-Prime 1.1 Software (Psychological Software Tools, Pittsburgh, PA). All stimuli were presented in white color on a black background measuring 600x800 pixels. Stimuli were presented equidistant from a fixation dot that appeared between individual trials.

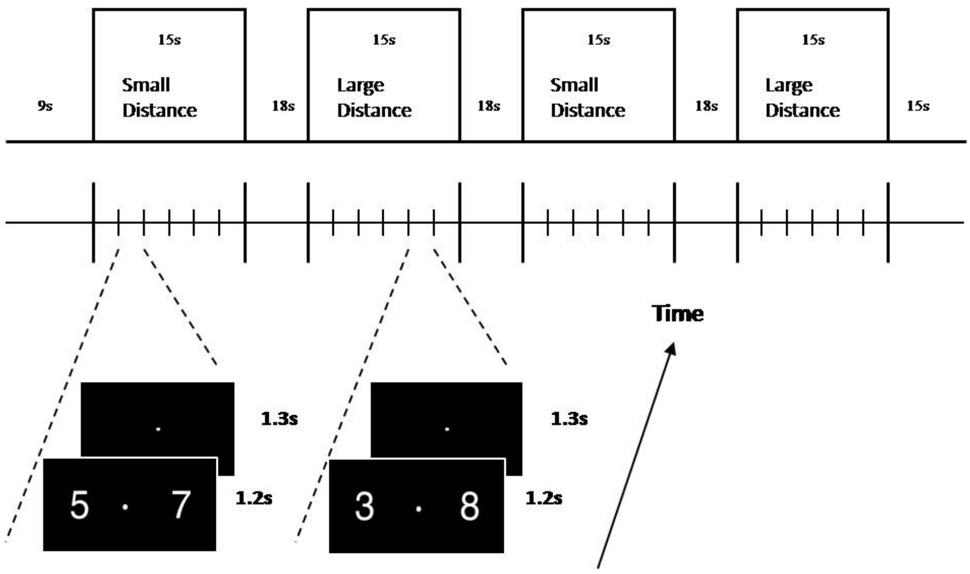


FIGURE 2 Symbolic Number Comparison Stimulus Timing and Paradigm Structure.

10.2.3 fMRI Parameters

The experiment was performed using Siemens Symphony 1.5 T MRI scanner. Before functional imaging, a T1-weighted high resolution 3D structural volume (3D-MPR, FOV = 256 × 256 × 176 mm^3, sampling = 0.97 × 0.97 × 1 mm^3) was acquired providing detailed anatomical information for defining the location of 36 axial slices acquired during functional imaging. For each run a time-series of 43 EPI volumes were acquired using BOLD sensitive interleaved gradient-echo sequence (sampling = 3× 3 × 4 mm^3, no gap, TR = 3 s, TE = 44 ms, FA = 90 ^{o}).

10.2.4 Behavioural Data Analysis

This study employed an experimental paradigm which was designed to ensure that all groups, typically and atypically developing, were able to perform the task with a high level of accuracy. This is an important dimension of task design particularly in the context of neuroimaging data, as in order to interpret activation patterns in terms of cognitive processes, the experimenter must be able to reasonably assume that all participants were performing the same task. If accuracy falls below a certain level it can no longer be assumed that the participant or groups were performing the task at hand. As a consequence of this design strategy, however, percent correct accuracy data tends to exhibit a negative skew and this was evident in the accuracy scores for all conditions and for all groups in the present study. In order to correct this skew a logarithmic transformation was applied to all accuracy data, however, this transformation did not correct the skew and therefore the transformed data was not used in the final analysis. Subsequently, an ARCSINE transformation was applied to the accuracy data, but again did not improve the skew, and thus the transformed data were not used in the final analysis. However, ANOVA is known to be robust statistical procedure and violations of parametric assumptions have little or no effect on the conclusions (Howell, 2001) and so nonparametric tests were not employed.

10.2.5 fMRI Data Analysis

Both structural and functional images were analyzed using Brain Voyager QX 1.8.6 (Brain Innovation, Maastricht, Netherlands). The functional images were corrected for head motion, linear trends in signal intensity, and low frequency non-linear trends in signal intensity using a high-pass filter set at 3 cycles per time course. Following initial automatic alignment of functional images to the high-resolution T1 structural images, the alignment was manually fine-tuned to ensure optimal spatial correspondence. The realigned functional data set was then transformed into Talairach space (Talairach & Tournoux, 1988). A two gamma hemodynamic response function was used to model the expected BOLD signal(Friston et al., 1998).

A random effects, whole-brain, analysis was carried out to assess which brain regions were significantly activated by numerical comparison versus rest in the first instance, and by distance (small – large) in the second instance. The resulting statistical maps were subsequently corrected for multiple comparisons using cluster-size thresholding (Forman et al., 1995; Goebel, Esposito, & Formisano, 2006).

In this method, an initial voxel-level (uncorrected) threshold is set (In the present study $p < .001$, uncorrected). Then, thresholded maps are submitted to a whole-slab correction criterion based on the estimate of the map's spatial smoothness and on an iterative procedure (Monte Carlo simulation) for estimating cluster-level false-positive rates. After 1,000 iterations, the minimum cluster-size that yielded a cluster-level false-positive rate (α) of .05 (5%) is used to threshold the statistical maps. Put another way, this method calculates the size that a cluster would need to be (the cluster threshold) to survive a correction for multiple comparisons at a given statistical level. Only activations whose size meet or exceed the cluster threshold are allowed to remain in the statistical maps.

The current set of analyses contained a combination of task versus rest within and between group, and within task within and between group contrasts. Thus, in order to address the progression from the most basic to higher level, multi-factorial analyses, and compensate the increasing risk of Type II errors with increasing analysis complexity, a different cluster corrected threshold was used for each level of analysis employed. For the first level of analysis, task versus rest across groups, a cluster level correction criteria of $p < 0.001$ ($p < 0.001$ uncorrected) was used. For the next level of analysis, task versus rest between groups and distance effect across groups a cluster level correction criteria of $p < 0.001$ ($p < 0.005$ uncorrected) was used, and finally the distance effect between groups analysis used a cluster corrected threshold of $p < 0.01$ ($p < 0.005$ uncorrected).

Functional activations were *z*-scored by estimating baseline signal from the rest periods of each functional run.

STUDY 1: BEHAVIOURAL ANALYSIS

11 INTRODUCTION

It is clear from the literature review above, that few studies have investigated the mental representation of numerical magnitude in dyscalculic populations that are both stringently defined and do not present with comorbid reading disorders. Although a growing body of behavioural research has begun to investigate impairments in basic numerical processing abilities which may underlie DD, such as estimating the approximate results of arithmetic equations, matching quantities to Arabic digits and naming digits and quantities from one to four (Jordan & Hanich, 2003; Jordan et al., 2003; van der Sluis et al., 2004), only a handful have investigated numerical comparison.

Bruandet, Molko, Cohen, & Dehaene (2004) compared typically developing controls to individuals with Turner Syndrome on a range of basic numerical tasks and found that during numerical comparison of Arabic digits there were no significant performance differences between Turner Syndrome patients and controls. Furthermore the authors found no Group x Distance interaction, with both groups showing classical behavioural distance effects. However, while Turner Syndrome patients have been shown to have mild to severe arithmetic deficits, these are present in the context of widespread visual memory, visual-spatial and attentional deficits (Mazzocco, 1998; C. M. Temple & Marriot, 1998). Thus, while Turner Syndrome may include some of the impairments seen in dyscalculia, studies of Turner syndrome patients cannot reliable elucidate the underlying causes of pure DD.

Landerl et al (2004) compared children with pure DD to typically developing children, those with dyslexia and comorbid dyscalculia and dyslexia. The authors found that during numerical comparison of Arabic digits, the dyscalculic and the double deficit groups were slower than the controls and dyslexics, but did not differ from each other. The control and dyslexic groups also did not differ from each other. This result suggests that the underlying deficit in the DD and double deficits groups is specific to numerical information and is not related to reading deficits. However, this study failed to observe a significant distance effect for any of the groups, or any Group x Distance interaction.

Although Landerl et al (2004) used strict selection criteria for defining the experimental groups, it is peculiar that a distance effect was not observed even for control children as the behavioural distance effect is a highly robust effect (Moyer & Landauer, 1967). The reasons for the lack of distance effect in this study are unclear, and the authors do not offer one, thus the findings of this study with regards to numerical comparison are in need of replication. Furthermore, this study did not include a nonsymbolic numerical comparison task, and thus the question remains whether the slower RTs in the dyscalculic and double deficit groups reflect an impairment dealing with Arabic digits or whether underlying numerical representations are impaired in one or other of those groups.

So far only one study appears to have investigated numerical comparison in DD using nonsymbolic stimuli. Rousselle & Nöel (2007) found that children with DD were slower and less accurate than controls in comparison of Arabic digits but not in comparison of collections of lines. This study also found that DD children showed a weaker distance effect than controls in symbolic comparison, but the distance comparison for nonsymbolic stimuli was not reported. Despite the interesting findings of this study there is a serious problem in interpreting the results with regards to pure DD. The "maths disabled" group was made up of children with pure DD and those with comorbid mathematical and reading disorders. The authors report that the groups were collapsed on the basis that they showed no differences in overall reaction time or accuracy for any of the experimental measures. However, it is still highly possible that group differences existed in the distance effects between groups as this effect in particular is thought to reflect access to numerical semantic information. Thus it is possible that the merging of the two maths disabled groups may have masked more subtle group differences in the representation and processing of numerical magnitude that would have been revealed by a contrast of distance effects.

Furthermore, Rousselle & Nöel included in their selection measures a subtest of Arabic number comparison. Thus, the comparison between symbolic and nonsymbolic number comparison is undermined because poor performance on symbolic comparison has already contributed to the initial group classifications.

Both Landerl et al (2004) and Rousselle & Nöel (2007) observed no differences in numerical comparison performance or in the numerical distance effect between DD and CM children. Landerl et al suggest that this reflects a shared deficit in the representation and processing of "specifically numerical information". While it is true that the two groups did not differ on a range on basic numerical tasks including number reading and writing and dot counting, these tasks all required either the use of Arabic digits or serial counting, and thus impaired performance on these tasks could reflect both a deficit in the representation of numerical magnitude or a deficit in accessing that representation through the use of visual symbols. It may be that had this study included a test of nonsymbolic numerical comparison different profiles may have emerged for the DD and CM groups.

Rousselle & Nöel (2007) on the other hand, tested both symbolic and nonsymbolic comparison, and found that the DD and CM groups when collapsed together performed worse than controls on symbolic comparison but not nonsymbolic comparison. The authors suggest that this reflects a deficit in the accessing numerical magnitude representations through the use of Arabic digits, while the underlying representations themselves remain intact.

However, these groups were selected on the basis of a composite score which included a test of symbolic comparison but not nonsymbolic comparison, thus inflating the chances of finding a group difference on this measure. Furthermore, the DD and CM groups were not compared directly with regards to the effects of distance on their numerical comparison performance, and thus it is possible that group differences in the distance effect in either symbolic or nonsymbolic comparison may have been present between the groups, but were masked by collapsing them into one. Thus it is possible that a deficit in the underlying representation of numerical magnitude was present in one or both of these groups, but was not revealed for the reasons above.

The Comorbid group may represent a subset of dyslexics who have a specific deficit in retrieval of semantic information from visual symbols, in addition to a phonological awareness core deficit, which impacts negatively on arithmetic performance. Many dyslexic children show a retrieval deficit measured by tasks such as rapid naming (Lyytinen, Erskine, Tolvanen et al., 2006) which has been suggested to represent a second core deficit in dyslexia (Wolf & Bowers, 1999).

Symbolic number comparison requires rapid recognition of Arabic digits, as well as access and integration of the semantic information underlying the symbols, and therefore, if the comorbid group's arithmetic deficits stem from retrieval or 'access' impairments, and not an impaired representation of numerical magnitude, then they could be expected to show impairments of symbolic number comparison but not nonsymbolic number comparison. An access deficit would also be expected to result in a stronger distance effect, as the access to and integration of semantic information underlying numerical symbols would become more difficult as that semantic information becomes more overlapping.

By contrasting symbolic and nonsymbolic numerical comparison performance and the in particular the effect of numerical distance between groups it is possible to probe at least one of the potential sources of comorbidity between dyslexia and dyscalculia, that is, the impairment of numerical magnitude representation. If the arithmetic impairments of the comorbid children stem from the same presumed impairment of numerical magnitude representation as those in the DD children, then both groups would be expected to show atypical effects of distance on numerical comparison in both the symbolic and nonsymbolic condition. If, however, this is not shown to be the case, then it paves the way for future research to focus on other potential sources of the comorbidity, such as a specific deficit in naming fluency.

In order to address the above concerns, this thesis compares dyscalculic (DD), dyslexic (DL), comorbid (CM) and typically developing (TD) children on both symbolic and nonsymbolic numerical comparison tasks. Furthermore an explicit comparison of the effects of distance on both reaction time and accuracy in both conditions is included so that the representation and processing of numerical magnitude both through the use of numerical symbols and directly may be compared between groups.

12 PARTICIPANTS

45 Children who completed the initial screening session were assigned to one of 4 groups based on their results (see General Methods section for selection criteria). A one-way Analysis Of Variance (ANOVA) revealed no main effect of Group on Age (years) $F(1,3) = 1.44$, $p > 0.05$, WISC-III Block Design scores $F(1,3) = 1.92$, $p > 0.05$, or WISC-III Similarities subtest scores $F(1,3) = 0.34$, $p > 0.05$. A one-way ANOVA revealed a significant main effect of Group on Nonword reading time (seconds) $F(1,3) =15.8$, $p < 0.001$. Post-hoc analyses using Tukey's criterion for post-hoc significance indicate that reading times were slower in the dyslexic and comorbid groups than the control and dyscalculic groups ($p < 0.05$), no other group differences were significant. A one-way ANOVA revealed a significant main effect of Group on Nonword reading error percentage $F(1,3) =3.46$, $p < 0.05$. Post-hoc analyses using Tukey's criterion for post-hoc significance indicate that the dyslexic group made more errors than the control group ($p < 0.05$), no other group differences were significant. A one-way ANOVA revealed a significant main effect of Group on Arithmetic $F(1,3) =28.83$, $p < 0.001$. Post-hoc analyses using Tukey's criterion for post-hoc significance indicate that arithmetic performance was lower ($p < 0.05$) in the dyscalculic and comorbid groups than the control and dyslexic groups, no other group differences were significant. These results support the validity of the screening measures, and confirm that the participant groups differ only along the dimensions on which they were intended to. Table 3 summaries the group profiles on the screening measures.

TABLE 3 Group Results for Behavioural Screening Measures.

	Group							
	Control n(13)		**Dyscalculic n(9)**		**Dyslexic n(11)**		**Comorbid n(12)**	
	Mean	*Std. Error*	*Mean*	*Std. Error*	*Mean*	*Std. Error*	*Mean*	*Std. Error*
Age (yrs)	11.74	0.43	11.46	0.52	10.99	0.35	10.64	0.4
Arithmetic Standard Score	9.54	0.83	3	0.58	9	0.54	3.58	0.45
Non-word Reading Time (secs)	28.38	3.34	28.94	2.59	53.73	3.83	70.75	8.18
Non-word Reading Error Percentage	1.48	0.49	3.21	1.2	9.1	2.63	8.17	2.77
WISC-III Block Design	103.64	1.92	91.11	5.88	94.55	5.93	103.0	2.71
WISC-III Similarities	105.45	3.78	105.0	4.64	100.45	2.56	102.5	5.28

13 NONSYMBOLIC NUMBER COMPARISON

13.1 Hypotheses

H1. If dyscalculia stems from an impaired or underdeveloped mental representation of numerical magnitude, the DD group is expected to show poorer performance on nonsymbolic number comparison than the TD and DL groups.

H2. If the arithmetic impairments in the comorbid group stem from the same impaired or underdeveloped representation of numerical magnitude as those in DD, then the CM group is expected to show poorer performance than the control and DL groups on nonsymbolic number comparison but equivalent performance to the DD group.

H3. As children show a stronger distance effect than adults, a stronger distance effect is assumed to represent a less well developed representation of numerical magnitude. If the mental representation of numerical magnitude is impaired or underdeveloped in the DD, then the DD group is expected to show a stronger distance effect than the TD and DL groups.

H4. If the arithmetic impairments in the comorbid group stem from the same impaired or underdeveloped representation of numerical magnitude as those in DD, then the CM group is expected to a stronger distance effect than the TD and DL groups but not than the DD group.

13.2 Results

13.2.1 Overall Comparison

13.2.1.1 Reaction Time

Mean reaction times (see TABLE 4) for correct responses were analysed in a one-way ANOVA with Group as the between subjects factor. Responses were classified as incorrect if the participant selected the smaller of the two numerosities, or if the participant did not respond within the 1.3s post stimulus period. This analysis revealed no main effect of group, [$F(1,3) = 1.25$, $p > 0.05$].

13.2.1.2 Accuracy

Accuracy was calculated as the percentage of trials in which a correct response was given (see TABLE 4). A one-way ANOVA with Group as the between subjects factor revealed no main effect of group on comparison accuracy [$F(1,3) = 1.11$, $p > 0.05$].

TABLE 4 Mean reaction times and percentage correct accuracy for nonsymbolic comparison.

	Typically Developing		**Dyscalculic**		**Dyslexic**		**Comorbid**	
	Mean	Standard Error	Mean	Standard Error	Mean	Standard Error	Mean	Standard Error
Reaction Time	673.87	23.24	675.19	34.27	705.02	22.09	731.34	21.82
Percentage Correct	93.27	0.89	88.89	1.46	89.77	3.15	91.55	1.2

13.2.2 Nonsymbolic Distance Effect

13.2.2.1 Reaction Time

In order to assess the effect of numerical distance on reaction time between groups, mean RTs were analyzed by means of a 2 x 4 mixed design analysis of variance (ANOVA), with Distance (small vs. large) as a within subjects factor and Group (Control vs. Dyscalculic vs. Dyslexic vs. Comorbid) as a between subjects factor. This analysis revealed a main effect of distance on reaction time [$F(1,41) = 284.04$, $p < 0.001$], with longer response times for small distance trials than large distance trials. The main effect of group was not significant [$F(1, 3) = 1.25$, $p > 0.05$]. No distance by group interaction was found [$F(3,41) = 0.34$, $p > 0.05$]. FIGURE 3 summarises reaction times for each group for small and large numerical distances, and shows that each group showed a classical distance effect.

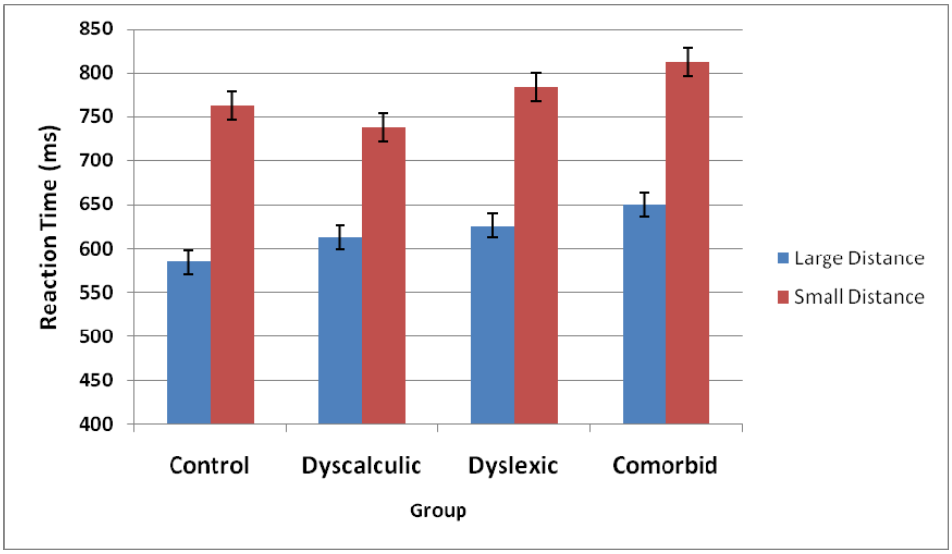


FIGURE 3 Reaction times for small and large distance nonsymbolic number comparison.

13.2.2.2 Accuracy

In order to assess the effect of numerical distance on comparison accuracy, 'Percentage Correct' accuracy data were analyzed by means of a 2 x 4 mixed design analysis of variance (ANOVA), with Distance (small vs. large) as a within subjects factor and Group (Control vs. Dyscalculic vs. Dyslexic vs. Comorbid) as a between subjects factor. This analysis revealed a main effect of distance on accuracy [$F(1,41) = 171.49$, $p < 0.001$], with greater accuracy for large distance trials than small distance trials. There was no significant main effect of group [$F(1,3) = 1.11$, $p > 0.05$]. This analysis revealed no significant distance by group interaction [$F(1,3) = 1.39$, $p > 0.05$]. Figure 4 summarizes accuracy data for small and large distance comparisons in terms of percent correct. It can be seen that all groups show a classical distance effect with decreased accuracy for smaller numerical distances.

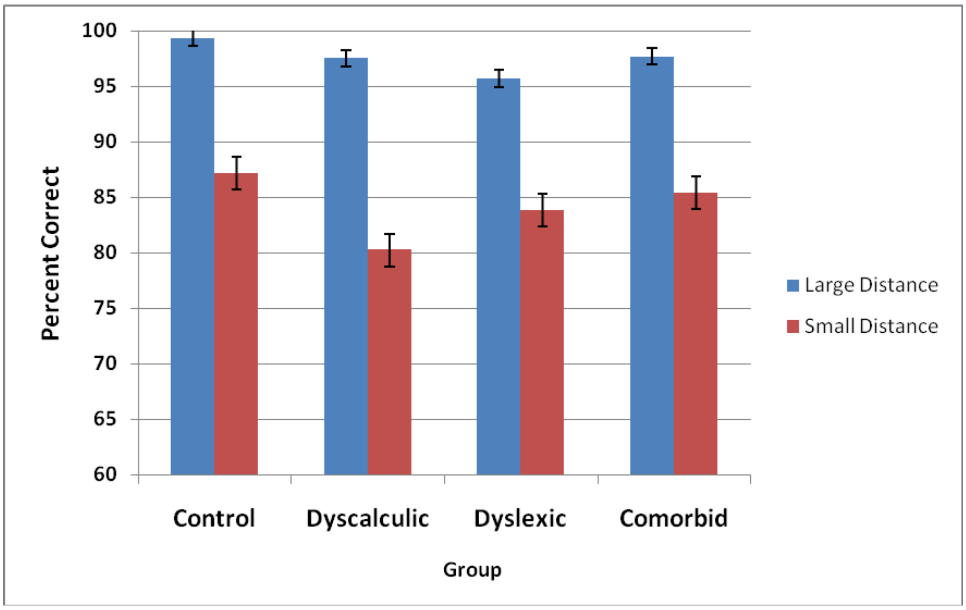


FIGURE 4 Percent correct data for small and large distance nonsymbolic number comparison.

Despite the lack of a significant Group x Distance interaction the dyscalculic group appeared on visual inspection of the data to show a stronger distance effect than the other three groups. Thus, on the basis of apriori hypotheses, a series of 2 x 2 mixed design ANOVAs were carried out, comparing at first each atypically developing group to the control group, then each atypically developing group with each other. The results of these analyses are summarised in TABLE 5.

It can be seen from TABLE 5 that for nonsymbolic number comparison, the Group x Distance interaction was marginally significant for controls versus dyscalculics while no other interactions approached significance. Independent samples t-tests showed that the DD group did not differ from controls in the large distance condition [$t(9.94) = 1.77$, $p > 0.05$], however the DD group were significantly less accurate in the small distance condition [$t(20) = 2.5$, $p < 0.05$].

TABLE 5 2 x 2 ANOVAs comparing nonsymbolic distance effects between each group.

	Main Effect of Distance		Group x Distance Interaction	
Group Contrast	**F-Value**	**Significance Level**	**F-Value**	**Significance Level**
Control–Dyscalculic	132.03	< 0.001	3.96	**0.06**
Control–Dyslexic	93.34	< 0.001	0.02	N.S.
Control–Comorbid	77.21	< 0.001	0.001	N.S.
Dyscalculic–Dyslexic	96.46	< 0.001	3.33	N.S
Dyscalculic–Comorbid	78.73	< 0.001	2.27	N.S.
Dyslexic–Comorbid	58.67	< 0.001	0.02	N.S.

13.3 Discussion

The first set of analyses of this section investigated general speed and accuracy differences between groups during nonsymbolic number comparison. The results above show that all groups performed with equal speed and accuracy when the small and large distance conditions were collapsed. Thus hypotheses 1 and 2 were not supported.

This finding supports the results of Rousselle & Nöel (2007) who found no difference in the speed and accuracy of nonsymbolic numerical comparison between DD and control children. The authors suggest that this reflects a fully intact mental representation of numerical magnitude in DD children, however, it is highly possible that the representation as a whole is intact at the most basic level, but not sufficiently strong to support more taxing numerical processing. In other words, the numerical magnitude representation in DD children may be sufficient to compare numbers separated by relatively large numerical distances, but is not able to perform as well with numbers separated by relatively small distances. Thus one could say the representation is not absent, it is simply underdeveloped and a more sophisticated within task manipulation is required to probe that impairment.

Therefore the second set of analyses in this section compared the numerical distance effect between groups and found no Group x Distance interactions for either speed or accuracy. However, when each group was compared to each other in a series of 2 x 2 ANOVAs a marginally significant Group x Distance interaction for accuracy was revealed when comparing the DD and TD groups. Further analysis revealed that while the groups did not differ in accuracy on the large distance condition the DD group was significantly less accurate in the small distance condition. Thus the predictions of hypothesis 3 were met. Although there was no significant Group X Distance interaction for reaction time, all groups showed a classical distance effect for reaction time, suggesting there was not a speed accuracy trade off.

These results suggest that the level of numerical representation in DD children is sufficient to perform the simplest of numerical comparisons in which a large numerical distance separates the two numbers. However, once the task places increasing demands on that representation it fails to support the same level of accurate performance as typically developing children. Thus, these results tentatively support the hypothesis that DD children have an impairment of the mental representation of numerical magnitude, and that it is revealed by a stronger distance effect than typically developing children. It should be noted, however, that this interpretation is based on a post-hoc interaction that was only marginally significant, and that the initial Group X Distance interaction was non-significant. However, the post-hoc test was justified on the basis of the apriori hypotheses, but nonetheless the result requires replication.

The comorbid and dyslexic groups showed no differences in the nonsymbolic distance effect to the typically developing group. This suggests that in these two groups the mental representation of numerical magnitude is equally as developed and supportive to numerical processing as that in typically developing children. Furthermore, this suggests that the arithmetic deficits observed in the CM group stem from a different source to those observed in pure DD and thus hypothesis 4 could not be accepted.

Rousselle & Nöel (2007) showed that when DD and CM children are collapsed into one group, they do not perform worse than control children on nonsymbolic number comparison. The authors suggest therefore, that the arithmetic impairments in both groups stem from a deficit in accessing underlying numerical representations through Arabic digits. However, the current results suggest that this may be the case only for the CM group, and that the failure of Rousselle and Nöel to elucidate these subtle group differences was due to the fact that they collapsed the groups and did not test for differences between CM and DD children in the effects of distance during nonsymbolic numerical comparison.

Thus, the results of the nonsymbolic comparison task suggest that pure dyscalculia is underscored by an underdeveloped representation of numerical magnitude. Children with comorbid dyslexia and dyscalculia, on the other hand do not show the same representational impairment. This suggests that the mental representation of numerical magnitude in the CM group is intact, and thus, the source of arithmetic impairments in comorbid children remains an open question. By comparing the numerical distance effect during symbolic number comparison, it is possible to investigate whether the comorbid group differ from the dyslexic and typically developing groups in their ability to access the mental representation of numerical magnitude through the use of Arabic digits, as the results of Rousselle and Nöel (2007) would suggest.

14 SYMBOLIC NUMBER COMPARISON

14.1 Hypotheses

H1. If dyscalculia stems from an impaired or underdeveloped mental representation of numerical magnitude, the DD group is expected to show poorer performance on symbolic number comparison than the control and dyslexic groups.

H2. If the arithmetic impairments in the CM group are a result of a deficit in accessing the mental representation of numerical magnitude through the use of Arabic digits, independent of their comorbid dyslexia, then the CM group is expected to show impaired performance in symbolic number comparison relative to the TD and DL groups.

H3. As children show a stronger distance effect than adults, a stronger distance effect is assumed to represent a less well developed representation of numerical magnitude. If the mental representation of numerical magnitude is impaired or underdeveloped in DD, then the DD group is expected to show a stronger distance effect than the control and dyslexic groups.

H4. If the arithmetic impairments in the CM group are a result of a deficit in accessing the mental representation of numerical magnitude through the use of Arabic digits, independent of their comorbid dyslexia, then the CM group is expected to show a stronger distance effect than TD and DL groups, but not than the DD group.

14.2 Results

14.2.1 Overall Comparison

14.2.1.1 Reaction Time

Mean reaction times for correct responses (see TABLE 6) were analysed in a one-way ANOVA with Group as the between subjects factor. Responses were classified as incorrect if the participant selected the smaller of the two numerosities, or if the participant did not respond within the 1.3s post stimulus period. This analysis revealed a marginally significant effect of group, [$F(1,3) = 2.78$, $p = 0.053$].

14.2.1.2 Accuracy

Accuracy was calculated as the percentage of trials in which a correct response was given (see TABLE 6). A one-way ANOVA with Group as the between subjects factor revealed no main effect of group on comparison accuracy [$F(1,3) = 1.91$, $p > 0.05$].

TABLE 6 Mean reaction times and percentage correct accuracy for symbolic comparison.

	Typically Developing		**Dyscalculic**		**Dyslexic**		**Comorbid**	
	Mean	Standard Error	Mean	Standard Error	Mean	Standard Error	Mean	Standard Error
Reaction Time	632.62	24.94	688.93	32.61	717.13	28.35	736.04	29.15
Percentage Correct	94.87	0.48	91.67	1.65	90.15	2.58	90.63	1.34

14.2.2 Symbolic Distance Effect

14.2.2.1 Reaction Time

In order to assess the effect of numerical distance on reaction time between groups, median RTs were analyzed by means of a 2 x 4 mixed design analysis of variance (ANOVA), with Distance (small vs. large) as a within subjects factor and Group (Control vs. Dyscalculic vs. Dyslexic vs. Comorbid) as a between subjects factor. This analysis revealed a main effect of distance on reaction time [$F(1,41) = 71.9$, $p < 0.001$], with longer response times for small distance trials than long distance trials, but no distance by group interaction [$F(1,3) = 0.4$, $p > 0.05$]. The main effect of group was marginally significant [$F(1,3) = 2.78$, $p = 0.053$). Post-Hoc Tukey's HSD tests revealed that the marginally significant main effect of group was driven by higher reaction times for the comorbid group relative to the control group ($p < 0.05$). All other comparisons were not significant. FIGURE 5 summarises the reaction time data for small and large distances. It can be seen that all groups showed a classical distance effect, with longer reaction times for the small distance condition.

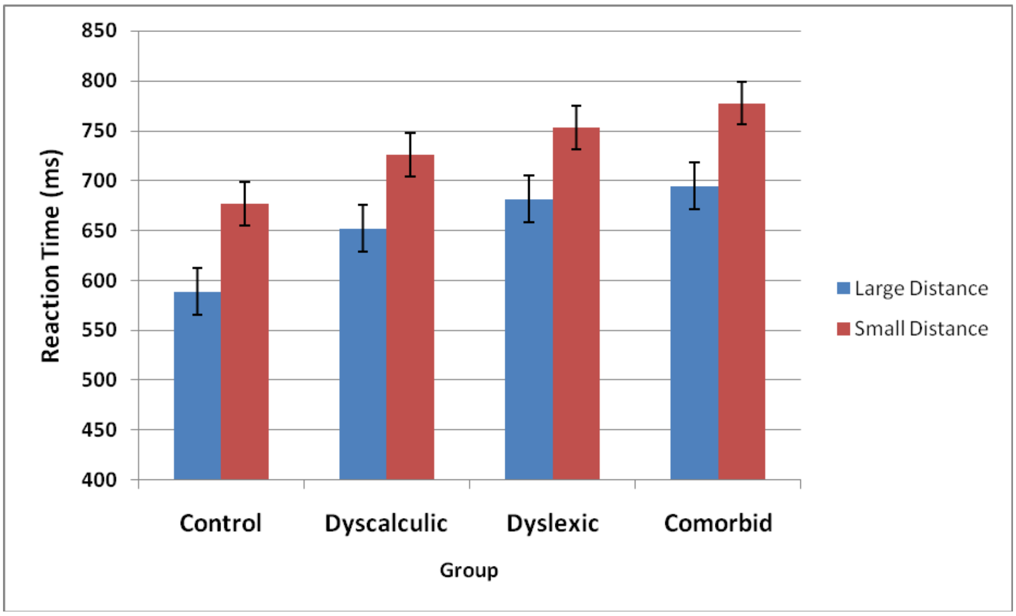


FIGURE 5 Reaction times for small and large distance symbolic number comparison.

14.2.2.2 Accuracy

In order to assess the effect of numerical distance on comparison accuracy, 'Percentage Correct' accuracy data (FIGURE 6) were analyzed by means of a 2 x 4 mixed design analysis of variance (ANOVA), with Distance (small vs. large) as a within subjects factor and Group (Control vs. Dyscalculic vs. Dyslexic vs. Comorbid) as a between subjects factor. This analysis revealed a main effect of distance on accuracy [$F(1,41) = 158.46$, $p < 0.001$], with greater accuracy for large distance trials than small distance trials. The main effect of group was not significant [$F(1,3) = 1.91$, $p > 0.05$). This analysis also revealed a significant distance by group interaction [$F(1,3) = 3.96$, $p < 0.05$].

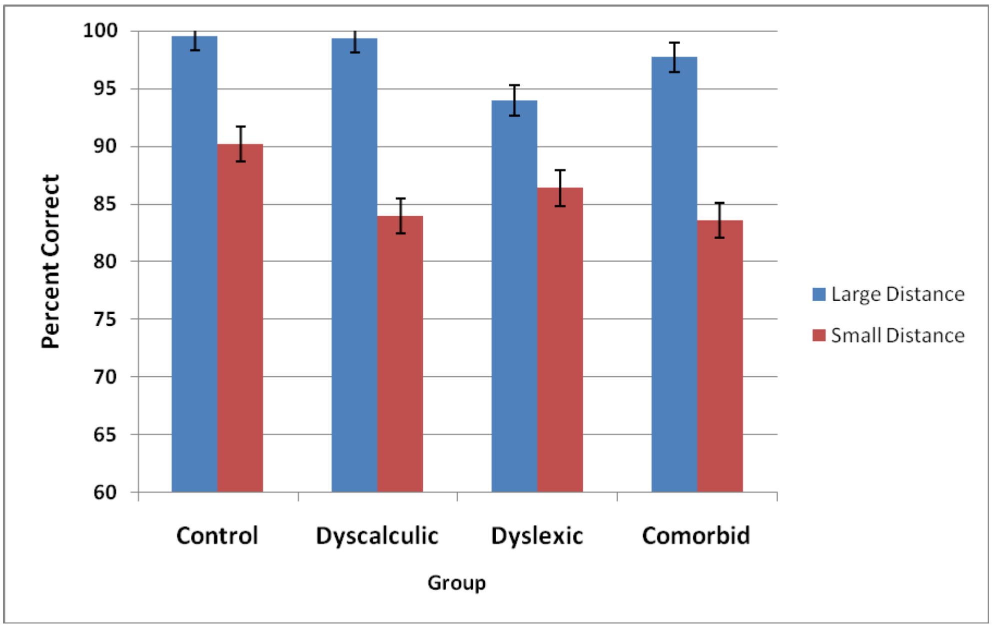


FIGURE 6 Percent correct data for small and large distance nonsymbolic number comparison.

In order to explore the source of the Group x Distance interaction, a series of 2 x 2 mixed design ANOVAs were carried out, comparing at first each atypically developing group to the control group, then each atypically developing group with each other. The results of these analyses are summarised in TABLE 7.

TABLE 7 2 x 2 Anova's directly contrasting each group with each other.

	Main Effect of Distance		**Group x Distance Interaction**	
Group Contrast	**F-Value**	**Significance Level**	**F-Value**	**Significance Level**
Control–Dyscalculic	85.61	< 0.001	5.05	**< 0.05**
Control–Dyslexic	72.8	< 0.001	0.84	N.S.
Control–Comorbid	128.65	< 0.001	5.18	**< 0.05**
Dyscalculic–Dyslexic	50.77	< 0.001	5.2	**< 0.05**
Dyscalculic–Comorbid	83.07	< 0.001	0.16	N.S.
Dyslexic–Comorbid	72.72	< 0.001	6.62	**< 0.05**

As can be seen from TABLE 7, all contrasts revealed a significant main effect of distance. TD versus DD, TD versus CM, DD versus DL, and CM versus DL contrasts all revealed significant Group x Distance interactions. Inspection of the means plots suggested that both the DD and CM groups showed a greater effect of distance than the TD and DL groups. In other words, the two groups with mathematical impairments showed stronger distance effects than the two groups without mathematical impairments. Independent-samples t-tests confirmed this interpretation, showing that the DD group did not differ significantly from the TD group in accuracy in the large distance condition [$t(20) = 0.39$, $p > 0.05$] but showed significantly lower accuracy during the small distance condition [$t(20) = 2.24$, $p < 0.05$]. The CM group who also showed a significant group by distance interaction with the TD group were found to have significantly lower comparison accuracy in both the large [$t(13.68) = 2.16$, $p < 0.05$] and small [$t(15.4) = 2.8$, $p < 0.05$)]distance conditions. When comparing the DD and DL groups, accuracy rates were not significantly different in either the small distance [$t(18) = -0.65$, $p > 0.05$] or the large distance [$t(18) = 1.55$, $p > 0.05$)]conditions. The significant Group X Distance interaction can be explained by marginally higher accuracy for the DL group relative to the DD group in the small distance condition, and marginally lower accuracy in the large distance condition. Thus, although percent correct was not significantly different between groups in either condition, the change in accuracy from large to small distance comparisons was greater for the DD group. Similarly, the CM group did not differ from the DL group in either the small [$t(21) = -0.9$, $p > 0.05$] or large [$t(21) = 1.2$, $p > 0.05$] distance conditions, despite showing a significant group by distance interaction.

14.3 Discussion

The first analysis in this section investigated overall speed and accuracy differences between groups during symbolic number comparison. The above results revealed no group differences in accuracy but did reveal a marginally significant main effect of group for reaction time, post-hoc tests showing that the effect was driven by longer reaction times for the comorbid group relative to the typically developing group. Thus Hypothesis 1 was not met, but hypothesis 2 was tentatively supported.

These results support previous findings by Landerl et al (2004) and Rousselle & Nöel (2007) both of which found a main effect of group on reaction time during symbolic comparison. Rousselle & Nöel also found a main effect of group on comparison accuracy. Landerl et al, however, did not find any accuracy differences between groups. Thus results from previous studies show that in untimed tasks, children with mathematical learning disorders are slower than typically developing children during symbolic number comparison. Accuracy comparisons, however, have yielded mixed results and the present set of results suggests that groups do not differ in overall symbolic accuracy with numbers 1 - 9.

The source of the main effect of group on reaction time in the present study was longer reaction times for the comorbid group than for the control group. No other comparisons were significant. This suggests that the comorbid group had a general problem in accessing numerical information through Arabic digits as suggested to underlie DD in general by Rousselle and Nöel (2007).

The lack of a group effect on overall accuracy is harder to explain however. The participants in the Landerl et al (2004) and the Rousselle & Nöel (2007) studies were 4 years old and 6-7 years old respectively, while the participants in the present study were approximately 11 years old. It is possible that the older age of the participants in the present study afforded them a great familiarity with Arabic digits, and thus the task was relatively simple for them, in comparison to the younger children in previous studies.

It is also possible that, as in the nonsymbolic condition reported above, collapsing small and large distance conditions masks subtle performance variations between groups, and thus the second set of analyses in this section compared the effect of distance on reaction time and accuracy between groups. This analysis revealed that both the dyscalculic and comorbid groups showed stronger accuracy distance effects than the typically developing and dyslexic groups. Although there were no differences between groups in the effect of distance on reaction time, all groups showed a classical distance effect for reaction time, suggesting that the results pattern did not reflect a speed accuracy trade off.

Exploration of these interactions revealed that the DD group did not differ in accuracy from the TD group during the large distance condition, but showed a significantly greater error rate during the small distance condition, suggesting that the underlying numerical representation in the DD group is sufficiently developed to perform the most simple numerical comparisons, but cannot support comparisons which require more fine grained access to the mental representation of numerical magnitude. Thus the predictions of hypothesis 3 were met.

The CM group, on the other hand, as well as showing a stronger accuracy distance effect than controls, made significantly more errors than the TD group in both the small and large symbolic distance conditions. Since they did not show an increased distance effect during nonsymbolic comparison, this result suggests that the CM group's arithmetic problems are related specifically to the use of Arabic digits rather than an impaired underlying representation of numerical magnitude. In combination with the significantly longer reaction times for the CM group relative to the TD group, these results suggest the while the underlying representation of numerical magnitude is intact in the CM group, they may have a deficit in accessing that representation through symbolic stimuli.

Hypothesis 4 predicts that if comorbidity is caused by a deficit in accessing numerical representations through Arabic digits, then the CM group but not DL group will show a stronger distance effect than the TD group. The results of this analysis showed that indeed the CM group showed a stronger distance effect than the TD group, but the DL group did not. Thus, hypothesis 4 was supported.

Rouselle & Nöel (2007) suggest that DD is caused by semantic access deficit whereby DD children are impaired in accessing numerical magnitude representations through the use of Arabic digits. In this account the underlying representation is intact, but the access to that representation through the use of symbols is impaired. The authors suggest that this access deficit underlies DD based on results from a study which collapsed DD and CM children into one group. The results of the present study, however, suggest that the access deficit may underlie comparison deficits in CM children since numerical comparison impairments in this group are apparent only during the symbolic condition. DD, on the other hand, appears to be caused by an underdeveloped representation of numerical magnitude as this group shows comparison deficits in both symbolic and nonsymbolic conditions.

Rousselle & Nöel (2007) report a significant Group x Distance interaction for symbolic comparison reaction times (the authors do not report whether the same interaction was significant for accuracy). However, in that study the DD group which comprised both DD and CM children showed a weaker distance effect than controls. The authors suggest that, since many of the DD children actually showed a reverse distance effect, they may have been reciting the counting sequence rather than directly comparing the numerical magnitudes of the two digits. Thus, the difference in the direction of the Group x Distance interaction between the Rousselle & Nöel study and the current study may be as a result of the fact that their paradigm was not time limited while the current study classified answers which took more than 2.5 seconds after stimulus onset as incorrect.

In summary, the results of the both symbolic and nonsymbolic comparison tasks suggest that the dyscalculic group have an underdeveloped representation of numerical magnitude which impairs their ability to make numerical comparisons as the numerical distance between comparators decreases in both symbolic and nonsymbolic tasks. The comorbid group, on the other hand, showed a stronger distance effect than typically developing children in the symbolic condition but not the nonsymbolic condition, as well as slower overall reaction times during symbolic comparison. This suggests that the CM group may represent a subgroup with a specific deficit in accessing numerical semantic information through the use of symbolic stimuli. It is possible that this deficit may stem from a wider deficit in semantic retrieval present in many dyslexic children (Lyytinen, Erskine, Tolvanen et al., 2006), and thus, such a deficit may represent a plausible explanation for the high rate of comorbidity between dyslexia and dyscalculia. The current thesis did not include a rapid naming test or any other test of general retrieval speed, and thus this hypothesis is a speculative, post-hoc one which requires further research to address. The present results do support, however, the conclusion that the representation of numerical magnitude is not impaired in CM children as it is in DD children. It should be noted that some of the present results were marginally significant, and thus should be treated as tentative preliminary findings which require replication.

In summary, the behavioural distance effect is robust and gives strong insight into the integrity of mental representations of numerical magnitude (see above). The current results are the first to examine the distance effect in both symbolic and nonsymbolic number comparison in children with pure dyscalculia, dyslexia, comorbid dyscalculia and dyslexia and typically developing controls. Subsequently they are the first results to reveal essential differences in the mental representation of numerical magnitude between children with pure dyscalculia and those with comorbid dyslexia. This is an important step in beginning to understand not only the roots of pure DD but the sources of comorbidity with dyslexia, and ultimately in developing focused educational interventions for each disorder.

The behavioural data reported above provide evidence of an impaired representation of numerical magnitude in developmental dyscalculia, however, in order to further strengthen this hypothesis it is necessary to examine this representation, which has reliable neural correlates, at the brain level. Although the comorbid and dyslexic groups participated in fMRI scanning, excess head motion in those groups caused their imaging data to be uninterpretable, and thus, the next chapter of this thesis investigates the neural correlates of the symbolic and nonsymbolic distance effects in the DD and TD groups.

STUDY 2: BRAIN IMAGING ANALYSIS

15 INTRODUCTION

It is clear from the literature review above that the intraparietal sulcus (IPS) plays a key role in the representation and processing of numerical magnitude information (Dehaene et al., 2003). Neuroimaging studies of healthy adults and children have shown the IPS to be active in numerical comparison with symbolic and nonsymbolic stimuli (Ansari & Dhital, 2006; Pinel et al., 1999). Furthermore IPS activation during numerical comparison increases as the numerical distance between the numbers being compared decreases both for adults and children (Ansari et al., 2006; Pinel et al., 2001). These results suggest that impairments in the representation and processing of numerical information thought to underlie DD (Butterworth, 1999; Dehaene, 1997) should be reflected in functional abnormalities in the IPS of DD children during numerical comparison.

However, despite several recent attempts, there is as yet no conclusive evidence regarding the functional integrity of the IPS in children with developmental dyscalculia (DD). Neuroimaging studies of patients with genetic syndromes such as fragile X syndrome and Turner's Syndrome have revealed functional and structural abnormalities in the IPS (Molko et al., 2003; Molko et al., 2004; Rivera et al., 2002). However, these populations show difficulties with arithmetic in the context of much wider behavioural impairment profiles, and thus it is impossible to extrapolate those results to the case of pure DD.

Recently imaging studies have attempted to focus on DD subjects with isolated mathematical learning disorders in the context of otherwise typical development. Kucian et al (2006) used fMRI to compare children with DD to typically developing peers during a nonsymbolic numerical comparison task. Participants had to compare the relative numerosity of sets of objects such as nuts or fruits. The study found that during comparison both groups of children showed task related activation in the right IPS, but in the control group this activation was bilateral across the IPS. However, a direct statistical comparison of the groups yielded no significant differences in brain activation during comparison versus rest.

The authors subsequently employed a Region of Interest (ROI) analysis to compare activity between groups in a predefined set of brain areas. These analyses also yielded no significant differences in any of the regions tested including both the left and right IPS. The lack of significant differences may be attributed to the fact that the stimuli used in this study were not controlled for physical variables which vary continuously with numerosity, such as surface area and density. Such variables have been shown to be used by children to aid numerosity judgements if not controlled for within the experimental design (Rousselle et al., 2004) and thus it is possible that the failure of Kucian et al to control continuous physical variables means that their comparison task did not require sufficient access to mental numerical magnitude representations and could instead be solved using spatial strategies. Furthermore, despite including a distance manipulation in the task design, Kucian et al did not report distance effect contrasts within or between groups.

More recently, Soltesz et al (2007) used an Event Related Potentials (ERP) paradigm to test for electrophysiological correlates of the distance effect during numerical comparison of Arabic digits. The authors observed that during an early time window there were no differences in the topography of the distance effect between control and dyscalculic participants. During a later time window, however, the control group show a non-significant distance effect over right parietal areas, while the Dyscalculic group did not. Thus, although these results do not provide conclusive evidence of an impaired neural distance effect in DD, they do hint at a weaker effect in the right parietal area.

One possible reason for the lack of significant differences in this study is the way in which the participants were selected. Dyscalculic children were selected purely on the basis of having been diagnosed with DD in school at least 2 years prior to the study, and having been unresponsive to special education. However, the authors do not provide details of how these diagnoses were carried out, and whether each diagnosis adhered to the same diagnostic criteria. Thus it is possible that the group contained a heterogeneous sample of dyscalculics with regards to the severity of the disorder.

A second issue is that all the dyscalculic participants had above average verbal skills, and the authors included only symbolic number comparison in the task design. It is possible that the DD group was able to employ verbal strategies such as counting or ordering in order to perform the task which would alleviate the need to access underlying numerical magnitude representations.

Thus, no study has thus far compared clearly defined dyscalculic and control groups on well controlled nonsymbolic and symbolic numerical comparison tasks as well as testing for the effects of numerical distance on brain activation in these groups.

In order to address the above concerns, the current thesis employs both symbolic and nonsymbolic numerical comparison tasks including within task distance manipulations. This allows both a comparison of the effects of stimulus format between groups during comparison versus rest, and beyond this a more fine grained analysis of the neural correlates of the distance effect within and between formats. Furthermore, the nonsymbolic comparison task is structured so that continuous physical variables such as overall surface area, item density and individual item size cannot be used to reliable predict numerosity of a set.

16 PARTICIPANTS

(For recruitment and group classification procedures see General Methods).

Head motion during fMRI reduces signal to noise ratio and introduces a highly possibility of false activations or "motion artefacts". Thus it is imperative to exclude from analysis those participants whose head motion exceeds an acceptable level, typically 3mm for a given functional run. Thus, in the present study head motion was quantified using BrainVoyager QX motion correction algorithms, and runs in which overall motion exceeded 3mm were excluded from analysis.

Unfortunately, children in the comorbid and dyslexic groups showed a high number of runs in which head motion exceeded the above criterion, so much so that as groups their imaging date revealed almost no reliable task related activations and instead showed what appeared to be extensive deactivations in areas canonically activated during the performance of any task such as contralateral motor cortex and primary visual areas. Thus both groups had to be excluded from further analysis.

Six (5 controls and 1 dyscalculic) subjects were also excluded entirely from analysis due to excess head motion. One subject (control) was excluded on the basis of extremely long RTs and poor accuracy (at least 4 standard deviations away from control mean in each condition), hence we were unable to be sure that the child had understood the purpose of the task and was performing with a focused strategy. Thus, from an initial sample of 45 children who underwent screening, eight right handed children diagnosed with DD on the basis of standardized math scores of at least 1.5 standard deviations below the standardized average, in the absence of any other cognitive or learning disabilities were compared to eight right handed, typically developing age-matched peers.

Control and dyscalculic groups differed significantly on standard math scores (t (14) = 5.72, p < .001), but not on Non-word reading time (t (14) = -.48, p > .05), or Non-word reading Errors (t (14) = -1.9, p > .05). The groups did not differ significantly on Similarities subtest (t (13) = .86, p > .05), but there was a significant group difference in the Block Design Subtest (t (13) = 2.58, p < .05). However, for the Block design subtests the group mean for the DD was within the normal range. TABLE 8 summarises the results of screening measures for both groups.

TABLE 8 Screening measures results for TD and DD groups.

	Controls (N=8)		**Dyscalculics (N=8)**	
	Mean	Std. Error	Mean	Std. Error
Age (yrs)	12.06	0.53	11.43	0.59
RMAT Standard Score	10.12	1.04	3.13	0.64
Non-word Reading Time (secs)	26.87	5.12	29.65	2.79
Non-word Reading Errors	0.38	0.18	1.75	0.7
WISC-III Block Design	106.43	2.1	88.75	6.11
WISC-III Similarities	110.71	3.69	105.00	5.26

17 NONSYMBOLIC NUMBER COMPARISON

17.1 Hypotheses

H1. Dyscalculic children are expected to show weaker activation in the intraparietal sulcus during nonsymbolic number comparison than typically developing children, reflective of weaker underlying mental representations of numerical magnitude.

H2. While typical developing children are expected to show a classical neural distance effect in the IPS, that is, increased activation in the small distance condition relative to the large distance condition, dyscalculic children are expected to show a weaker neural distance effect reflective of weaker underlying representations of numerical magnitude.

17.2 Results

17.2.1 Behavioural

17.2.2 Overall Comparison

17.2.2.1 Reaction Time

Mean reaction times for correct responses were analysed in a one-way ANOVA with Group as the between subjects factor. Responses were classified as incorrect if the participant selected the smaller of the two numerosities, or if the participant did not respond within the 1.3s post stimulus period. This analysis revealed no main effect of group, [$F(1,14) = 0.79$, $p > 0.05$].

17.2.2.2 Accuracy

Accuracy was calculated as the percentage of trials in which a correct response was given. A one-way ANOVA with Group as the between subjects factor revealed a significant main effect of group on comparison accuracy [$F(1,14) = 5.41$, $p < 0.05$] with the dyscalculic group showing lower accuracy than the typically developing group.

17.2.3 Nonsymbolic Distance Effect

17.2.3.1 Reaction Time

Mean reaction time data (TABLE 9) for nonsymbolic numerosity comparison were analyzed by means of a 2 x 2 mixed design analysis of variance (ANOVA), with Distance (small vs. large) as a within subjects factor and Group (Control vs DD) as a between subjects factor. This analysis revealed a main effect of distance on reaction time [$F(1,14) = 115.75$, $p < 0.001$] with longer response times for small distance trials, but no distance by group interaction [$F(1,14) = 2.13$, $p > 0.05$].

17.2.3.2 Accuracy

Percentage of correct responses (TABLE 9) for nonsymbolic numerosity comparison were analyzed by means of a 2 x 2 mixed design analysis of variance (ANOVA), with Distance (small vs. large) as a within subjects factor and Group (Control vs DD) as a between subjects factor. This analysis revealed a significant main effect of distance [$F(1,14) = 85.58$, $p < 0.001$] on accuracy, with more errors in the small distance condition than the large. Additionally, a significant group by distance interaction was found [$F(1,14) = 5.09$, $p < 0.05$], with DD subjects showing a greater effect of distance on response accuracy. Independent samples t-tests revealed that the DD group did not differ from the TD group in the large distance condition ($t(14) = 1.14$, $p > 0.05$) but showed significantly lower accuracy in the small distance condition ($t(14) = 2.41$, $p < 0.05$).

TABLE 9 Accuracy and Reaction Time Data by Distance Condition for Nonsymbolic Comparison.

	Control (N = 8)		Dyscalculic (N = 8)	
	Average	**Std. Error**	**Average**	**Std. Error**
Small Distance Mean RT(ms)	718.82	26.96	740.57	44.47
Large Distance Mean RT(ms)	554.85	26.79	615.79	35.98
Small Distance Percent Correct	88.19	2.21	79.86	2.66
Large Distance Percent Correct	98.96	0.51	97.6	1.11

17.2.4 fMRI

17.2.4.1 Task Vs Rest Across Groups

A random effects whole brain analysis was carried out to assess which regions were significantly activated by numerical comparison relative to rest across all participants. Greater activation for nonsymbolic comparison vs. rest was found at cluster corrected threshold of $p< 0.001$ (cluster-level threshold calculated on the basis of interaction t-map thresholded at $p < 0.001$, uncorrected) in bilateral primary visual cortices, bilateral superior parietal lobes, left inferior parietal lobe, dorsal anterior cingulate cortex, left primary motor cortex extending into primary somatosensory cortex, right rostral middle frontal gyrus, right dorsolateral prefrontal cortex, right insula extending including the claustrum, right cerebellum, and the right lentiform nucleus including the Putamen (see TABLE 10).

TABLE 10 Brain regions active during nonsymbolic comparison versus rest across groups.

Region	Brodmann Area	Voxel Cluster Centre of Mass Talairach Coordinates (x, y, z)	Cluster Size	Average Statistic t(15)
Right Superior Parietal	BA7	29, -57, 45	9933	5.63
Left Superior Parietal	BA7	-27, -55, 48	8380	5.72
Left Inferior Parietal	BA40	-43, -28, 45	3814	5.49
Left Primary Motor Cortex	BA4	-37, -17, 54	2921	4.87
Dorsal Anterior Cingulate Cortex	BA32	1, 16, 43	8137	5.1
Right Rostral Middle Frontal Gyrus	BA10	38, 40, 20	5548	5.17
Right Dorsolateral Prefrontal Cortex	BA9	44, 7, 30	696	4.64
Right Lentiform Nucleus	N.A.	18, 11, 2	597	5.26
Right Insula	BA13	37, 17, 5	1503	4.55
Right Primary Visual Cortex	BA17/18/19	25, -78, 0	27293	6.04
Left Primary Visual Cortex	BA17/18/19	-24, -79, -2	26829	6.05
Right Cerebellum	N.A.	23, -48, -13	9978	5.3

17.2.4.2 Task vs. Rest Between Groups

In order to assess which brain regions were differentially modulated by nonsymbolic numerosity comparison between groups, we carried out a random-effects, whole brain, voxel-wise analysis testing for Task by Group interactions. Interactions were investigated at a cluster-level correct threshold of $p < 0.001$ (cluster-level threshold calculated on the basis of interaction t-map thresholded at $p < 0.005$, uncorrected). This analysis revealed no brain regions more active for Task vs. Rest that were more active for one group than the other i.e. no significant Task x Group interactions. In other words, there were no significant differences in the brain regions employed by controls or dyscalculics during nonsymbolic numerosity comparison relative to rest.

17.2.4.3 Distance Effect Across Groups

In order to assess which brain regions were differentially modulated by numerical distance across both groups, we carried out a random-effects, whole brain, voxel-wise analysis testing for regions which showed stronger activation for small distance comparisons than large distance comparisons. In other words we tested for regions which showed stronger activation in the small distance condition relative to the large distance condition across both control and dyscalculic groups. As this comparison contrasted a within subjects factor which was a within task manipulation, as opposed to the coarse Task vs. Rest contrasts reported above, a more liberal uncorrected threshold of $p < 0.005$ was used to calculate the cluster-level corrected threshold. Significant interactions were observed at cluster corrected threshold of $p < 0.001$ (cluster-level threshold calculated on the basis of interaction t-map thresholded at $p < 0.005$, uncorrected) in the right superior parietal lobe, anterior cingulate gyrus, bilateral posterior cingulate gyrus, right lingual gyrus, right inferior temporal gyrus and the right claustrum (see TABLE 11).

TABLE 11 Brain regions more active in the small distance condition relative to the large distance condition across groups.

Region	**Brodmann Area**	**Voxel Cluster Centre of Mass Talairach Coordinates (x, y, z)**	**Cluster Size**	**Average Statistic t(15)**
Right Superior Parietal Lobe	BA7	22, -54, 51	560	3.83
Anterior Cingulate Gyrus	BA32	0, 18, 37	953	3.87
Left Posterior Cingulate Gyrus	BA23	-8, -71, 7	1433	3.4
Right Posterior Cingulate	BA30	9, -58, 6	1077	3.74
Right Lingual Gyrus (Prestriate Cortex)	BA18	11, -72, 0	528	373
Right Inferior Temporal Gyrus	BA37	42, -51, -4	552	3.71
Right Claustrum	N.A.	32, 10, 2	1270	3.95

17.2.4.4 Distance Effect Between Groups

In order to assess which brain regions were differentially modulated by distance between groups, we carried out a random-effects, whole brain, voxel-wise analysis testing for Group x Distance interactions. Significant interactions were observed at cluster corrected threshold of $p < 0.05$ (cluster-level threshold calculated on the basis of interaction t-map thresholded at $p < 0.005$, uncorrected) in three separate neural loci (see TABLE 12). Interactions were found in the right intraparietal sulcus (FIGURE 7), left fusiform gyrus (Figure 8), and left medial prefrontal cortex (FIGURE 9).

TABLE 12 Brain Regions showing Group X Distance interactions during nonsymbolic comparison.

Region	Brodmann Area	Voxel Cluster Centre of Mass Talairach Coordinates (x, y, z)	Cluster Size	Average Statistic t(15)
Right Intraparietal Sulcus	BA7	33, -50, 52	219	4.09
Left Medial Prefrontal Gyrus	BA10	-13, 54, -2	199	3.91
Left Fusiform Gyrus	BA37	-36, -54, -13	324	3.92

FIGURE 7 Group X Distance interaction in the Right Intraparietal Sulcus

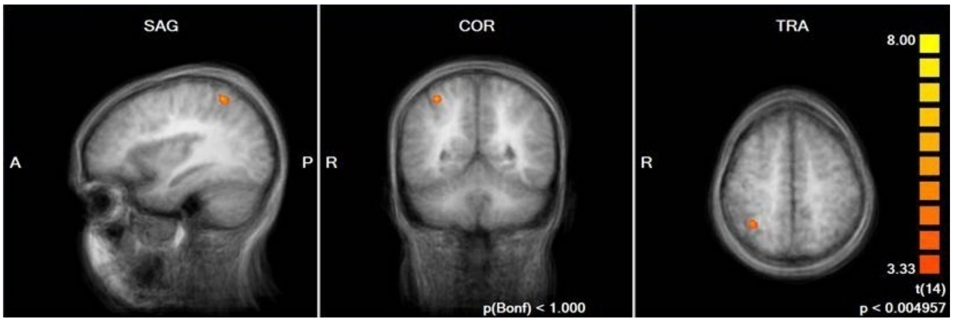


FIGURE 8 Group X Distance Interaction in Left Fusiform Gyrus.

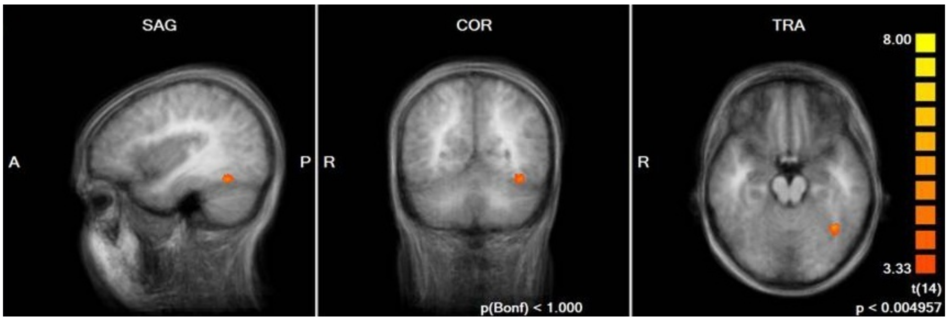
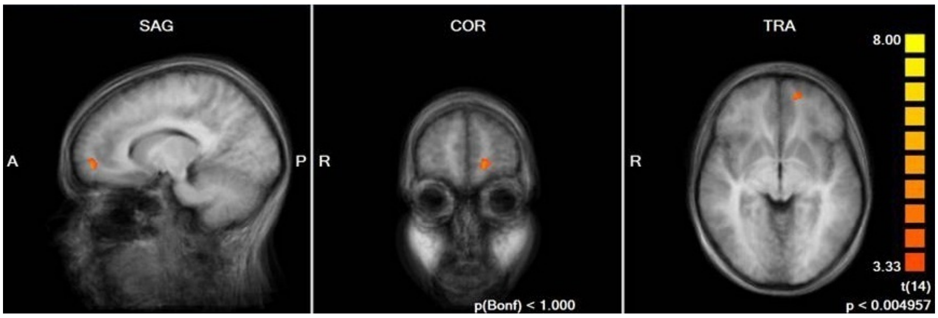


FIGURE 9 Group X Distance interaction in the left medial prefrontal cortex



As can be seen from the Bar chart in FIGURE 10 the interaction in the IPS was characterized by a stronger distance effect in the control group compared to the DD group, and the same pattern was observed in the left fusiform area, as shown in FIGURE 11. The interaction in the MPFC region shown in FIGURE 12, on the other hand, was characterized by a greater deactivation in the DD group for Small *vs.* Large distances while showing equal positive activations in the Control group.

FIGURE 10 Beta weights extracted from right intraparietal region showing distance effect in TD group and no distance effect in DD group.

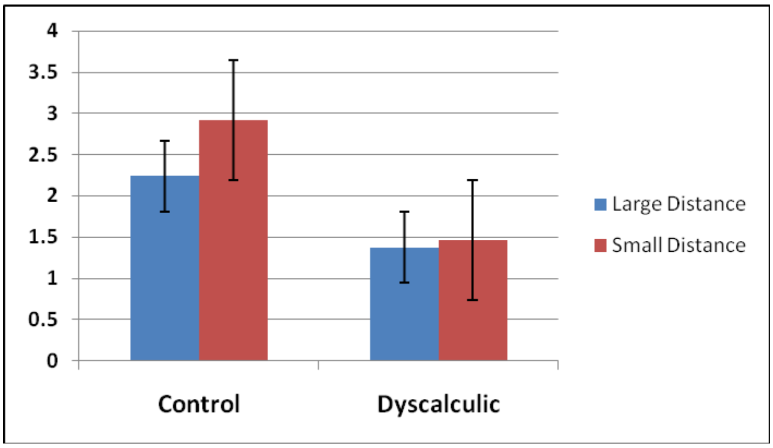


FIGURE 11 Beta weights extracted from left fusiform gyrus region showing distance effect in TD group and no distance effect in DD group.

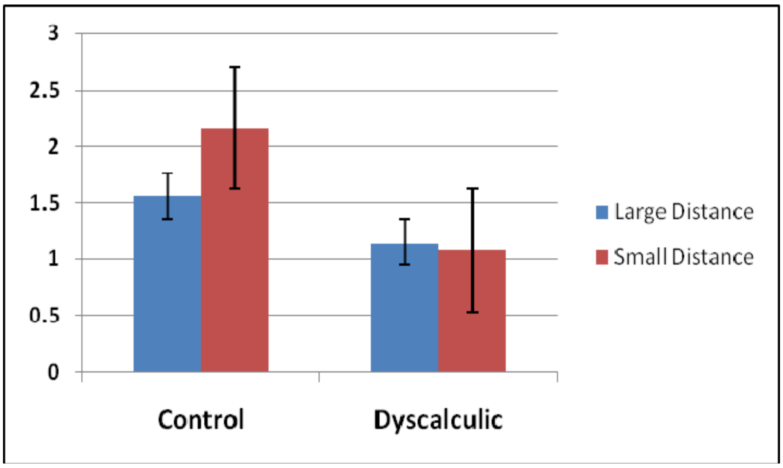
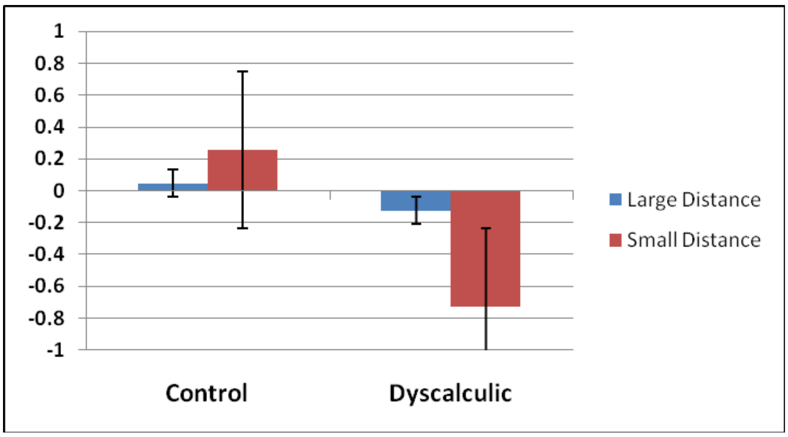


FIGURE 12 Beta weights extracted from left medial prefrontal region showing no distance effect in TD group and reverse distance effect in DD group.



In order to further explore the strength of the distance effect in each group in each of these ROIs, paired samples t-tests were performed on signal change values for small and large distance conditions in each ROI. These analyses revealed that in the right IPS, the TD group showed a significant increase in signal strength from the large distance condition to the small distance condition

($t(7) = 4.59$, $p < 0.05$) while the DD group showed no difference in signal strength between the two conditions ($t(7) = 0.64$, $p > 0.05$). The same pattern was true in the left fusiform area, with the TD group showing a significant increase in signal strength from large to small distance conditions ($t(7) = 4.51$, $P < 0.05$), while the DD group showed no significant change ($t(7) = -1.14$, $p > 0.05$). In the left medial prefrontal cortex however, the TD group showed no significant effect of distance ($t(7) = 2.12$, $p > 0.05$) while the DD group showed a significantly greater deactivation during the small distance condition compared to the large distance condition ($t(7) = -6.9$, $p < 0.05$).

17.2.4.5 Baseline Activation Levels

The paucity of previous fMRI research in developmental dyscalculia leaves open the possibility that the present results could be the consequence of lower activation levels throughout the whole brain in DD participants. In order to rule out this possibility and ensure that the observed results were indeed reflective of a deficit of the cognitive mechanism for numerical magnitude processing, ROI analyses were performed on left and right hemisphere primary visual areas. Left hemisphere V1 (-32, -83, -1) showed no main effect of distance [$F(1,14) = 3.11$, $p > .05$], and no Group x Distance interaction [$F(1,14) = 2.51$, $p > .05$]. The same pattern was true of activations in right hemisphere V1 (27, -86, 10) for both the main effect of distance [$F(1,14) = 1.72$, $p > .05$], and the Group x Distance interaction [$F(1,14) = .68$, $p > .05$]. These results suggest that the observed group differences in brain activation during nonsymbolic number comparison are indeed task related and not the consequence of general lower activation levels across the whole brain.

17.3 Discussion

The first analysis in this section compared the neural activation patterns associated with nonsymbolic magnitude comparison across both large and small distances. The results of this analysis show that during nonsymbolic numerical comparison in general, both DD and TD children activate a canonical network of brain regions associated with the representation and processing of numerical magnitude.

The observed regions of task related activation included bilateral superior parietal lobes as well as prefrontal and inferior frontal areas. These regions have been found to be active in the processing of nonsymbolic numerical stimuli in typically developing adults and children (Ansari & Dhital, 2006; Cantlon et al., 2006; Piazza et al., 2004) and so the present findings support the results of previous studies with regards to the role of a fronto-parietal network in the processing of numerical magnitude through nonsymbolic stimuli. Furthermore, these findings replicate those of Kucian et al (2006) who found no differences between DD children and typically developing controls on a nonsymbolic numerical comparison task. Thus, Hypothesis 1 was not supported.

The present results are in agreement with previous literature when distances are collapsed. However, the behavioural results show significant differences in the effect of distance on comparison accuracy between groups. In the large distance condition the DD and TD groups performed with equivalent accuracy but in the small distance condition the DD group showed a significantly sharper decline in accuracy than the TD group. Thus it is possible that simply comparing the groups on general numerical comparison without contrasting numerical distances does not sufficiently probe the integrity of the underlying numerical representations and at the neural level averaging comparison across distances may mask more subtle group differences in those representations.

Therefore, the next analysis contrasted the neural correlates of the distance effect between groups. Smaller numerical distances have been shown to correlate with stronger activation in the IPS in typically developing adults and children (Ansari et al., 2005; Pinel et al., 2001). However, no studies to date have contrasted the neural distance effects between DD and TD children during nonsymbolic number comparison.

The results of the present analysis revealed that the TD group showed significant neural distance effects in the right IPS and left fusiform gyrus, while the DD group showed no modulation by distance in these areas. The lack of a neural distance effect in the IPS of DD children supports Hypothesis 2, and provides the first direct evidence of an underdeveloped brain level representation of numerical magnitude in dyscalculia. The IPS region showing the Group x Distance interaction overlaps directly with an area identified in a meta analysis by Dehaene et al (2003) as in the representation and processing of numerical quantity (mean Talairach coordinates for hIPS:41, –47, 48; standard deviations for these mean coordinates: 7, 7, 5). Furthermore Transcranial Magnetic Stimulation to this region resulted in impaired automatic activation of numerical magnitude information in a numerical stroop task in healthy adults (Cohen Kadosh, Cohen Kadosh, Schuhmann et al., 2007), mimicking a behavioural characteristic of adults with DD (Rubinsten & Henik, 2005).

Thus, these results suggest an impaired parietal representation of numerical magnitude in DD that is able to support numerical comparisons in the large distance condition, but not in the small distance condition. This supports the pattern of behavioural results reported above which show that DD and TD groups perform equally well during large distance comparisons, but the DD perform significantly worse during small distance comparisons and suggests that this occurs because the underlying mental representations of numerical magnitude in DD are insufficiently developed to support more demanding numerical processing.

The same pattern was observed in the left fusiform gyrus, whereby the TD group showed a significant neural distance effect while the DD group showed no modulation by distance. This area has been associated with the identification of visual word forms (e.g. Cohen et al., 2002) but is also active in object naming and visual form processing in general (Price & Devlin, 2003). The exact cognitive function of this area is as yet unresolved, however, Price & Devlin (2003) suggest that its role may be specified on the basis of the network of regions with which it interacts during a given task. Thus, in the current study the lack of distance effect in this region in the DD group may reflect a deficit in the function of visual mechanisms used to extract the semantic dimension of numerosity from a set of objects. However, this interpretation is speculative and this finding is in need of further replication in order to gain a better understanding of its cognitive function in numerical comparison.

While the left fusiform gyrus and right IPS appear to be involved in the visual extraction and mental representation of numerical semantic information respectively, the left medial prefrontal cortex appears have a more domain general role. In this region the TD group showed no activation differences between small and large distance conditions, while the DD group showed a significant decrease in activation in response to small distance comparisons compared to large distance comparisons. This area is suggested to be part of the so-called resting stating network (Gusnard & Raichle, 2001) and thus it is possible that the distance related deactivation for DD children reflects the greater level of subjective task difficulty and the need for more effortful processing in order to compensate for the failures of the parietal magnitude system.

The present results provide the first direct evidence of parietal dysfunction in pure developmental dyscalculia and thereby support the hypothesis that DD is caused by a disruption of the neural circuitry that supports a domain specific mental representation of numerical magnitude.

18 SYMBOLIC NUMBER COMPARISON

18.1 Hypotheses

H1. Dyscalculic children are expected to show weaker activation than control children in the intraparietal sulcus during symbolic number comparison reflective of weaker underlying mental representations of numerical magnitude.

H2. While Typical Developing children are expected to show a classical neural distance effect in the IPS, that is, increased activation in the small distance condition relative to the large distance condition, dyscalculic children are expected to show a weaker neural distance effect reflective of weaker underlying representations of numerical magnitude.

18.2 Results

18.2.1 Behavioural

18.2.2 Overall Comparison

18.2.2.1 Reaction Time

Mean reaction times for correct responses were analysed in a one-way ANOVA with Group as the between subjects factor. Responses were classified as incorrect if the participant selected the smaller of the two numerosities, or if the participant did not respond within the 1.3s post stimulus period. This analysis revealed no main effect of group, [$F(1,14) = 2.13$, $p > 0.05$].

18.2.2.2 Accuracy

Accuracy was calculated as the percentage of trials in which a correct response was given. A one-way ANOVA with Group as the between subjects factor revealed no main effect of group on comparison accuracy [$F(1,14) = 3.45$, $p > 0.05$].

18.2.3 Symbolic Distance Effect

18.2.3.1 Reaction Time

Mean reaction time data (Table 13) for Symbolic Number comparison were analyzed by means of a 2 x 2 mixed design analysis of variance (ANOVA), with Distance (small vs. large) as a within subjects factor and Group (Control vs. DD) as a between subjects factor. This analysis revealed a main effect of distance on reaction time [$F(1,14) = 93.49$, $p < 0.001$] with longer response times for small distance trials. Additionally, a significant distance by group interaction was revealed [$F(1,14) = 6.16$, $p < 0.05$]. Paired samples t-tests revealed that both groups showed a significant increase in reaction time for small distance comparisons compared to large distance comparisons, however, the effect was weaker in the DD group. Independent samples t-tests revealed that reaction time was not significantly different between groups in either the small distance [$t(14) = -1.15$, p = $p < 0.05$] or large distance conditions [$t(14) = -1.8$, $p < 0.05$].

18.2.3.2 Accuracy

Percentage of correct responses (TABLE 13) for symbolic comparison were analyzed by means of a 2 x 2 mixed design analysis of variance (ANOVA), with Distance (small vs. large) as a within subjects factor and Group (Control vs. DD) as a between subjects factor. A significant main effect of distance [$F(1,14) = 45.21$, $p < 0.001$] on the number of errors was found, with more errors in the small distance condition. Additionally, a marginally significant group by distance interaction was found [$F(1,14) = 4.44$, $p = 0.05$], with DD subjects showing a greater effect of distance on response accuracy. Independent samples t-tests revealed that comparison accuracy was equivalent between groups in the large distance condition ($t(14) = 0.00$, $p < 0.001$) but in the small distance condition the DD group showed a marginally significant lower accuracy rate than the TD group ($t(14) = 2.0$, $p = 0.065$).

TABLE 13 Accuracy and reaction time data for symbolic comparison.

	Control (N = 8)		Dyscalculic (N = 8)	
	Average	**Std. Error**	**Average**	**Std. Error**
Small Distance Mean RT(ms)	657.22	36.34	714.91	36.84
Large Distance Mean RT(ms)	559.19	33.77	647.65	35.85
Small Distance Percent Correct	91.32	1.11	84.03	3.47
Large Distance Percent Correct	99.31	0.45	99.31	0.45

18.2.4 fMRI

18.2.4.1 Task vs. Rest Across Groups

A random effects whole brain analysis was carried out to assess which regions were significantly activated by symbolic number comparison relative to rest across all participants. Greater activation for task vs. rest was found at cluster corrected threshold of $p < 0.001$ ($p < 0.001$ uncorrected) in bilateral primary visual cortices, bilateral cerebellum, right superior parietal lobe, anterior cingulate gyrus, left pre-central and post-central gyri (see TABLE 14).

TABLE 14 Brain regions active during symbolic comparison versus rest across groups.

Region	**Brodmann Area**	**Cluster Centre of Mass Talairach Coordinates (x, y, z)**	**Cluster Size**	**Average Statistic t(15)**
Right Superior Parietal	BA7	31, -54, 42	1591	4.69
Left Precentral & Postcentral Gyri	BA3/4	-39, -22, 53	3734	4.77
Anterior Cingulate Gyrus	BA32	-2, 10, 46	3457	4.87
Right Primary Visual Cortex	BA 17/18/19	25, -78, -7	9313	4.92
Left Primary Visual Cortex	BA 17/18/19	-12, -84, -4	1023	4.64
Left Cerebellum	N.A.	-29, -69, -17	4583	4.84
Right Cerebellum	N.A.	25, -72, -15	4021	4.71

18.2.4.2 Task vs. Rest Between Groups

In order to assess which brain regions were differentially modulated by symbolic number comparison between groups, we carried out a random-effects, whole brain, voxel-wise analysis testing for Task by Group interactions. Interactions were investigated at a cluster-level correct threshold of $p < 0.001$ (cluster-level threshold calculated on the basis of interaction t-map thresholded at $p < 0.005$, uncorrected). This analysis revealed no brain regions more active for Task vs. Rest that were more active for one group than the other i.e. no significant Task by Group interactions. In other words, there were no significant differences in the brain regions employed by controls or dyscalculics during basic symbolic numerosity comparison relative to rest.

18.2.4.3 Distance Effect Across Groups

In order to assess which brain regions were differentially modulated by numerical distance across both groups, we carried out a random-effects, whole brain, voxel-wise analysis testing for regions which showed stronger activation for small distance comparisons than large distance comparisons. In other words we tested for regions whose activation strength was negatively correlated with numerical distance across both control and dyscalculic groups. As this comparison contrasted a within subjects factor which was a within task manipulation, as opposed to the coarse Task vs. Rest contrasts reported above, a cluster-level correction threshold of $p < 0.05$ ($p < 0.005$ uncorrected) was used. This analysis revealed no brain regions that were more active for small distance comparisons than large distance comparisons across groups.

18.2.4.4 Distance Effect Between Groups

In order to assess which brain regions were differentially modulated by distance between groups, we carried out a random-effects, whole brain, voxel-wise analysis testing for Group x Distance interactions. Significant interactions were observed at cluster corrected threshold of $p < 0.05$ (cluster-level threshold calculated on the basis of interaction t-map thresholded at $p < 0.005$, uncorrected) in three regions (see TABLE 15), the left middle temporal (FIGURE 13), right mid-occipital gyrus (FIGURE 14) and right lateral prefrontal cortex (pars triangular) (FIGURE 15)

TABLE 15 Brain Regions showing Group X Distance interactions during symbolic comparison.

Region	Brodmann Area	Cluster Centre of Mass Talairach Coordinates (x, y, z)	Cluster Size	Average Statistic t(15)
Left Mid-Temporal Gyrus	BA21	-46, -31, -6	300	3.90
Right Mid-Occipital Gyrus	BA19	44, -69, 6	805	3.95
Right Inferior Frontal Lobe (Pars Triangular)	BA45	32, 18, 17	361	3.92

FIGURE 13 Group X Distance interaction in the Left Middle Temporal Gyrus

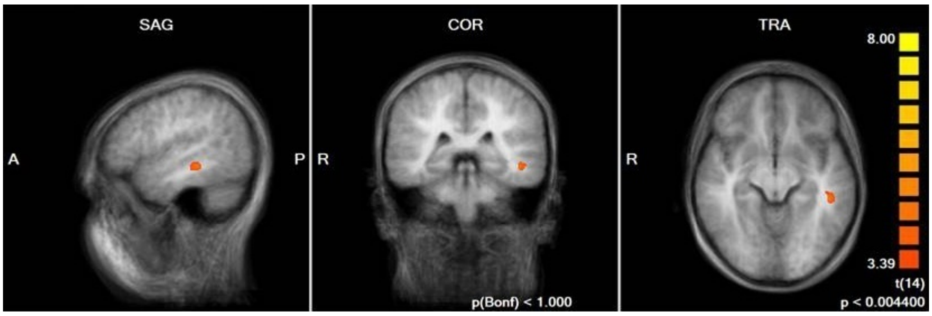


FIGURE 14 Group X Distance interaction in the Right Middle Occipital Gyrus

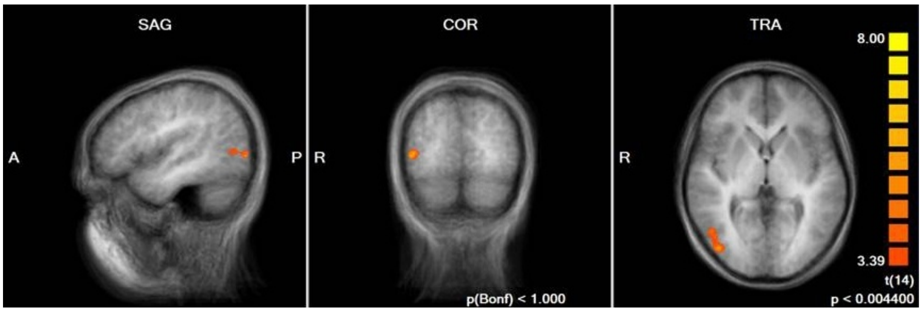
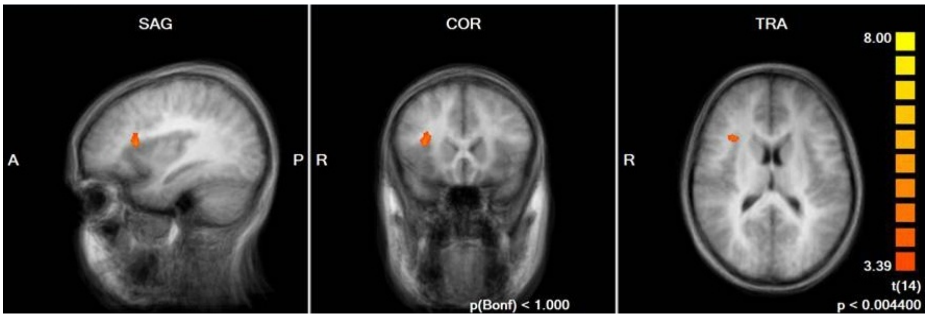


FIGURE 15 Group X Distance interaction in the Right Inferior Frontal Lobe



As can be seen from the Bar chart in FIGURE 16 the interaction in the left middle temporal region was characterized by an increase in activation from large distances to small distance in the TD group, and a decrease in activation from large to small distances in the DD group. The same pattern was observed in the left middle occipital area, as shown in FIGURE 17, and in the right inferior frontal area (FIGURE 18).

FIGURE 16. Beta weights extracted from left middle temporal region showing distance effect in TD group and reverse distance effect in DD group.

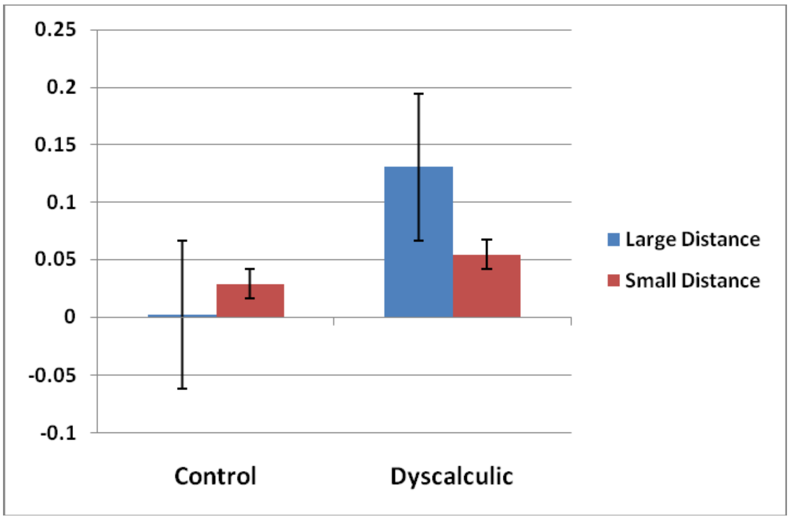


FIGURE 17 Beta weights extracted from right middle occipital region showing distance effect in TD group and reverse distance effect in DD group.

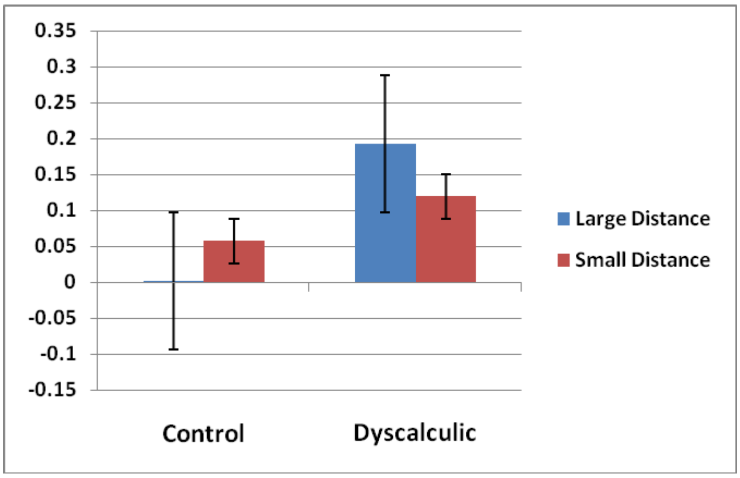
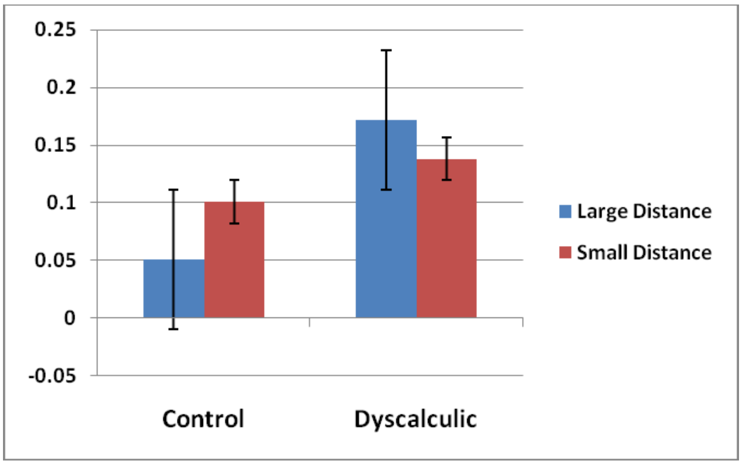


FIGURE 18 Beta weights extracted from right inferior frontal region showing distance effect in TD group and reverse distance effect in DD group.



In order to further explore the strength of the distance effect in each group in each of these ROIs, paired samples t-tests were performed on signal change values for small and large distance conditions in each ROI. These analyses revealed that in the left middle temporal region, the TD group showed a significant increase in signal strength from the large distance condition to the small distance condition ($t(7) = 2.62$, $p < 0.05$) while the DD group showed a significant reverse distance effect with signal strength decreasing from large to small distance comparisons ($t(7) = -4.12$, $p < 0.05$). The same pattern was true in the right middle occipital area, with the TD group showing a significant increase in signal strength from large to small distance conditions ($t(7) = 2.97$, $P < 0.05$), while the DD group showed a reverse distance effect ($t(7) = -2.6$, $p < 0.05$). In the right lateral prefrontal cortex the TD group again showed a significant effect of distance ($t(7) = 2.93$, $p < 0.05$) while the DD group showed a significant reverse distance effect ($t(7) = -2.63$, $p < 0.05$).

18.3 Discussion

The first analysis in this section investigated the neural correlates of symbolic number comparison in general, collapsing small and large distance conditions. The results reveal a network of brain regions involved in comparing the numerosity of Arabic digits across groups, including bilateral primary visual cortices, bilateral cerebellum, right superior parietal lobe, anterior cingulate gyrus, left pre-central and post-central gyri.

These results replicate the findings of previous studies which show activation of the intraparietal sulcus during symbolic number comparison in typically developing children (Ansari et al., 2005) and adults (Pinel et al., 1999). A comparison of groups, however, revealed no differences in the activation of regions supporting symbolic number comparison. To date, no fMRI studies have compared DD and TD children during symbolic number comparison, and thus it is impossible to interpret these results in the context of previous research. Hypothesis 1 predicted that DD children would show weaker activation than TD children in this contrast, and this was not supported by the present set of results. The TD and DD groups did not differ in overall accuracy or reaction time for symbolic comparison, and thus it is possible that collapsing small and large distance conditions masks more subtle between group differences in the underlying representation of numerical magnitude.

Thus, brain activations during small distance comparisons were contrasted to those during large distance activations both across and between groups. Across groups no brain regions revealed a significant effect of distance. Between groups, however, Distance x Group interactions were revealed in the left middle temporal gyrus, right mid-occipital gyrus and right lateral prefrontal cortex (pars triangular). In all three of these areas the interactions were explained by a significant classical distance effect in the TD group (i.e. Stronger activation for smaller distances) but a significant reverse distance effect in the DD group (i.e. stronger activation for large distances).

The left middle temporal gyrus has been associated with the processing of auditory stimuli (Scott, Blank, Rosen, & Wise, 2000) and in particular phonemic discrimination during speech sounds (Ashtari et al., 2004). This suggests therefore that while the TD children were able to perform the task without explicit mental manipulation of the digits during the large distance condition.

During the small distance condition, however, the increased task difficulty lead them to employ a verbal strategy involving mentally reciting the counting sequence. The DD group on the other hand, who showed less activation in this region during the small distance condition, were perhaps already employing a verbal strategy involving reciting the counting sequence already during the large distance condition, and the degree of subjective task difficulty experienced during the small distance condition lead to a decrease in the engagement of this phonological processing mechanism as DD children failed to fully or accurately mentally recite the digit names.

The right middle occipital area has been shown to be involved in symbolic number comparison (Fias et al., 2003a), judging the orientation of Arabic digits (Pesenti et al., 2000), counting relative to random number generation (Jahanshahi, Dirnberger, Fuller, & Frith, 2000) and letter matching (Temple et al., 2001). In tandem with the present results this suggests that this area plays a role in representation and processing of Arabic digits as visual objects. Thus it is possible that in the TD group, as the distance between the numbers being compared decreases, participants are forced to engage in more effortful retrieval of visual representations of the Arabic digits in order to aid successful numerical comparison. In the DD group, however, activation in this region decreased in the small distance condition, suggesting that either the visual representation of Arabic digits is undermined in this group, or that simply attention to the task was reduced in this condition as a consequence of subjective task difficulty.

The right inferior frontal region which shows a classical distance effect in the TD group and a reverse distance effect in the DD group has previously been shown to be involved in symbolic number comparison (Chochon et al., 1999), the backward recall of digits (Sun et al., 2005) and specifically in conflict resolution during numerical comparison of Arabic Digits (Tang, Critchley, Glaser, Dolan, & Butterworth, 2006). In addition to these numerically specific findings, the region has been shown to be involved in cognitive conflict resolution in go/no go tasks (Durston et al., 2002). In combination with the present results these findings suggest that the role of this region in symbolic number comparison is related to executive control over response selection, and that the reverse distance effect observed in the DD group may relate simply to reduced effort and attention to the experimental task.

No previous fMRI studies have contrasted symbolic comparison distance effects between TD and DD children, and thus the present results require further replication in order to understand whether the reverse distance effects in the DD group are the result of underlying cognitive impairments, or whether due to the subjective task difficulty, perhaps as a result of the DD children's numerical processing impairments, the DD group simply attended to the task less in the small distance condition, causing a decrease in activation in those areas. In other words, are the decreased activations during small distance symbolic comparisons in DD the result or the cause of their poor performance?

To date only one other imaging study has examined the neural correlates of the symbolic distance effect in DD. Soltesz et al (2007) observed that both TD and DD children showed distance effects over multiple parietal and frontal electrodes at an early time window, but at a later time window the TD children showed aright parietal distance effect while the DD children did not, although the difference between groups was nonsignificant. The authors suggest that in concert with their neuropsychological profile of their DD group, their results suggest deficient executive functioning in DD children during symbolic comparison.

In contrast to Soltesz et al, the present results did not show any parietal distance effect during symbolic number comparison. A possible explanation for this is that Soltesz et al used a paradigm which required participants to select whether or not a single digit was larger or smaller than 5, while the present study present two digits simultaneously in horizontal orientation. Thus it is possible task that performance in the present study was supported by visualising and/or reciting the ordinal number sequence in order to make numerosity judgements, rather than comparing the underlying numerical magnitudes. Thus, while overall the task did activate some level of parietal magnitude representation as evidenced by the task versus rest contrast across groups, it did not require a deeper access to parietal magnitude systems during the small distance condition. Thus it did not yield parietal distance effects in either group, but rather engaged cognitive mechanisms involved with the representation of the Arabic digits themselves.

In summary, the results above show that during symbolic number comparison compared to rest, TD and DD children activate a network of regions typically involved in numerical comparison, in particular the right IPS. However, when small distance and large distance trials are contrasted the two groups show dramatically different neural activation profiles. While the TD group show classical distance effects in a network of regions involved in the visual and phonological representation of Arabic digits as well as executive control over response selection, the DD group show a reverse distance effect in these areas. Thus the results of the symbolic number comparison task do not show an underdeveloped representation of numerical magnitude in DD children, but it may be that the task structure simply did not require deep enough access to those representations to yield brain level group differences.

19 GENERAL DISCUSSION

19.1 Summary

Some researchers have suggested that dyscalculia is caused by a core deficit in the mental representation of numerical magnitude (Butterworth, 1999; Dehaene, 1997). Furthermore a high rate of comorbidity exists between dyscalculia and dyslexia, and in order to develop effective educational interventions it is important to investigate whether the arithmetic deficits in comorbid children stem from the same core deficit as those in dyscalculic children. Thus, the aim of the present thesis was to investigate the integrity of the mental representations of numerical magnitude in developmental dyscalculia using both behavioural and brain-imaging methods, as well as to investigate the representation of numerical magnitude in children with comorbid dyscalculia and dyslexia.

The distance effect, whereby decreasing numerical distance between two numbers causes an increase in reaction time and errors when comparing the numerical value of those numbers, is a well replicated effect and is presumed to reflect the nature of mental representations of numerical magnitude, in that numbers which are closer together overlap in representational space. Therefore the current thesis investigated the representation of numerical magnitude in dyscalculic (DD), dyslexic (DL), comorbid (CM) and typically developing (TD) children using symbolic and nonsymbolic numerical comparison tasks, contrasting small and large distance comparisons.

Behavioural results from all four groups revealed that during nonsymbolic comparison, all groups showed a classical distance effect. The DD group, however, showed a marginally significantly stronger effect of distance on accuracy than the TD group on accuracy (i.e. a stronger decline in accuracy in response to decreased numerical distance). None of the other groups differed from the TD group or each other. Symbolic number comparison, on the other hand, revealed stronger distance effects for both the DD and CM groups.

Not only does the distance effect have a robust and highly replicated behavioural pattern, but it also has a well replicated neural signature as well. In both healthy adults and children, as numerical distance decreases, brain activation increases in intraparietal sulcus (Ansari et al., 2005; Pinel et al., 2001), an area thought to house a domain specific, abstract representation of numerical magnitude (Dehaene et al., 2003).

Unfortunately, due to a high level of head motion in the dyslexic and comorbid groups their fMRI data could not be included in the neuroimaging analysis, although the behavioural data alone provides highly novel insight into the mental representation of numerical magnitude in comorbid children as well as pure dyscalculics. Thus, only the dyscalculic and typically developing groups are discussed with regard to fMRI results.

During nonsymbolic number comparison versus rest, a whole brain analysis of both groups revealed classical distance effects in a network of regions frequently found to be active during numerical comparison and processing, including bilateral superior parietal and prefrontal regions. A direct comparison of groups during task versus rest revealed no regions of differential brain activation. However, when testing for the effects of distance on brain activation, significant Group x Distance interactions were revealed in three loci, the right IPS, the left fusiform gyrus, and the right medial prefrontal cortex. In all of these areas the TD group showed classical neural distance effects (i.e. increased activation for small relative to large distances) while the DD group showed no distance related changes in activation strengths.

During symbolic number comparison versus rest, a whole brain analysis of both groups revealed task related activation in the bilateral cerebellum, right superior parietal lobe, anterior cingulate gyrus, left pre-central and post-central gyri. A direct comparison of groups during task versus rest revealed no regions of differential brain activation. However, when comparing the effects of distance on brain activation between groups, significantly stronger distances effects in the TD group relative to the DD group were revealed in the left middle temporal gyrus, right mid-occipital gyrus and right lateral prefrontal cortex (pars triangular). In all three of these areas the TD groups showed a classical neural distance effect while the DD group actually showed reverse distance effects (i.e. lower activation for small distance comparisons).

The principle aims of this thesis were firstly to investigate the integrity of numerical magnitude representations in children with pure developmental dyscalculia, and secondly to investigate the sources of comorbidity between dyscalculia and dyslexia. The results of this work will now be discussed in relation to these aims in turn.

19.2 Numerical Magnitude Representation in Developmental Dyscalculia

Domain specific theories of dyscalculia hypothesise a core deficit in the mental representation of numerical information (Butterworth, 1999; Dehaene, 1997). However, only recently have studies begun to investigate the most basic numerical processing abilities in children with DD, having previously focused on higher level arithmetical abilities (Ansari & Karmiloff-Smith, 2002). It is especially important to investigate the existence of a core deficit in DD in order to ultimately develop focused and effective interventions.

The results of this thesis revealed that while dyscalculic children did not differ from controls in overall accuracy and error rates during either symbolic or nonsymbolic comparison, they did show a stronger effect of distance on accuracy in both conditions. In other words, DD children were significantly poorer than controls at comparing numbers which are separated by a relatively small numerical distance.

According to Dehaene & Cohen (1995), the internal representation of numbers is organised along a mental number line with its neural locus in the IPS (Dehaene et al., 2003). The closer two numbers are on this number line the more they overlap in terms of representational space, thus making it harder to distinguish one from the other. It is this representational overlap which is thought to give rise to the numerical distance effect. The size of the distance effect decreases over the course of development (Duncan & McFarland, 1980; Sekuler & Mierkiewicz, 1977) and furthermore, larger distance effects have been linked to poorer arithmetic performance (Holloway & Ansari, in press). These findings are an important precursor to the current work because they suggest that, firstly, a larger distance effect reflects a less developed mental representation of numerical magnitude, and secondly, that a less developed representation of numerical magnitude has a significant negative influence on arithmetic performance.

Thus, the results of the present thesis, showing a stronger distance effect in dyscalculia, suggest that the underlying representation of numerical magnitude is underdeveloped in these participants, and that this underdeveloped representation is a plausible candidate for a core deficit underlying poor arithmetic achievement. In the current work, however, the size of the distance effect did not correlate with standardised maths scores for any of the groups. The lack of effect in this case may be due to low subject numbers and low variability in reaction time and accuracy.

It should also be noted that Holloway & Ansari (in press) observed a correlation between arithmetic fluency and the symbolic reaction time distance effect. Rousselle & Nöel (2007) have suggested that DD stems not from an underdeveloped representation of numerical magnitude, but rather a deficit in the ability to access those representations through the use of Arabic digit symbols. The limitations of Rousselle and Nöel's study in support of this access deficit hypothesis are discussed above and do not need to be repeated here. However, the results of Holloway and Ansari (in press) may lend support to the access deficit hypothesis in that it was only the symbolic distance effect and not the nonsymbolic distance effect which correlated with math fluency.

Behavioural evidence, then, has yet to resolve the question of whether DD is caused by an underdeveloped representation of numerical magnitude or a deficit in accessing that representation through the use of Arabic digits. Thus it becomes even more important to investigate the neural processes which underlie numerical processing in DD. If the core deficit hypothesis is correct, then the larger distance effect in DD children should be underscored by atypical activation in those brains regions thought to support the representation of numerical magnitude, particularly the IPS. If, on the other hand, as the access deficit hypothesis suggests, the representation of numerical magnitude is intact in DD, then the IPS should not show any atypical activation patterns.

The present thesis is the first work to examine the neural correlates of both the symbolic and nonsymbolic distance effects in DD children. The results show that during nonsymbolic number comparison, the TD group shows a classical distance effect in the right IPS and left fusiform gyrus. The DD group on the other hand, show equivalent activation to the TD group during large distance comparisons but no increase in activation during small distance comparisons (i.e. no distance effect). In other words, the larger behavioural distance effect in the DD group is mirrored by the lack of distance effect in the IPS, the brain region principally thought to house the representation of numerical magnitude (Dehaene et al., 2003). Thus the results of the nonsymbolic number comparison paradigm appear to support the core deficit hypothesis and contradict the access deficit hypothesis.

The results of the symbolic comparison paradigm, however, are not as conclusive. The TD group showed a classical distance effect in three brain regions which the DD group did not, namely the left middle temporal gyrus, right mid-occipital gyrus and right lateral prefrontal cortex (pars triangular). In all three of these regions the DD group actually showed a decrease in activation during small distance comparisons relative to large distance comparisons. The left middle temporal region has previously been associated with auditory word processing (Price et al., 1996), phonemic discrimination (Ashtari et al., 2004) and auditory speech perception (Scott et al., 2000). This suggests that during the symbolic number comparison task participants were accessing and perhaps repeating sub-vocally the names of the Arabic digits to be compared. They could also have been reciting counting sequences. Seemingly the TD group employed the strategy more during the small distance condition while the DD group did so less for small distances than for large distances. No other fMRI study has investigated the neural correlates of the symbolic distance effect in DD children, and so this interpretation is highly speculative, and requires replication in theoretically focused empirical studies.

The right middle occipital region which includes the occipito-temporal junction has previously been found to respond the judgement of Arabic digit orientation more than numerical comparison (Pesenti et al., 2000), but is active during symbolic number comparison (Fias et al., 2003a). Thus it appears that although this region is involved in the visual processing of Arabic digits, it is not related to the underlying semantic representations of numerosity as it is less active during comparison than orientation judgement. It is possible that the increased activation for small distances in the control group simply reflects the greater application of this cognitive mechanism during the more difficult of the two conditions. The decreased activation in the DD group on the other hand may simply reflect reduced application in line with falling error rates. Given the existing literature on the function of this region it is difficult to see why it should show a distance effect in either group, given that the visual stimulation between conditions was not different, and the region does not appear to play a role in semantic access to numerical information. As with the middle temporal region, the role of this area in numerical comparison requires further focused investigation.

Finally, the right inferior frontal region which shows a classical distance effect in the TD group and a reverse distance effect in the DD group has previously been shown to be involved in symbolic number comparison (Chochon et al., 1999), the backward recall of digits (Sun et al., 2005) and specifically in conflict resolution during numerical comparison of Arabic Digits (Tang et al., 2006). In addition to these numerically specific findings, the region has been shown to be involved in cognitive conflict resolution in go/no go tasks (Durston et al., 2002) and error monitoring (Carter et al., 1998). As with the other two regions, the classical distance effect in the TD group suggests increased application of domain general cognitive processes during the harder of the two comparison conditions, the DD group, on the other hand, appear to decrease their application of these processes, and subsequently show a great increase in error rates.

The lack of a neural distance effect in the IPS during symbolic comparison was unexpected. Previous neuroimaging studies which have investigated the symbolic distance effect have observed distance related modulation in parietal regions in both adults and children (Ansari et al., 2005; Pinel et al., 2001). Ansari et al used a paradigm almost identical to the current study, albeit with more subjects, so it is unclear why their paradigm should yield a parietal distance effect and the current study not. It is possible that the participants in the current study simply employed a different cognitive strategy to those in the Ansari et al study. Although highly speculative, this interpretation is supported by the fact that the brain regions showing neural distance effects in the current study were not present in the Ansari et al study. As the current set of regions suggest the use of a strategy which was based primarily on visual recognition of the Arabic digits themselves, it is possible that the current sample of TD children were retrieving the correct answer from memory of the ordinal counting sequence rather than accessing the underlying quantity representations.

If we assume then, that the TD children in the current study were employing an ordinal strategy to carry out the comparison task, then the question remains why the DD group showed a classical behavioural distance effect but reverse neural distance effects in those regions showing classical distance effects in the TD group.

It is possible that the failure to compare the numerosity of Arabic digits as effectively as controls is the result of a deficit in the link between the digits symbols and the underlying mental representations. Rousselle & Nöel (2007) argue that DD is caused by an impairment of the ability to access numerical magnitude representations through the use of Arabic digits. However, it is unclear why such a deficit would occur only in the context of Arabic digits, while the underlying representations themselves remain intact. Thus it seems more likely that such an access deficit may indeed be present, but it stems from an underdeveloped representation rather than a specific impairment of the access process. This would explain why DD children show a stronger distance effect both in nonsymbolic numerical comparison, which requires direct access to numerical magnitudes, and symbolic comparison, which requires fluent use of Arabic digits. However, this is the first work to compare the neural distance effect in both symbolic and nonsymbolic comparison between TD and DD children, and thus these interpretations are necessarily speculative.

Although the behavioural and neuroimaging results of this thesis support a domain specific impairment of numerical magnitude representation in DD, it should also be noted that the DD group had significantly lower spatial IQ than the TD group, albeit within the normal range. There is an acknowledged link between spatial attention and numerical processing, evidenced from numerical deficits in spatial neglect patients (Zorzi, Priftis, & Umilta, 2002), behavioural interference between spatial location and numerical magnitude (Dehaene, Bossini, & Giraux, 1993), and shared neural circuitry in the parietal lobes for attention to external space and the representation of numerical information (Hubbard et al., 2005). Furthermore, a recent study by Geary, Hoard, Nugent, & Byrd-Craven (2008) showed that DD children are less accurate than controls in estimating the midpoint of a number line from 0-100.

These results suggest that the underdeveloped representation of numerical magnitude in DD suggested by the present thesis cannot be entirely extricated from deficits in visuo-spatial processing. Several studies which investigated mathematical difficulties as opposed to pure DD have observed poorer visuo-spatial skills in AD children (e.g. McLean & Hitch, 1999; Rourke, 1993). However, several studies of DD have failed to find a specific pattern of relationships between general visuo-spatial ability and DD (Shalev, Manor, Amir, Wertman-Elad, & Gross-Tsur, 1995; Shalev et al., 1997). Thus the relationship between visuo-spatial processing and DD remains unclear. However, both the reduced spatial IQ and the lack of distance effect in the left fusiform gyrus of DD children in the current study suggest that perhaps there is a relationship between visuo-spatial ability and the development of numerical magnitude representation.

It is possible that a developmental visuo-spatial deficit could undermine the development of a typical numerical magnitude representation by impairing the ability to extract numerosity from visual displays and organise numbers on a mental number line. However, given the lack of consistent evidence of visuo-spatial deficits in DD, a more likely explanation is that there is simply an overlap between a domain specific impairment of numerical magnitude representation and visuo-spatial impairments due to the close proximity of the two neural mechanisms. The exact relationship between visuo-spatial processing and DD remains an open question, and one that requires truly developmental longitudinal research to answer. The results of the present study, however, are the first to provide direct support the existence of a domain specific core deficit in the brain-level representation of numerical magnitude.

19.3 The Causes of Comorbidity

The second aim of this thesis was to investigate the representation of numerical magnitude in children with comorbid dyscalculia and dyslexia. The high rate of comorbidity makes this an important issue in the context of developing focused interventions for the remediation of arithmetic learning disorders, as different subtypes may present different behavioural profiles and developmental trajectories (Fletcher, 2005).

The principle question addressed in this thesis is whether children with comorbid dyscalculia and dyslexia have arithmetic learning difficulties as the result of an impaired representation of numerical magnitude, as appears to be the case in pure dyscalculia, or whether, as suggested by Rousselle & Nöel (2007) both DD and CM children's deficits stem from an impairment in accessing numerical semantic information through the use of Arabic digits..

This question was addressed by probing the mental representation of numerical magnitude in dyscalculic, dyslexic, comorbid and typically developing children as manifest through behavioural symbolic and nonsymbolic distance effects during numerical comparison. Unfortunately, due to head motion in the CM and DL groups their data had to be excluded from fMRI analysis, and so the second aim of this thesis is addressed solely by behavioural data.

Despite the divergence in theoretical perspectives, the majority of behavioural evidence suggests that DD and CM children do not differ in terms of their basic numerical abilities, but may differ in their ability to compensate poor numerical skills with linguistic abilities (Geary et al., 2000; Geary & Hoard, 2001; Jordan et al., 2003; Jordan et al., 2002). However, much of this work is compromised by liberal selection criteria when diagnosing DD. Two recent studies have employed more stringent selection criteria observed similar results, but arrived at opposing theoretical interpretations. Landerl et al (2004) observed that DD and CM children did not differ on a range of basic numerical tasks and concluded that the arithmetical deficits in both groups stemmed from the same core deficit in numerical representation. Rousselle & Nöel (2007) also found that DD and CM children did not differ on a range of basic numerical tasks. However, because in this study the DD and CM groups (collapsed) were impaired relative to controls in symbolic but not nonsymbolic comparison the authors concluded that DD is caused by a deficit in accessing numerical magnitude information through the use of Arabic digits.

The results of this thesis revealed that during nonsymbolic comparison the DD group showed a marginally significantly stronger distance effect than the TD group. No other group comparisons for this condition approached significance. During the symbolic condition, on the other hand, both the DD and CM groups showed stronger distance effects than the TD and DL groups, and furthermore, the CM group showed slower overall reaction time for symbolic comparison relative to the TD group.

These results suggest that while the DD group has an underdeveloped representation of numerical magnitude that impairs both symbolic and nonsymbolic processing of numerical information, the CM groups impairment is limited to symbolic number processing. However, it is important to note that the dyslexic group did not show any impairment of symbolic number comparison, and thus the performance of the CM grouped cannot be attributed solely to the presence of comorbid phonological awareness deficits associated with dyslexia. Thus it is possible that the comorbid group represents a subgroup of children who have a specific deficit in accessing mental numerical representations through the use of visual symbolic stimuli. Whether or not this 'access deficit' extends to other domains is an open question.

Some researchers have suggested that dyslexia may be associated with a core deficit in both phonological awareness and in naming fluency (i.e. semantic retrieval) (e.g. Manis et al., 1999; Wolf & Bowers, 1999) and longitudinal research has shown that many children with dyslexia show a specific impairment in retrieval, indexed by tasks such as rapid naming (Lyytinen, Erskine, Tolvanen et al., 2006). Thus, if semantic retrieval requires a combination of visual recognition of feature elements and integration of semantic and conceptual information (Wolf & Bowers, 1999), then it is plausible that an impairment of this cognitive process would impair both arithmetic performance and result in a stronger distance effect during symbolic number comparison, as both arithmetic and numerical comparison require fluent access to semantic information on the basis of visual symbolic stimuli. The current thesis did not, however, include a specific test of rapid naming, and thus this interpretation is speculative, but provides a highly plausible explanation for testing in future research.

Although Rousselle and Nöel (2007) suggested that this "access deficit", which may be analogous to a naming fluency or semantic retrieval deficit, was the root cause of arithmetic impairments in both the CM and DD groups, they did not compare the two groups in terms of distance effects before collapsing them into to one larger group. Had the groups remained separate, the authors may have observed group differences in the nonsymbolic condition related to the distance effect, which were masked as a result of collapsing the two groups.

Similarly, Landerl et al (2004), who found no differences between CM and DD groups in basic numerical tasks, did not include a nonsymbolic number comparison task. The current results show that the differences between the CM and DD groups emerge in the nonsymbolic and not the symbolic distance effect, and thus had the authors included such a contrast differences between the CM and DD groups may have emerged.

Thus, the present results suggest that the arithmetic deficits in children with comorbid dyscalculia and dyslexia do not stem from an impaired mental representation of numerical magnitude, but rather from an impairment of accessing the semantic information represented by numerical symbols. Future research will be able to focus on identifying the cognitive impairments which lead to this 'access deficit'.

19.4 Intervention

The natural goal of research into learning disorders is to ultimately develop effective educational interventions which allow children to achieve their full potential. Several researchers have already begun to develop focused interventions which attempt to improve the basic representation of numerical magnitude or "number sense", (Griffin, 2007; Wilson, Dehaene et al., 2006).

The theory that the development of strong sense of quantity or number sense is essential to the development of arithmetic proficiency has, however, been used in the development of educational interventions long before the emergence of the triple code model. In the 1980s and 1990s Griffin and Case developed the "Number Worlds" (formerly "Rightstart'") program which was specifically designed to teach Number Sense, initially to Kindergartners and later extended to grades one and two. The program aims to build upon and improve children's existing knowledge levels and follows the natural developmental pathway to develop both computational fluency and conceptual understanding in mathematics learning. The program is founded on the development of the understanding of three 'Number Worlds', quantity, number words and symbols and has been found to be highly successful in helping children from lower socio-economic backgrounds attain the same level of numerical competence as those from more affluent backgrounds (Griffin & Case, 1997). The 'Number Worlds' program, although highly successful in improving the arithmetic performance of children with low socio-economic status has not yet been shown to be effective in the remediation of pure DD.

The term "Number Sense" has different connotations in education and in cognitive psychology however (Berch, 2005). More recently, the neuropsychological concept of 'number sense' derived from the 'triple code model' (Dehaene, 1995) has been directly applied in the construction of intervention software, specifically designed to remediate children with DD. Wilson and colleagues (Wilson, Dehaene et al., 2006; Wilson, Revkin, Cohen,

Cohen, & Dehaene, 2006) have developed the "Number Race" computer game for the remediation of dyscalculia stemming from a core deficit either in number sense or in the access to it through symbolic number information. In the Number Race programme "Number Sense" is defined as the ability to "represent and manipulate numerical quantities non-verbally".

The game uses a structure similar to a board-game, with numerical comparison as its main task, employing repeated associations between different number representations and quantity, as well as a spatial progression along the game path to emphasize associations between number and space. "Number Race" shares some features with "Number Worlds' in that both also attempted to improve fluency in very basic calculation. A key feature emphasized in both projects was that the programs should be relevant to child's own ability, and hence the "Number Race" game incorporates a computerized, multidimensional adaptive algorithm which assesses response patterns and adjusts task difficulty accordingly. Open trial assessments have shown positive effects of the game in improving basic numerical skills including speed of subitizing and numerical comparison, and accuracy of some simple subtraction (Wilson, Revkin et al., 2006).

The development of focused and effective teaching and remediation methods can be positively informed by cognitive neuroscience research, helping educators and scientists to understand how the brain acquires basic numerical skills and the nature of developmental abnormalities which can impair those processes. Despite the advancement of interventions focused on developing core number sense, the results of this thesis are the first to provide direct evidence of a brain level impairment in pure dyscalculia, and thus highlight the importance of the development of the mental representation of numerical magnitude in acquiring arithmetic proficiency. Furthermore, the lack of distance effect in the fusiform gyrus in DD subjects suggests that visuo-spatial processing may play a role in extracting the dimension of numerosity from a set of objects.

Such findings may be useful in the refinement of educational interventions in allowing developers a better understanding of which additional cognitive mechanisms may be employed to bolster the focused development of numerical representation. For example, an increased focus not just on understanding the relationship between quantities and symbols, but also on the low level visual processes which allow numerosity information to be extracted from visual displays may be beneficial in building a strong number sense.

Furthermore, the behavioural results presented in this thesis show that the arithmetic deficits in children with pure dyscalculia and comorbid dyscalculia and dyslexia may stem from different root causes. Thus, while the pure DD group may benefit from a focused intervention which seeks to bolster the mental representation of numerical magnitude through associations with numbers and space, the CM group may benefit more from interventions which seek to increase the fluency with which numerical representations are accessed through the use of symbols.

It is important, however, to avoid an extreme position in adapting educational practices to such an extent that children are learning only those basic processes which are well described at the neural level, such as basic magnitude comparison. It is highly important that proficiency in processes such as simple magnitude comparison are not viewed as the learning end states, but continue to be viewed as cognitive foundations on which more sophisticated learning can be built.

19.5 Dyscalculia: Cause or effect of atypical development of the intraparietal sulcus.

The IPS is frequently active in tasks requiring numerical magnitude processing (Dehaene et al., 2003). There are at least two possible explanations for this specialisation. First, that the IPS becomes specialised during ontogenetic development for the processing of numerical magnitudes by means of a so called 'Neuronal Recycling' mechanism (Dehaene, 2005). By this method neuronal populations innately specialised for processing domain general magnitudes would become assimilated for the preferential processing of numerical magnitudes, perhaps by an educational or cultural system which highlights the magnitude dimension of numerical information.

The second possibility is that the right IPS is phylogenetically specified for numerosity processing, and upon this evolutionary foundation, our culturally embedded systems of number are based. Thus the properties of evolutionarily recent numerical systems would be at least similar in part to the properties of the numerical magnitude system located in the IPS. This second possibility is supported by evidence showing number selective neurons in regions of the monkey brain which are analogous to intraparietal regions in the human brain (Nieder, 2005) and evidence of numerical processing abilities in untrained animals (e.g. McComb et al., 1994; Wilson et al., 2001).

If the intraparietal sulcus is ontogenetically specialised for numerical processing, then DD children should show functional impairments of this region only secondary to one or more functional impairments of more fundamental processing mechanisms, those that allow the IPS to become specialised for numerical processing. The current data show that the right IPS is functionally impaired in DD independent of impairments in any other primary processing brain regions, with the exception of the left fusiform gyrus. Thus, while the results of this thesis support the existence of a deficit in the mental representation of numerical magnitude in DD, there remains an open question as to whether that impaired representation occurs independently or is the consequence of the failure of lower level visual impairments to extract the dimension of numerosity from visual stimuli.

19.6 Conclusions and Future Directions

The results reported above support the existence of a core deficit of numerical magnitude representation in dyscalculia. Furthermore they suggest that the arithmetic impairments shown by children with comorbid dyscalculia and dyslexia may stem from an alternative core deficit, perhaps in the cognitive mechanism responsible for accessing semantic information through visual symbols.

Domain specific theories of dyscalculia are rooted in adult neuropsychological evidence and as such follow similar theoretical conceptualisations of which processes may be impaired. In the initial stages of developing our understanding of DD, analogies between behavioural deficits acquired as a result of brain damage and developmental disorders are a useful first step (Denckla, 1973). However, the behavioural manifestations of acquired brain damage differ in many ways from those of developmental disorders, given that acquired cognitive deficits stem from a focal lesion which might disrupt one or more mature brain mechanisms, while in children the damage occurs often as a result of prenatal and postnatal developmental abnormalities, which rather than 'knocking out' a given system, impair the ontogenetic growth of that system. Furthermore, brain-behaviour relationships in adults tend to be much more static than they are in childhood (Rourke & Conway, 1997).

The consequence of brain damage in an adult brain is the partial or complete loss of one or more cognitive functions. In children however, the issue is rather how brain level abnormalities will affect future development and learning capacity. The behavioural impact of brain dysfunction in a child is a consequence of the present and future developmental environments, as well as the neuropathological characteristics of the brain dysfunction (Karmiloff-Smith, 1998; Rourke, Bakker, Fisk, & Strang, 1983). The behavioural impairments present in infancy may fall away and even be supplanted by alternative impairments over the course of development (Paterson, Brown, Gsodl, Johnson, & Karmiloff-Smith, 1999). Thus, despite the heuristic utility of the neuropsychological approach to the study of DD, a truly development approach is required which considers the impact of brain development abnormalities on the ontogenetic learning trajectory of mathematical skills.

The results of this thesis reveal a domain specific impairment of numerical magnitude representation in DD. However, it can presently merely be concluded that at some point in the course of development, pre or post natal, DD children appear to have suffered a disruption to the domain-relevant system responsible for developing the ability to manipulate numerical quantities. Whether the system that was originally impaired is numerically domain specific or linked to low level perceptual processes is a question that can only be answered by true developmental research (Karmiloff-Smith, 1998).

Thus, future research should aim to chart developmentally the functional development of both parietal magnitude systems as well as lower level visual mechanisms such as those supported by the fusiform gyrus in order to understand whether the functional impairments of these regions demonstrated in the current thesis occur independently or are causally linked, and if the latter, then in which direction does the causal influence flow? This thesis also revealed differing activation patterns in temporal and occipital regions between TD and DD children during symbolic number comparison. However, the exact roles of these regions in numerical comparison need to be further elucidated, and these findings need to be replicated before they can be practically interpreted. Future studies of symbolic number comparison should seek to use paradigms such as those used by Pinel et al (2001) which place more demand on numerical magnitude systems and are not readily solvable using ordinal strategies. In this way it may be possible to examine whether intact or impaired magnitude representations underlie performance in symbolic as well as nonsymbolic number comparison.

The present results also suggest that children with comorbid dyscalculia and dyslexia have a cognitive deficit in accessing numerical semantic information through the use of visual symbols, and that impairs arithmetic performance, but is not shared with either pure dyscalculics or dyslexics. Thus, a major area for future research is to investigate the nature of the 'access deficit' in comorbid children. Exploratory research is required in order to understand whether the access deficit is specific to the use of numerical symbols, or whether these children have a wider deficit in mapping symbols onto referents, an impairment which could also possibly account, in part, for their reading impairments. Both behavioural and neuroimaging comparisons between dyscalculic, dyslexic and comorbid children are required and need to extend to cognitive tasks beyond those which probe core deficits in either numerical or phonological representation.

Finally, the wide variation in terms used in research on mathematical learning difficulties has perhaps dissipated some of the focus from past research findings. Thus, in order that research findings from one study can be easily and accurately compared to those from another, there needs to be some agreement on exactly which populations are defined by different terms. To some extent this is already developing, with mathematics or arithmetic difficulties referring to populations with milder deficits than those observed in pure dyscalculia.

The results reported in this thesis represent a key step in the identification of both a core deficit in pure dyscalculia, as well as a second, as yet unclear, core deficit in comorbid children. Significant work is still required in order to build a more complete understanding of these deficits, their causes and developmental trajectories and ultimately to develop effective educational interventions.

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