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Behavior and neuroimaging at baseline predict individual response to combined mathematical and working memory training in children

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ABSTRACT

Mathematical performance is highly correlated with several general cognitive abilities, including working memory (WM) capacity. Here we investigated the effect of numerical training using a number-line (NLT), WM training (WMT), or the combination of the two on a composite score of mathematical ability. The aim was to investigate if the combination contributed to the outcome, and determine if baseline performance or neuroimaging predict the magnitude of improvement.

We randomly assigned 308, 6-year-old children to WMT, NLT, WMT + NLT or a control intervention. Overall, there was a significant effect of NLT but not WMT. The WMT + NLT was the only group that improved significantly more than the controls, although the interaction NLTxWM was non-significant. Higher WM and maths performance predicted larger benefits for WMT and NLT, respectively. Neuroimaging at baseline also contributed significant information about training gain. Different individuals showed as much as a three-fold difference in their responses to the same intervention.

These results show that the impact of an intervention is highly dependent on individual characteristics of the child. If differences in responses could be used to optimize the intervention for each child, future interventions could be substantially more effective.

1. Introduction

Academic abilities, like mathematical attainment, are dependent on not only ability-specific training but also general cognitive skills. Mathematical performance is highly correlated with non-verbal reasoning abilities (Geary, 2011), working memory (WM) capacity (Gathercole et al., 2004; Bull et al., 2008; Dumontheil and Klingberg, 2012) and processing speed (Geary, 2011).

Given the close link between cognitive and academic abilities, one would expect that enhancing cognitive capacity through training would also improve academic performance. However, the results to date have been inconsistent with both positive and negative findings (Dahlin, 2011; Dunning et al., 2013; Bergman-Nutley and Klingberg, 2014; Cheng and Mix, 2014; Holmes and Gathercole, 2014; Schwaighofer et al., 2015). In this study, we explored the hypothesis that a combination of content-specific (i.e. mathematics) and WM training (WMT) might provide a greater benefit to improving mathematical ability when they are used in combination than when they are used individually. Key questions for such an approach are what the optimal combination is, and to what extent and for what reasons this differs between individuals. The second aim was thus to find predictors of the training gain. Both psychological testing and neuroimaging could potentially contribute to such predictions. Imaging has previously been used to predict the magnitude of response to a particular intervention (Hoeft et al., 2011; Supekar et al., 2013), but it has never been used to predict the amount of improvement among alternative interventions in children. In this study we try to make a step forward and inquire the differential predictive power of neuroimaging measures for different training types.

The current study included preschool (i.e. 6-year old) children because of the evidence that early academic skills are predictive of later achievements. For example, a meta-analysis of several longitudinal studies showed that mathematical ability at school entry was the best predictor of achievement in mathematics at age 13–15 (Duncan et al., 2007). Similarly, Jordan et al. (2009) measured num-

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ber competency in kindergarten, as well as the growth of number competency from kindergarten to middle of first grade. Both measures explained the achievements in mathematics in third grade, emphasizing the importance of early number competence in order to set the children's learning trajectories. In an evaluation of different aspects of early mathematical ability, performance on the number-line task in 6-year olds predicted the rate of development during the next five years (Geary, 2011). In the same study, cognitive performance, including visuo-spatial working memory, was also a significant predictor of future mathematical achievements. In the light of these previous results aiming at improve mathematical competencies in pre-school children seems to be the most effective ways to achieve stable and long lasting improvement.

In the current training, numbers were always represented using number-line. Addition and subtraction were performed through movements to the right and the left. Number-line training (NLT) was used because the number-line is an important construct in mathematics, and there is a strong tendency to represent numbers along a single spatial dimension (Hubbard et al., 2005; Booth and Siegler, 2008; Fischer et al., 2011). Moreover, this spatial representation is located in the intraparietal cortex (Simon et al., 2002; Cohen Kadosh and Walsh, 2009; Knops et al., 2009; Arsalidou and Taylor, 2011), possibly in areas shared by visuo-spatial representations used in WM tasks (Rotzer et al., 2009; Dumontheil and Klingberg, 2012). There has also been several studies showing that training using the number-line enhance mathematical performance (Kucian et al., 2011; Kaser et al., 2013; Link et al., 2013; Looi et al., 2016).

In order to acquire neural predictors of training-related improvement we chose to use BOLD activity during a WM task and grey matter volume (GMV). In a previous study BOLD signal during a WM task predicted math performance two years later in a developmental sample (Dumontheil and Klingberg, 2012). The use of a WM task for scanning had the additional benefit of providing less variability in behavioral performance within the scanner relative to an arithmetic task, as there is a great variability in number and basic arithmetic operation knowledge in 6 years old. The second measure used for prediction was GMV. It has been repeatedly shown that GMV in the parietal cortices is correlated to mathematical abilities, at least in dyscalculic children (Rotzer et al., 2008), premature born children (Starke et al., 2013), and children born with low weight (Isaacs et al., 2001). Moreover, a recent study found that GMV measured in the parietal cortex when children were in the first grade could predict mathematical performance in second grade (Price et al., 2016).

To investigate these questions, we randomly assigned 6-year-old children to four different combinations of NLT, WMT and reading training (RT). The RT was intended as active comparison training. Our hypothesis was that a combination of WMT and NLT would be more effective than either WM or NLT alone. Statistically, we evaluated the effect of NLT and WMT as well as the interaction between them. The outcome measure in all analyses was a combined measure of mathematical performance. Secondly, our aim was to investigate if the magnitude of the training grain could be predicted by baseline performance in mathematics or WM, or neuroimaging data. We therefore statistically evaluated the interaction between baseline data and type of training on the outcome measures.

2. Materials and methods

2.1. Subjects

The study participants, which included 239 typically developing 6-year-old children and 69 children who were included after screening with measures of WM performance, where subjects with lowest 20% performance on the WM tasks were included. No subjects had neurological or psychiatric diagnosis. To include a large number of children in this study, the project spanned two school-years; 160 of the children participated in the training in 2015 and 147 participated in 2014. Only children who trained for at least 30 days (mean = 38.1, SD = 3.4) were included in the analysis, which included 259 children (210 typically developing and 49 low WM; 132 boys; mean age = 80.3 months, SD = 3.5).

The children included in the behavioral study were invited to participate in the neuroimaging part of the study. Of the 308 children participating in the behavioral study, 62 agreed to participate in the neuroimaging study and 58 completed the neuroimaging protocol. In the analyses, we used an index of the subject's movement in the scanner derived from fMRI acquisition, and only those subjects who completed at least one fMRI run (N = 45) were retained for further analysis. Movement parameters were also used as covariates in the analysis of BOLD signals. The imaging sample included 11 WMT/Read children (3 low WWM) 11 NLT/Read (2 low WM), 10 NLT/WMT (2 low WM) and 13 Read/Read (4 low WM).

2.2. Procedure

Two schools were contacted for the study, and they agreed to participate. A letter was sent to all families with a child attending the respective school. Written informed consent from both caregivers was obtained for all subjects.

Before and after the training period, subjects underwent a set of cognitive tests measuring abilities, including WM and mathematical abilities.

Participants were assigned to one of four training groups and underwent 30 min of training each school day for approximately 8 weeks. After performing a stratification based on a math test (verbal arithmetic WISC), school class and MR-participation, participants were assigned to one of the following groups: 50% WMT and 50% NLT, 50% WMT and 50% Reading, 50% NLT and 50% Reading, or 100% Reading.

The training took place in the classes, during regular school hours, always at the same time of the date, were compatible with regular curricular activity. For each class a teacher was responsible for ensuring the compliance of children with the training regime, and monitors the children during training.

2.3. Training programs

The training program was developed within our lab and is not available for commercial use. The program was designed for 6-year-old children and did not require previous knowledge of math, reading or tablets. The training program automatically logged out after 30 min of training and automatically switched between training programs after 15 min for the groups performing two types of training (e.g., WMT + NLT).

The WMT consisted of four different visuo-spatial working memory tasks. In each task a sequence of spatial positions had to be kept in WM and then reproduced by pointing on the screen. WM training with predominantly visuo-spatial tasks has previously been shown to be effective in increasing WM capacity (Klingberg et al., 2005). WM training using exclusively visuo-spatial tasks has also been shown to be effective in younger children (Thorell et al., 2009; Bergman-Nutley et al., 2011). Furthermore, the NLT was based on using a spatial representation of numbers, as explained in the introduction.

The NLT training consisted of tasks in which children used their index finger to drag along a number-line in order to respond. At the lowest and easiest level, Arabic numbers (e.g. "5") was presented and the child then used a finger to drag out a line from zero to the