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Development of verbal short-term memory and working memory in children with epilepsy: Developmental delay and impact of time-related variables. A cross-sectional study

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ABSTRACT

While short-term memory (STM) and working memory (WM) are understood as being crucial for learning, and children with epilepsy often experience learning difficulties, little is known about the age-related development of memory span tasks in children with epilepsy. Short-term memory and WM, operationalized as digit span forwards (DSF) or digit span backwards (DSB), respectively, were studied. Participants were 314 children with epilepsy and 327 typically developing children in ages between 5 and 15 years and full scale intelligence quotient (FS-IQ) ≥ 75. Cross-sectional analyses of the data were done with analyses of variance and analyses of covariance ((M)ANCOVAs) and generalized linear analyses. The analyses revealed that STM problems in epilepsy were mediated by age-related gains in WM as well as by differences in IQ. Working memory developed at a quick pace in the younger children, the pace slowed down to some extent in the later primary school years and resumed again later on. Working memory problems prevailed in epilepsy, independent of IQ and development of STM. Timing of the epilepsy in terms of age at onset and duration determined memory development. The youngest children with epilepsy showed age-appropriate development in STM but were the most vulnerable in terms of WM development. Later in the course of the epilepsy, the WM problems of the young children attenuated. In later onset epilepsy, WM problems were smaller but persisted over time.

1. Introduction

Although working memory (WM) is generally recognized to be a system essential for learning [1], and children with epilepsy are known to have cognitive and learning problems [2–4], studies on the development of WM in children in the context of epilepsy are still scarce. Also, little is known about the factors affecting WM development in children with epilepsy.

Verbal short-term memory (STM) is often regarded as a subcomponent of WM [5]. Short-term memory refers to the temporary storage of verbal information. Verbal WM refers to the simultaneous storage and processing of verbal information [6,7]. The difference between the two systems is that, beyond retention, WM implies mental manipulation of the information. In this sense, it is considered an executive function [8]. In contrast to the sheer limited capacity of long-term memory, the capacity of both STM and WM in man is limited.

Individual differences in both STM and WM are important for scholastic achievement like reading and mathematics [9–11]. With its higher processing load, WM is more strongly associated with school learning than STM [1,12]; deficits are associated with learning disabilities [13]. Some evidence even suggests that WM is a more powerful predictor of academic success than IQ ([1], but see [14]). McGrew [15] discussed the possibility that WM may be one of the important abilities *underlying* general intelligence.

1.1. Development of verbal STM and WM

Studies on development of STM and WM in typically developing children and adolescents have found steady increases in capacity over time [11,16,17]. For children aged 6 to 15 years, this increase was found to be linear [11,17], but the rate of growth was likely to decrease from childhood toward late adolescence [18].

1.2. Brain areas involved in WM

A common measure for verbal STM is digit span forwards (DSF). The DSF task requires the repetition of a series of orally presented digits in the order of presentation. Digit span backwards (DSB) is often taken as a measure of WM. On this task, the series of orally presented digits have to be repeated in backward order [1,10,16,17,19]. Both span

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tasks are believed to recruit multiple brain areas. These areas show overlap for both tasks as well as distinct areas recruited only in DSB. Functional Magnetic Resonance Imaging (MRI) studies have shown that the right dorsolateral prefrontal cortex, the right parietal cortex (inferior parietal lobule), the anterior cingulate, as well as the medial occipital cortex are involved in DSF and DSB [20]. In DSB, bilateral involvement of the dorsolateral prefrontal cortex and involvement of the right inferior parietal lobule and Broca's area may also be seen [20]. Structural MRI studies have indicated involvement of the parietal lobe in DSF and involvement of frontal and prefrontal areas, as well as of the left anterior insular cortex in DSB [21]. Overall, the studies suggest involvement of more posterior areas, mainly the parietal areas, in digits forwards tasks and of anterior areas in the more demanding digit backwards tasks [8,18,20,21]. In addition, cortical changes in bilateral prefrontal and posterior parietal regions were seen as children grow older [18].

1.3. STM and WM in children with epilepsy

Children with epilepsy have been reported to have STM and WM problems. On the Wechsler Intelligence Scale for Children - IVth edition (WISC-IV), children with low full scale intelligence quotients (FS-IQs) performed worse on the WM factor, which contains both types of span tasks, than on the verbal or the perceptual factors [22]. Working memory problems were already present early in the course of the epilepsy and were seen to remain stable over time when children were retested several times within a year [23]. Deficits on memory span tasks have been found in children with benign epilepsy with centrotemporal spikes [24], as well as frontal and temporal lobe epilepsy [25,26]; no effect of seizure frequency has been reported [27]. The studies reviewed have included either separate or combined measures for DSF and DSB. Given the differences in STM and in WM, also in terms of brain areas involved, in the present study separate measures of STM and WM were included.

2. Present study

Given the importance of STM and particularly WM for scholastic achievement and given that children with epilepsy have learning disorders [3,4] and changing cognitive patterns over time [28], it is worthwhile to pursue a better understanding *of the development* of STM and WM in children with epilepsy. In addition to age-related changes, STM and WM were studied in relation to demographic and epilepsy variables. The study addressed the following three research questions:

1. Does the development of STM and WM follow the same pattern in children with epilepsy compared with typically developing children? The hypothesis in the present study was that children with epilepsy follow a similar – predominantly linear [11,18] – developmental pattern at a slower pace.
2. To what extent can development of WM be accounted for by the development of STM — and vice versa? Are individual differences the result of differences in intellectual development? While STM is thought of as being less complex than WM, both abilities develop alongside each other [5], and a mutual interaction between STM and WM is proposed in the model on WM [6,29]. Lower IQ in children with epilepsy is a general finding [3,28]. Working memory has been found to be correlated with IQ but could just as well be a factor underlying FS-IQ [15]. From this point of view, low WM would contribute to a low IQ. The hypotheses tested were that STM and WM influence each other's development and that STM and WM are compromised in children with epilepsy, beyond IQ differences.
3. Which demographic and epilepsy-related variables are associated with STM and WM in children with epilepsy? It is hypothesized that children with greater scholastic needs (i.e., children enrolled in special education), from families with lower education [28], would have lower STM and WM capacity. Based on the literature, it was hypothesized that frontal or posterior epilepsy will be associated with STM proficiency and that frontal lobe involvement may negatively impact on WM, but that age-related differences may be seen [18,20]. Based on earlier findings highlighting the impact of time-related variables on cognitive development in children [28], it was also hypothesized that younger age at onset has a more detrimental impact on STM and WM than later onset of epilepsy.

3. Methods

3.1. Participants

Participants were 327 typically developing children and 314 children with epilepsy, between 5 and 15 years of age. The typically developing children had participated in a larger study that aimed to provide national norms for a variety of neuropsychological tests, including STM and WM. They had been tested in regular schools for primary and secondary education in The Netherlands. To ensure that the children belonged to the "typically developing children", together with the informed consent form, parents filled in a query on their child's development; teachers were also consulted on this topic. The typically developing children were enrolled in regular primary and secondary schools and were hence assumed to have normal IQs.

The children with epilepsy were clinically referred for comprehensive neuropsychological evaluation to a tertiary epilepsy center (Epilepsy Institute in the Netherlands Foundation (SEIN)) or its associated school for children with epilepsy because of concerns about their cognitive development. They were included in the study if their FS-IQ on the Wechsler tests was equal or larger than 75 and if data on DSF and DSB were present. Data concerning only IQ patterns on part of these children have been reported earlier by the authors (i.e., [3]). Table 1 shows the numbers of children per age group, mean age, and percentages of boys for the typically developing group and the group with epilepsy.

Comparison of the group of typically developing children with the group of children with epilepsy indicated no difference with a t-test in mean age ($t = -0.17$, $p = 0.865$) and no differences in the proportions of children in each age group (X^2 (8633) = 10.3, $p = 0.240$). A smaller proportion of boys was seen in the group with typically developing children compared with the group with epilepsy (X^2 (1, 640) = 13.62, $p < 0.001$). Therefore, sex was included as a covariate in the analyses.

3.2. Measures

3.2.1. Forward and backward span

The DSF and DSB were taken from the digit span subtest of the Dutch WISC-III^{NL} [30]. Digit span was given to all children. In the DSF task, the child is asked to repeat a series of orally presented digits in the order of presentation. If the child succeeds, the length of the series is progressively increased until the child fails the two presentations in a row of the same length. In DSB, the same procedure is followed, except that the series of digits have to be repeated in reverse order. The lengths of the longest series correctly reproduced forwards and backwards were the measures of interest in the present study. For the second part of the analyses, raw scores were converted into standardized scores for all children based on the normed data from the typically developing control group.

3.2.2. Intelligence

Intelligence was assessed with age-appropriate Wechsler scales, which included either the full Dutch Wechsler Preschool and Primary Scale for Intelligence- III edition (WPPSI-III^{NL}) [31], the full Dutch Wechsler Intelligence Scale for Children - III edition (WISC-III^{NL}) [30], or a 4-subtest short form of the WISC-III^{NL} [32]. The short form was developed for use for the screening of children attending the Child

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