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Developmental dyscalculia in adults

Current issues and open questions for future research

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Abstract: Developmental dyscalculia (DD) is a chronic condition that poses not only a barrier to employment and socio-emotional wellbeing but that also persists into adulthood. Thus, understanding the neuro-cognitive foundations of DD is relevant for both children and adults with DD. However, so far the vast majority of scientific research endeavours has been dedicated to the study of DD in children only. Consequently, our current understanding of DD in adulthood is rather patchy. The main aim of the present review is to summarize the scientific findings on DD in adults by focusing on its cognitive manifestations and neural substrates in adults. For instance, research on DD in adulthood suggests that – beyond an outstanding deficiency in number processing – the processing of non-numerical magnitudes and domain-general skills seem to be also impaired in adults suffering from persistent DD. A secondary aim of this review is to delineate future lines of research that will provide us with a more elaborate understanding of the neurocognitive underpinnings of DD in adults (thus fostering the development of sensitive diagnostic marker tasks), and to formulate potential intervention areas targeting deficiencies frequently characterizing DD in adults.

Keywords: Developmental dyscalculia, adults, number magnitude processing, neural correlates

Entwicklungsbedingte Rechenstörungen im Erwachsenenalter – Aktueller Forschungsstand und offene Fragestellungen

Zusammenfassung: Entwicklungsbedingte Rechenstörungen ('developmental dyscalculia' / DD) bleiben unbehandelt bis ins Erwachsenenalter bestehen und haben einen negativen Einfluss auf die Berufsmöglichkeiten (und somit auf das Einkommen) sowie die sozio-emotionale Gesundheit der Betroffenen. Daher ist ein besseres Verständnis der neurokognitiven Grundlagen von DD bei Erwachsenen äußerst relevant. Das Hauptziel der vorliegenden Übersichtsarbeit ist die Darstellung der bisherigen wissenschaftlichen Befunde zu DD im Erwachsenenalter, wobei der Fokus auf den kognitiven und bildgebenden Studien liegt. Nach aktuellem Forschungsstand scheinen die kognitiven Defizite von Erwachsenen mit der Diagnose DD nicht auf Schwierigkeiten bezüglich der Zahlenverarbeitung im engeren Sinn beschränkt zu sein, sondern betreffen auch die Verarbeitung von nicht-numerischen Größen und domänen-übergreifende Fertigkeiten. Weitere Ziele der vorliegenden Arbeit sind die Skizzierung zukünftiger Forschungsfragen, die helfen sollen, (i) ein detaillierteres Verständnis der neurokognitiven Grundlagen von DD im Erwachsenenalter zu gewinnen (als Voraussetzung zur Entwicklung von sensitiven diagnostischen Instrumenten), und (ii) potentielle Interventionen zu definieren, die an den mit DD im Erwachsenenalter assoziierten kognitiven Defiziten ansetzen.

Schlüsselwörter: Entwicklungsbedingte Dyskalkulie, Erwachsene, Zahlenverarbeitung, neuronale Korrelate

Introduction

Developing good numeracy and calculation skills is important for adult life. Poor numeracy in adults is related to higher unemployment (KPMG, 2008; Parsons & Bynner, 2005), lower salary (OECD, 2012), depression (KPMG, 2008) and poorer health (Carpentieri, Lister & Frumkin,

2009). In the developmental literature, various terms and diagnostic criteria are used to classify individuals with difficulties in numeracy. The term developmental dyscalculia (DD) describes a rather circumscribed deficit in basic number processing (that in some affected individuals might be accompanied by poor attention, working memory, visual-spatial processing etc.; for respective reviews,

see Kaufmann & von Aster, 2012; Rubinsten & Henik, 2009).

The prevalence of DD is rather high, affecting 5–7% of the general population (Gross-Tsur, Manor & Shalev, 1996; Rubinsten & Henik, 2009; Schulz et al., 2018). Notably, affected children do not ‘grow out’ of DD. Rather, arithmetic difficulties tend to persist into adulthood if untreated (e.g., Ashkenazi & Henik, 2010; Cappelletti, Freeman & Butterworth, 2011; De Visscher, Noel, Pesenti & Dormal, 2018; Gliksman & Henik, 2018, 2019; McCaskey, von Aster, O’Gorman Tuura & Kucian, 2017; for a detailed description of a single-case study of adult DD, see Kaufmann, Pixner & Göbel, 2011a). However, most research to date has focused on children with DD, neglecting the large number of adults suffering from DD. Notably, DD has to be differentiated from acquired acalculia, which is a consequence of brain damage and has been studied rather extensively (e.g., Ardila & Rosselli, 2002; see Willmes, 2008, for an overview). For the sake of simplicity and because the vast majority of the research on non-acquired (i.e., developmental) mathematical difficulties in adulthood investigated DD, we will here use the term DD whenever refer-

ring to adults presenting with severe and persistent number-related difficulties.

Current diagnostic classifications of DD

According to the most recent versions of clinical diagnostic manuals, severe difficulties in learning arithmetic are considered to be a nosological entity and consequently, are assigned to a specific diagnostic category: ‘developmental learning disorders with impairment in mathematics’ in the ICD-11 (WHO, 2017) and, within the category of ‘neurodevelopmental disorders’: ‘specific learning disorder with impairment in mathematics’ in the DSM-V (APA, 2013). Importantly, the DSM-V acknowledges that specific learning disorders tend to persist into adulthood, and thus, should be considered as a life-long disorder. In contrast to the previous version of the internationally used clinical diagnostic manual DSM-IV (APA, 1994), DSM-V criteria do not require an IQ-achievement discrepancy. The abandonment of the IQ-achievement discrepancy is based on the fact that multi-com-

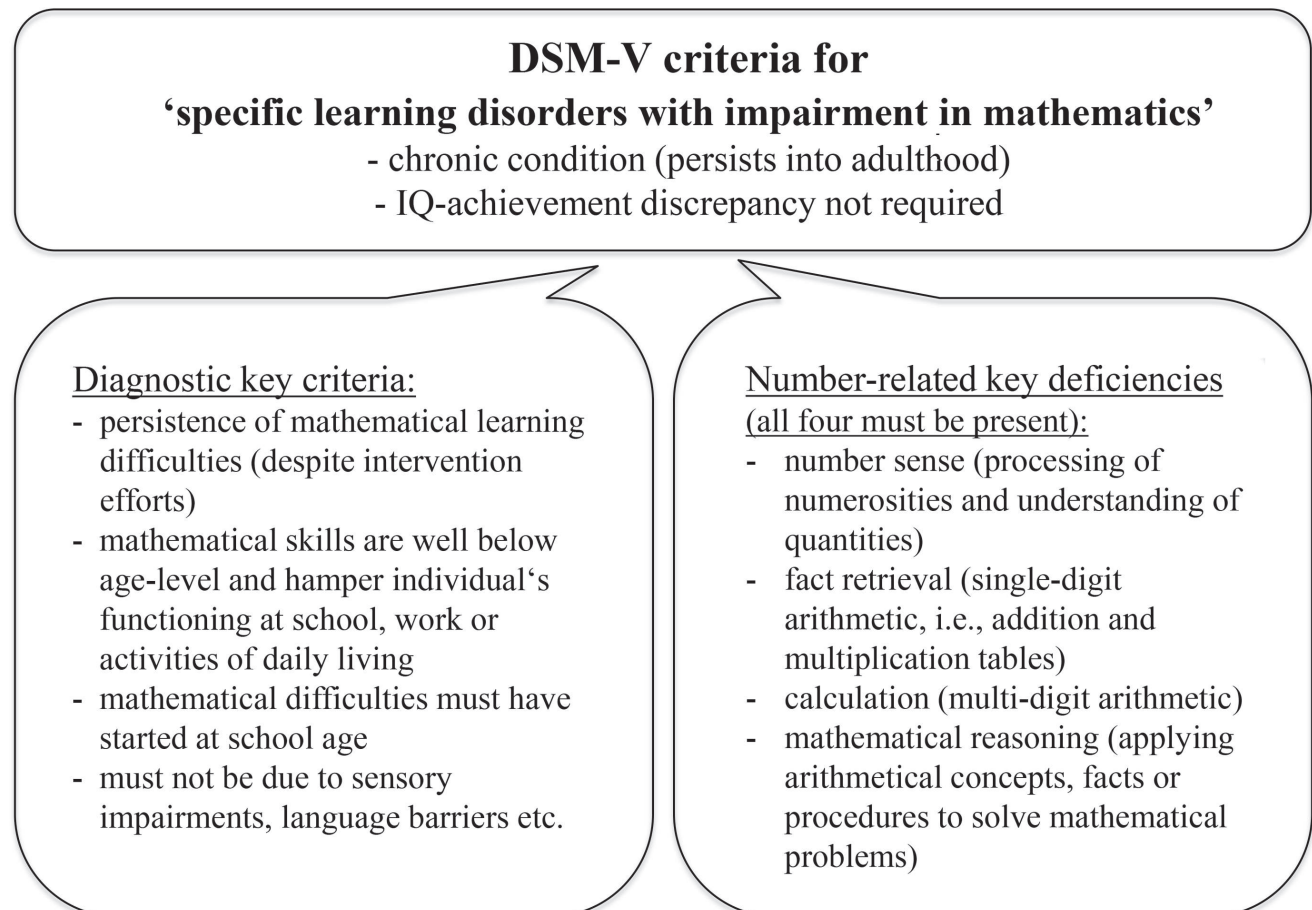


Figure 1. Current diagnostic criteria for identifying developmental dyscalculia (DD) in adults according to DSM-V (APA, 2013).

ponential IQ-tests frequently include subtests assessing reading, writing, or arithmetic performance (which in the presence of a specific learning disability inevitably cause a decrease of the total IQ score). Figure 1 depicts the diagnostic key criteria of ‘specific learning disorders with impairment in mathematics’ put forward by DSM-V (APA, 2013).

Before presenting an overview of the relevant literature on DD in adults, we briefly summarize our current understanding of numerical processing in the adult brain.

Theoretical models of number processing and calculation

Various number processing models were proposed in the 80s and 90s (for an overview, see Deloche & Willmes, 2000). The most influential one is the Triple-Code-Model (TCM) developed by Dehaene (1992; Dehaene & Cohen, 1995, for an elaborated model integrating cognitive and neurofunctional aspects; Dehaene, Piazza, Pinel & Cohen, 2003, for detailed specification of the parietal involvement). According to the TCM, numerical information is processed by three distinct representational codes that are supported by regionally and functionally distinct neural substrates. First, the *analogue magnitude representation* (i.e., II) mediates a core quantity system needed for both approximate quantity representations [also coined as ‘approximate number system/ANS’, tapped by tasks like estimation, approximate calculation as well as discrete quantity representations (which are supposed to house the core semantic number representation thought to be activated by number comparison tasks, among others)]. Second, the *visual Arabic number form* (i.e., ‘2’) supports the processing of visually presented number processing and arithmetic problems that require the recognition of Arabic numerals (as required upon solving multi-digit operations). Third, the *auditory verbal word frame* (i.e., ‘two’) is used for verbally mediated operations like counting, number naming or other tasks that require the active manipulation of sequences of number words. Also, the auditory verbal word frame is recruited whenever arithmetic problems are solved by direct arithmetic fact retrieval from memory and not by active magnitude manipulation (e.g., multiplication tables such as 2×3 and results of simple addition problems).

Up till now, the TCM has shaped decades of numerical cognition research investigating number processing and arithmetic in healthy adults and patients. Even in the developmental literature, the TCM served as conceptual framework to formulate research hypotheses and to interpret data derived from behavioural and brain imaging studies. However, because the TCM is based on adult data and

thus, mature brain systems, it might not be directly applicable to developmental brain systems (see Kaufmann et al., 2013, for the need to establish true developmental models of number processing and calculation).

Neural correlates of number processing and calculation

With regard to the neural underpinnings of the aforementioned representational codes, the TCM (Dehaene & Cohen, 1995; Dehaene et al., 2003) identifies the intraparietal sulcus (IPS) as a key region supporting the representation of approximate or discrete quantities (often called the ‘number sense’). According to the TCM, other key regions for number processing are left-hemispheric perisylvian language regions and the angular gyrus/AG (supporting verbally mediated processing of numerical information within the auditory verbal word frame) and bilateral inferior occipito-temporal regions including the fusiform gyri (supporting the visual processing of Arabic digits and letter strings from number words within the Visual Number Form Area/VNFA; e.g., Grotheer, Herrmann & Kovács, 2016).

An alternative account proposes that (intra)parietal cortices support an overarching concept of ‘magnitude’ in a rather generalized manner (Walsh, 2003; Walsh, 2015). In particular, the ATOM (A Theory of Magnitude) theory suggests that numerical quantity, time and space share common parietal processing mechanisms. In a similar vein, evidence from the developmental literature suggests that early in life, the processing of numerosity, space and time are frequently intermixed in the natural environment of humans and animals alike (e.g., de Hevia, Izard, Coubart, Spelke, & Streri, 2014). Notably, recent brain imaging studies support the idea of overlapping neurofunctional circuits mediating such a generalized magnitude system (e.g., humans: Dormal, Dormal, Joassin, & Pesenti, 2012; McCaskey et al., 2017; Skagerlund, Karlsson, & Träff, 2016; animals: Tudusciuc & Nieder, 2009; but see Anobile et al., 2018; Kucian, McCaskey, von Aster & O’Gorman Tuura, 2018). For example, the fMRI study of Skagerlund and colleagues (2016) is among the first that directly compared neurofunctional activation patterns across the three magnitude dimensions (i.e., number, time, line length) in healthy adults. Their findings are clearly compatible with the hypothesis of a generalized magnitude system. In particular, fMRI responses were found to substantially overlap across all three magnitude dimensions in several right-lateralized brain regions including the IPS and the insula (thought to support the magnitude processing system) as well as premotor cortex/supplementary motor areas and inferior frontal gyrus (thought to support more domain-general processing mechanisms).

Recently, the TCM was challenged by Skagenholt, Träff, Västfjäll and Skagerlund (2018) who tested all three numerical representational codes in healthy adults within one fMRI study. Based on the results of their study, the authors claimed that the TCM needs to be further elaborated by acknowledging interactions with attentional processes, thus strongly arguing for a fronto-parietal network of number processing involving the inferior and superior frontal gyrus, the dorsolateral prefrontal cortex and the anterior cingulate cortex, among others (for similar findings in adults, see Arsalidou & Taylor, 2011; Klein et al., 2016; Menon, 2015). Importantly, the involvement of (pre)frontal cortex in number processing has been repeatedly reported in developmental studies and has been interpreted to reflect compensatory strategies (for a meta-analysis of developmental fMRI studies, see Kaufmann, Wood, Rubinstein & Henik, 2011b). Possibly, children (compared with adults) and even more so children with DD need to employ more effort to solve even simple number tasks (Ashkenazi, Mark-Zigdon, & Henik, 2013; Kaufmann et al., 2011b; Kucian et al., 2006; Peters & De Smedt, 2018). Moreover, in children and adults alike it is plausible that the frequently reported co-activations in (pre)frontal brain regions during numerical and arithmetical tasks are attributable to task difficulty (Arsalidou & Taylor, 2011).

Finally, the results of a meta-analysis of adult fMRI studies comprising 53 data sets (Arsalidou & Taylor, 2011) revealed that number processing and calculation are crucially supported by both a number-relevant fronto-parietal neural circuit including number-specific regions (inferior and superior parietal lobes) and several other brain regions mediating number-unspecific (domain-general) skills such as attention, working memory, task difficulty (inferior frontal gyrus), error monitoring, response execution, switching, initiation of motivational behaviour (cingulate gyri and insula), visual encoding and object categorization and possibly a 'visual number form' (occipital regions including the left fusiform gyrus), coordination of visual-motor sequencing as required in experimental tasks (cerebellum). Please see Figure 2 for a schematic representation of the brain regions and neurofunctional circuits involved in number processing and calculation in adults.

DD in adults

Only recently, DD in adults has received increasing scientific interest because it finally has been acknowledged that – without specific and tailored treatment – dyscalculia should be considered a life-long learning disability (DSM-V, APA 2013). In the following sections we will provide an overview of our current understanding of the cognitive manifesta-

tions and neural underpinnings of DD in adults. Notably, the current evidence is based on only a handful of studies. Thus, in a concluding section, we will first delineate the needs for future research to aim at a better understanding of the neurocognitive underpinnings of DD in adults before we outline how such knowledge may inform and ameliorate the diagnosis of DD as well as intervention tools.

Cognitive characteristics of DD in adults

Below, we briefly present the current behavioural literature on adults with DD by focusing on number-specific and number-unspecific (domain-general) processing mechanisms characterizing DD in adults.

Enumeration/subitizing

Recently, Gliksman and Henik (2019) assessed enumeration skills (and alertness) in adults with DD. Enumeration is defined as the ability to name the number of elements in a set. Importantly, while in the counting range (i.e., 5 to 9 elements) response latencies increase linearly as a function of set size, smaller set sizes (< 4 elements) are processed rapidly and almost simultaneously. The latter quick enumeration process was coined 'subitizing' and is thought to reflect pre-attentive processes (e.g., Trick & Pylyshyn, 1994), pattern recognition (e.g., Ashkenazi et al., 2013; Mandler & Shebo, 1982) or visuo-spatial working memory limits (e.g. Feigenson, 2008; Piazza, Fumarola, Chinello, & Melcher, 2011). According to Gliksman and Henik (2019), adults with DD have a smaller subitizing range (i.e., 3 instead of 4 elements) compared with controls and moreover, present a larger alerting effect (i.e., alerting cues yielded quicker RTs). However, alerting did not facilitate or enhance subitizing performance of adults with DD. Consequently, the authors concluded that enumeration draws on number-specific and domain-general processes alike, both of which are deficient in adults with DD (i.e., impaired subitizing performance reflecting number-specific deficits, and atypical attentional abilities caused by domain-general deficits). In another study, Cohen, Gliksman and Henik (2019) investigated whether subitizing deficits of adults with DD are restricted to the numerical dimension or not. Participants carried out both a visual and a tactile task requiring the enumeration of canonical/neighbors and random/non-neighbors sets (comprising 1 to 10 elements). Importantly, stimulus presentation time was rather long, thus facilitating pattern recognition and reducing potential interaction effects with domain-general attentional resources. The results partly confirmed and extended the findings of Gliksman and Henik (2019) by showing that adults with DD were less accurate in visually enumerating random dot arrangements

(however, they performed equally well as controls when processing canonical sets). While controls' performance was highly accurate for random sets up to 5, for adults with DD this was only the case for random sets comprising up to 4 elements. Furthermore, adults with DD were less accurate than controls for sets in the counting range. Likewise, they were less accurate than controls upon performing tactile enumeration (on neighboring fingers only, and especially when neighboring fingers resembled counting patterns). The latter findings are interpreted to reflect modality-independent deficits in enumeration performance that might be caused by impaired pattern recognition and working memory (Cohen, Gliksmann & Henik, 2019).

Automatic activation of number magnitude

A popular task thought to tap automatic number magnitude activation (as well as interference processing) is the Number Stroop task (Cohen Kadosh et al., 2007). In the Number Stroop task, participants perform either physical or numerical magnitude comparisons of two simultaneously presented Arabic numerals (which digit is physically or numerically larger, respectively). Typically, the numerical and physical sizes of the digits interfere with each other (Number Stroop Effect [NSE]; e.g., 5 2). In adults with DD, a significantly reduced NSE was reported during physical comparison (Rubinsten & Henik, 2005) suggesting that the numerical magnitude of the digits led to less interference in adults with DD than in controls. Interestingly, a reduced NSE similar to that observed in adults with DD (Cohen Kadosh et al., 2007) has been reported in healthy participants when Transcranial Magnetic Stimulation [TMS], a method to temporarily interfere with normal brain activity, was applied over their right IPS. This finding has been interpreted as a temporary induced virtual dyscalculia. Hence, the authors suggested that automatic activation of magnitude processing depends on the right IPS solely. The laterality-specific effect is somewhat unexpected because previous findings revealed left or bilateral IPS involvement in number processing. Possibly, the left hemisphere (including the IPS) might support verbal components of number processing (Cohen Kadosh & Walsh, 2009).

Arithmetic fact retrieval

Adults suffering from DD (like affected children) frequently need to employ back-up strategies such as finger usage to solve even simple arithmetic problems (Kaufmann et al., 2011). These back-up strategies are often time-consuming and error prone. Generally, back-up strategies involve multi-step procedures that place high demands on domain-general working memory resources. As working memory deficiencies are frequently associated with DD (and learning disabilities in general, for over-

views, see Kaufmann & von Aster, 2012; Rubinsten & Henik, 2009), a high load on working memory even worsens the solution outcome, thus rendering the back-up strategies maladaptive. Kaufmann et al. (2011) reported a case study of a female undergraduate student who – despite average intelligence, reading, spelling and working memory – presented with severe calculation difficulties. When solving single-digit additions, subtractions and multiplications, the young adult was able to retrieve rule-based arithmetic facts (e.g., $n + 1$, $n + 0$, $nx1$, $nx0$) directly from memory, but frequently had to recruit procedural strategies (including counting by finger usage) on the remaining single-digit problems. Clearly, reaction times on these procedurally solved problems were remarkably longer than on those solved by direct memory retrieval. Thus, the latter findings revealed that finger usage to solve single-digit problems, which are typically solved by direct memory retrieval (in good calculators), is not limited to children (in the beginning of formal schooling as well as to individuals diagnosed with DD), but can also be observed in adults with DD. Most interestingly, the findings of Cappelletti and Price (2014) suggested that longer response latencies in adults with DD seem to be number-specific. In particular, compared with controls, adults with DD needed longer to solve tasks requiring numerical magnitude judgements, but were as fast as controls in tasks involving non-numerical semantic categorizations (cf. De Visscher et al., 2018, for similar findings).

Arithmetical conceptual understanding

Adults with DD were found to have difficulties with basic arithmetical concepts such as the base-10 system and calculating with decimals and fractions (Eckstein, 2016).

Time/duration processing

Theories postulating a deficit in the generalized magnitude processing system were further corroborated by the fact that adults with DD exposed difficulties with numerical and temporal processing, while length processing (and also face categorization) was preserved (De Visscher et al., 2018). The latter findings were interpreted as being compatible with a non-symbolic magnitude deficit in DD including numerosity and duration (but excluding length processing). However, in a study by Cappelletti, Freeman and Butterworth (2011), adults with DD presented with preserved temporal discrimination abilities (as long as non-numerical stimuli had to be processed), while in controls temporal discrimination abilities did not decrease in the presence of task-irrelevant numerical stimuli material (for similar findings, see Cappelletti et al., 2014). The authors interpreted their findings as supporting 'a partially shared quantity system across numerical and temporal dimensions'.

Length/spatial processing

Length may be considered a spatial stimulus property. Current findings on length processing are inconclusive to date. While the findings of Ashkenazi and Henik (2010) disclosed deficient length processing in adults with DD, other authors were not able to replicate these results (e.g., length comparison of lines: Cappelletti et al., 2014; spatial task comparing the physical distance of Arabic number triplets, i.e., judging the spatial location of the middle number relative to the two outer numbers: Musolin, Martin, & Schiltz, 2011). Interestingly, when using a physical line bisection task (requiring participants to mark the middle point of lines varying in length), Ashkenazi and Henik (2010) found that adults with DD did not display the expected leftward bias (often called pseudoneglect), which has been interpreted as reflecting visual attentional difficulties. On the contrary, adults with DD displayed a larger than expected leftward bias on a number line bisection task (requiring participants to estimate the numerical midpoint between two horizontally presented Arabic numerals). This typically-observed leftward bias (similar to pseudoneglect) is thought to reflect the logarithmic property of the so-called ‘mental number line’, on which numerals are ordered in a left-to-right orientation for Western participants (from small to large; smaller numerals being farther apart from each other compared with larger numerals; Dehaene, 1997). Hence, the larger leftward bias observed in adults with DD was interpreted to reflect a stronger logarithmic representation of the mental number line and thus, impaired (access to) number magnitude representations (Ashkenazi & Henik, 2010).

(Conceptual) Size processing

Recently, adults with DD were reported to display deficient conceptual size processing despite preserved physical size processing (Gliksman & Henik, 2018). In this study, students with DD and developmental dyslexia were asked to compare two simultaneously presented pictures regarding their conceptual size (i.e., small mouse, large elephant) or their actual physical size. Conceptual and physical sizes were manipulated to create congruent (e.g., physically small fish compared to a physically large turtle) or incongruent trials (e.g., physically large fish compared to a physically small turtle). Generally, congruent stimulus pairs are processed faster and more accurately than incongruent ones. This response pattern was coined ‘congruity effect’ and is thought to reflect automatic activation of the irrelevant stimulus dimensions. The results of the latter study showed that adults with DD (unlike those with developmental dyslexia or controls) showed no congruity effect when making physical judgments (in which the conceptual dimension

was irrelevant), but when making conceptual judgments (in which the physical dimension was irrelevant) they showed a congruity effect similar to controls and adults with developmental dyslexia. This dissociation (i.e., automatic activation of physical size, but not of conceptual size) led Gliksman and Henik (2018) to conclude that adults with DD might have a weaker magnitude representation, specifically regarding non-countable magnitudes (thus supporting theories of shared neurocognitive substrates for different types of magnitude; i.e., the ATOM theory, Walsh, 2003, 2015).

Attention

Ashkenazi and Henik (2010) assessed attentional functions in adults diagnosed with DD. In particular, using the attention network task (ANT-I, Callejas, Lupianez, & Tudela, 2004) the authors reported deficient alerting and executive attention in adults with DD (in the presence of preserved orienting attention). Consequently, the authors concluded that DD in adults (without comorbid conditions including attention disorders) is characterized not only by a core deficit in number processing, but also by deficient attentional processes. Furthermore, Ashkenazi and Henik (2010) suggested that the observed attentional (i.e., alerting) difficulties in adults with DD can most likely be explained by an abnormal functioning of the IPS (which is not only a key region for number/quantity processing, but also crucially involved in attentional processes, e.g., Fan, McCandliss, Fossella, Flombaum, & Posner, 2005). In a similar vein, the authors proposed that the executive attention deficits displayed by their participants may be attributable to (pre)frontal dysfunctions (which are also frequently associated with DD in children; for overviews, see Kaufmann et al., 2011; Peters & De Smedt, 2018). Accordingly, Ashkenazi and Henik (2010) propose that multiple deficiencies at the brain level might cause the multiple cognitive deficits associated with DD.

Neural manifestations of DD in adults

To date, there are only a handful brain-imaging studies investigating number processing in adults with DD.

Early on, Cappelletti and Price (2014) designed an elegant paradigm to investigate whether adults with and without DD display differential behavioural and brain responses when making comparative judgements involving either number semantics or word semantics. Across both domains (i.e., symbolic Arabic numerals or words), the experimental task required participants to compare two simultaneously presented stimuli according to quantity or category. At the brain level, number-related processing yielded comparable fMRI responses in bilateral IPS as well

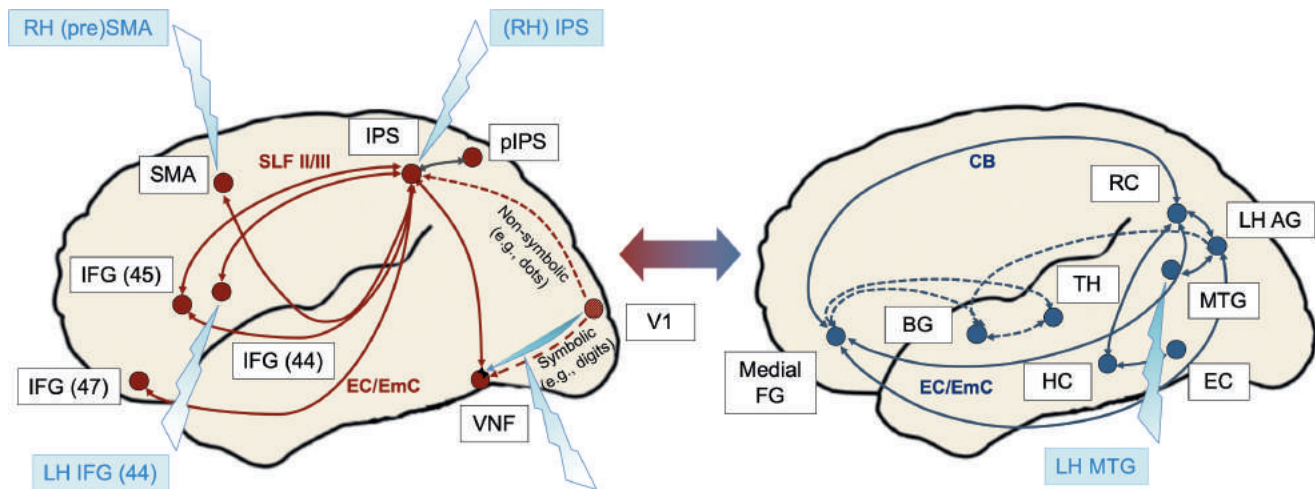


Figure 2. Cortical networks and processing pathways for magnitude-related number processing (left panel, red) and verbally mediated arithmetic fact retrieval (right panel, dark blue) in adults with and without DD. Two anatomically largely distinct networks with dorsal and ventral fiber pathways for magnitude-related processing (left panel) and for arithmetic fact retrieval (right panel) in adults based on the assumptions of the triple code model (TCM, Dehaene & Cohen, 1995, 1997; Dehaene et al., 2003), fMRI meta-analyses (Arsalidou & Taylor, 2011; Arsalidou et al., 2018), diffusion data (Klein et al., 2016) and neuropsychological data on acquired acalculia (for an overview see Willmes & Klein, 2014). The colour-changing arrow between the two panels reflects that these two anatomically separate networks operate together as functionally integrated circuits in numerical cognition. In the left panel, dashed lines depict the object recognition pathways from primary visual cortex to number-specific association cortex: non-symbolic stimuli such as dots are processed and transmitted from V1 along the dorsal path of visual object recognition to the magnitude representation in IPS. Symbolic stimuli such as Arabic digits are processed from V1 along the ventral path to the visual number form (VNF) in fusiform gyrus. In the right panel, dashed lines depict connections that have not been directly documented by fiber tracking so far but can be indirectly inferred from studies on patients with acquired acalculia (for overviews see Claros Salinas, Nuerk & Willmes, 2009; Willmes & Klein, 2014).

Note: The flashes in light blue mark brain structures in which deviations in activity or connectivity were reported for adults with DD. *Abbreviations:* AG – angular gyrus; BG – basal ganglia; CB – callosal bundle; EC/EmC – external/extreme capsule system; EC – entorhinal cortex; HC – hippocampus; LH – left hemisphere; IFG – inferior frontal gyrus; IPS – intraparietal sulcus; Medial FG – medial frontal gyrus; MTG – middle temporal gyrus; pIPS – posterior intraparietal sulcus; RC – retrosplenial cortex; RH – right hemisphere; SLF – superior longitudinal fascicle; SMA – supplementary motor area; V1 – primary visual cortex; VNF – visual number form; TH – thalamus. Numbers in parentheses depict the area according to the Juelich cytoarchitectonic maps (http://www.fz-juelich.de/ime/spm_anatomy_toolbox).

as in the right supramarginal gyrus and the right inferior frontal cortex in adults with and without DD (thus suggesting a fronto-parietal network mediating symbolic number processing). However, adults with DD exhibited stronger activations in the right superior and left inferior frontal gyrus for solving number (but not word) semantic tasks. Most interestingly, and despite comparable response accuracies across groups, adults with DD displayed stronger frontal activations that were associated with quicker response latencies (a pattern which was not found in controls). Consequently, Cappelletti and Price (2014) suggest that (right inferior and left superior) frontal activations in adults with DD might reflect compensatory mechanisms in the presence of inefficient functioning in number-relevant parietal brain regions (for similar views in the developmental literature, see Kaufmann et al., 2011b; Kucian et al., 2006; McCaskey et al., 2017; Peters & De Smedt, 2018). With respect to brain structure, Cappelletti and Price

(2014) conducted voxel-based-morphometry to investigate whether DD in adults might be accompanied by grey matter abnormalities. Despite comparable grey-matter volumes at the whole brain level, group differences emerged in a right parietal region-of-interest analysis (adults with DD displaying significantly reduced grey-matter volumes).

Very recently, Bulthé et al. (2019) employed a multi-method brain imaging approach to assess whether adults with DD have deficient magnitude representations or deficient access to those representations. Notably, functional and structural connectivity methods were combined with uni- and multivariate analyses in this study. Their results showed that (f)MRI responses of adults with DD were clearly distinguishable from those of controls during a non-symbolic magnitude comparison task (i.e., participants had to decide whether an Arabic one-digit number or a dot collection was numerically smaller or larger than 5). Notably, though adults with and without DD achieved

comparable accuracy rates, group differences emerged regarding reaction times (adults with DD being significantly slower; for similar findings, see Cappelletti & Price, 2014) and notation format [longer response times for non-symbolic magnitudes (i.e., dot collections) compared with symbolic magnitudes (i.e., Arabic digits) in adults with DD]. Most interestingly, at the brain level, group differences emerged during non-symbolic (but not symbolic) magnitude judgements in parietal regions (including the IPS) as well as in extra-parietal regions (i.e., superior and inferior frontal gyri as well as temporal regions; however, see Cappelletti & Price, 2014). Neurofunctional parietal deficiencies were interpreted to reflect deficient (non-symbolic) magnitude representations, while extra-parietal activations might be related to domain-general processes involved in accessing these magnitude representations (Bulthé et al., 2019). Moreover, functional (but not structural white-matter) connectivity analyses disclosed hyperconnectivity in temporo-occipital cortex in adults with DD (i.e., between fusiform gyrus and primary visual cortex as well as between inferior occipital cortex and primary visual cortex), most probably reflecting compensatory processes, namely the need for more elaborate processing of complex visual objects (i.e., dot collections in the present study). Hence, Bulthé et al. (2019) interpreted their findings as reflecting a combined deficit encompassing both the representation of (non-symbolic) magnitude knowledge and the access to these representations.

Interestingly, Bulthé et al.'s (2019) failure to find structural brain abnormalities in white-matter connectivity is further corroborated by the findings of Moreau, Wilson, McKay, Nihill and Waldie (2018). They used diffusion tensor imaging (i.e., measures of fractional anisotropy/FA) to investigate fiber tracts previously reported to be related to arithmetic skills (i.e., arcuate fasciculus which is a fiber bundle connecting frontal, temporal and parietal areas; e.g., Catani, Jones, & Ffytche, 2005; Klein, Moeller, Glauche, Weiller & Willmes, 2013, for arithmetic; for a review, see Matejko & Ansari, 2015). Their findings revealed no structural group differences regarding FA in the arcuate fasciculus between adults with and without DD. Thus, the latter result is not fully compatible with a previous study that reported decreasing FA values in the arcuate fasciculus of non-DD children with decreasing math proficiency (van Eimeren, Niogi, McCandliss, Holloway & Ansari, 2008). According to Moreau and colleagues (2018) potential explanations for these contradictory results may include differences regarding participants' age or strategy use as well as methodological differences (related to MRI parameters, such as voxel size and number of directions used for data collection).

In summary, neuroimaging studies so far suggest that adults with DD show abnormalities in grey matter density in right parietal regions, functional hyperconnectivity in

temporo-occipital regions and abnormal functional activation in fronto-parietal regions during number processing. Given the very limited evidence to date, however, those current findings on the neural underpinnings of DD in adults need to be interpreted with caution.

Future research on DD in adults

As the current review shows, research on DD in adults is quite sparse to date. Consequently, our understanding of the cognitive manifestations and neural underpinnings of DD in adults is rather patchy, thus calling for further systematic investigations. Future investigations should aim to (i) elucidate how DD in adults manifests at cognitive/behavioural and brain levels, and (ii) develop and evaluate diagnostic marker tasks (to identify DD in adults) as well as intervention tools (to ameliorate core deficiencies which in turn should enhance occupational opportunities and social wellbeing of affected individuals).

At the cognitive level, future research is needed to further delineate the reported core deficiencies of number-related and domain-general skills in adults with DD. In particular, key questions for future research are (i) whether these deficits can be found in (almost) all adults with DD; (ii) how much each specific deficit is contributing to the deficit and (iii) how much the specific contributions vary between individuals.

At the brain level, a significant issue for studies of adults with DD is that research is focused on the final stage of the disorder. The behaviours observed and its neural substrates may reflect not only the disorder but also the strategies that the individual has adopted during the life course in order to compensate for the underlying weaknesses. Thus, there is an urgent need for further longitudinal and cross-sectional group and single-case studies, provided they are grounded on sound conceptual knowledge and conducted according to the current scientific psychometric standards.

Moreover, future research endeavours should address explicitly the issue of compensation by investigating the role of any deviating, potentially compensatory brain activation in adults with DD. To this end, neurostimulation techniques such as TMS could be used to manipulate brain activity as an independent variable and to investigate its influence on the performance of different cognitive tasks. In combination with results from fMRI studies TMS can be used to identify causal structure-function relations, e.g. by investigating whether areas that were significantly activated during a certain task in an fMRI experiment in one individual make a crucial (possibly causal) contribution to task performance or not. Finally, structural and functional con-

nectivity studies may shed light on the fiber tracts involved in both residual and deficient neurocognitive processes underlying the observed core and associated deficits characterizing DD in adults.

So far, to the best of our knowledge no controlled and systematic intervention studies were reported for adults with DD. In order to develop effective intervention tools, future research should be dedicated to the formulation of a conceptual framework incorporating core deficiencies as well as associated (i.e., number-specific and number-unspecific) processing difficulties. Importantly, without an empirically driven conceptual framework, any intervention efforts remain unscientific and nonreplicable. However, just like in children suffering from DD (e.g., Cohen Kadosh, Dowker, Heine, Kaufmann, & Kucian, 2013), intervention methods are likely to be most effective when directly targeted at the observed cognitive core deficiencies, that may include both number-related (e.g., number magnitude knowledge, enumeration/subitizing, fact retrieval) and number-unspecific / domain-general skills (e.g., attention, working memory). Moreover, like in any other cognitive domain, effective interventions will benefit from incorporating preserved and well-

established skills that may be used to compensate for the observed deficiencies. Thus, any diagnostic assessment should identify cognitive deficits and preserved skills alike. Drawing such a comprehensive picture of the affected individual clearly goes beyond the routine clinical assessment, but would greatly enhance the chance to develop and implement effective and tailored intervention methods that will improve the status of (neuro)cognitive functioning of adults with DD. In turn, this is assumed to ameliorate the occupational situation as well as the social wellbeing of the affected individuals (in our case the adult with DD).

Discussion

The present review was targeted at summarizing the relevant neurocognitive literature on adults with DD. Importantly, research on DD in adults is sparse and, not surprisingly, pure cognitive / behavioural studies by far outweigh brain imaging studies. Nonetheless, we are confident that the current evidence provides a first informative sketch

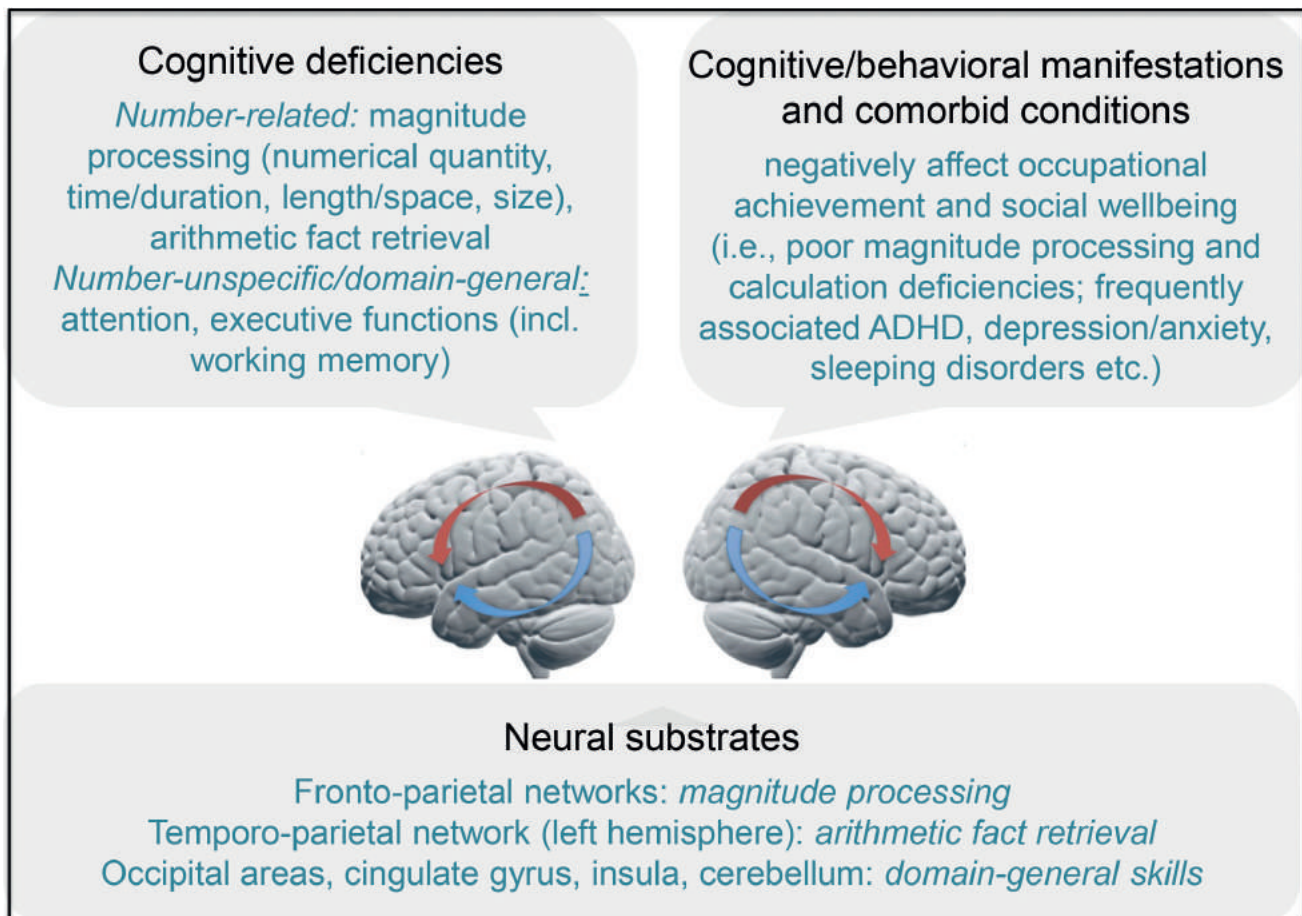


Figure 3. Cognitive characteristics and neural correlates of developmental dyscalculia (DD) in adults: A tentative working model.

that might be used by future studies (i) to formulate more differentiated research questions and working hypotheses, (ii) to develop sensitive diagnostic marker tasks, and (iii) to develop and evaluate effective intervention methods for adults with DD.

Overall, the empirical evidence to date suggests that DD in adults involves both number-specific and number-unspecific (i.e., domain-general) cognitive deficits. As such, number-unspecific dysfunctions were reported regarding attentional processes (i.e., alerting and executive attention: Ashkenazi & Henik, 2010; working memory: Kaufmann et al., 2004) and response latencies (e.g., Bulthé et al., 2019; Kaufmann et al., 2011; possibly, prolonged response times may be number-specific, Cappelletti & Price, 2014). With regards to number-related core deficiencies, the following areas of number processing have so far been reported to be deficient in adults with DD: automatic activation of number magnitude knowledge (Rubinsten & Henik, 2005), enumeration (Gliksman & Henik, 2019), arithmetic fact retrieval (Kaufmann et al., 2004, 2011a) and arithmetic conceptual knowledge (Eckstein, 2016). Furthermore, acknowledging the accumulating empirical evidence for a (partially) shared neurocognitive substrate that supports numerical and non-numerical magnitude processing (Salillas et al., 2019), it is plausible to assume that adults with DD have deficits related to a common magnitude system that includes – beyond their numerical key deficits – also non-numerical magnitude processing deficits including conceptual size (Gliksman & Henik, 2018), time/duration (De Visscher et al., 2018) and length (Ashkenazi & Henik, 2010).

In general, however, neuropsychological and brain imaging findings should be validated by clinical and longitudinal developmental evidence. In particular, the persistent nature of DD (if not detected and treated early-on) may be explained to a considerable part by experiences of chronic failure during the school years. This then – in addition to causing anxiety, avoidance, low self-concept and self-esteem regarding specific skills – may also cause depressive symptoms that account for a low self-concept of general abilities and low educational outcome. In a similar vein, attentional and executive deficiencies in adults with DD may therefore not only be conceptualized as cognitive characteristics of DD, but could also be regarded as secondary deficiencies caused by the increasing executive demands when monitoring and controlling socially blaming cues and regulating uncomfortable emotional and affective inner states.

Limitations of the review

Due to the rather scarce body of scientific evidence related to DD in adults to date, the present review should be

regarded as preliminary. Moreover, it is important to note that it is often difficult to directly compare reported findings from different studies due to methodological differences. In particular, differences across studies exist, among others, with respect to the methods (i.e., experimental tasks, data analyses) and diagnostic criteria used (i.e., DSM-V was released in 2013, and some of the reported studies were conducted before 2013). Notably, DSM-V (APA, 2013) has been the first clinical diagnostic manual acknowledging that DD is a chronic condition that frequently persists into adulthood. Especially with respect to brain imaging studies, the reported findings should be compared and interpreted with caution because of considerable methodological differences across studies (such as employed paradigms, selected statistical thresholds for data analyses, type of data analyses such as whole-brain vs. region-of-interest analyses, quantitative diffusivity measures vs. qualitative fiber tracking etc.). Nonetheless, we believe that the time is ripe to summarize and integrate the reported findings. We hope this review will be helpful and used as a building block (and possibly tentative working model, see Figure 3) for future research that will further elaborate our current – rather patchy – understanding of the cognitive and neural underpinnings of DD in adults.

Relevance for diagnosis and intervention

The present review, which summarizes and integrates the reported findings on DD in adults, may be used as a building block for future research endeavours. As depicted in Figure 3, the present findings suggest a differentiation between number-related and number-unspecific (domain-general) deficiencies characterizing DD in adulthood (at the cognitive and brain level alike). In order to develop sensitive diagnostic marker tasks, future research endeavours should be targeted at identifying neurocognitive core deficiencies of DD in adults. As evident in our review and across the existing literature, DD in adults is an important issue because it has a negative impact on the occupational achievement (i.e., income) and social and emotional well-being of affected individuals. In consequence the urgent need for (currently lacking) conceptually driven and empirically evaluated intervention studies becomes readily apparent.

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