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Mapping mental number line in physical space: Vertical and horizontal visual number line orientation in asymptomatic individuals with HIV

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ABSTRACT

Multiple studies have implicated frontostriatal dysfunction in human immunodeficiency virus (HIV) and described cognitive deficits with a focus on executive function and memory. Remarkably little is known about visuospatial and number processing in HIV, though these capacities are also supported by frontostriatal circuits and their parietal connections. We investigated the relation of numerical and spatial cognition in asymptomatic individuals with HIV and explored physical and mental number orientation using several modes of presentation and response: mental number line bisection, physical line bisection, and physical number line orientation on visually-presented horizontal and vertical number lines. The asymptomatic HIV+ group was significantly slower and produced more errors on visuospatial and number processing tasks than the HIV− group ($n = 37$/group). Both groups showed significant correlations between number processing and visuospatial performance. These findings demonstrate that HIV-related brain damage early in the disease course can alter the spatial representation of numerical distance, providing evidence for disruption of frontostriatal circuits and their parietal projections underlying numerical processing in HIV. Besides disease-related effects, this study demonstrates that the physical number line preserves its numerical and spatial integrity in both the vertical and horizontal physical dimensions, as all participants exhibited underestimation of numerical distance, i.e. leftward bias (for horizontal presentation) and downward bias (for vertical). Our results also revealed a dissociation between the processing components of numerical distance and physical space, suggesting differentiation between the neural networks involved in number lines and physical line orientation.

1. Introduction

The human immunodeficiency virus (HIV) crosses the blood–brain barrier and affects the brain early in the course of the disease (Avison et al., 2004; Gray et al., 1996; Power et al., 1993), causing neurochemical changes that alter functioning in selective populations of neurons (Kaul, Garden, & Lipton, 2001; Mattson, Haughey, Nath, & 2005). The neuropsychological and neuroimaging literature suggests that frontostriatal pathology is especially prominent in HIV (Chang et al., 2004, 2001; Ernst, Chang, Jovicich, Ames, & Arnold, 2002; Heaton et al., 1995; Paul, Cohen, & Stern, 2003; Paul et al., 2007). The basal ganglia, in particular, are subject to pathology early in the course of the infection (Berger & Nath, 1997). There is evidence that blood–brain barrier disruption, resulting from direct infection or apoptotic changes in endothelial cells, may increase the viral burden in this region and allow entry of substances that are damaging for basal ganglia (Berger et al., 2000). HIV infection is also associated with tissue loss in frontal and parietal areas (Thompson et al., 2005). Neuroimaging studies of cognitive activation in HIV positive (HIV+) individuals have found increased activation in frontal and parietal cortical regions that are adjacent to those activated by the HIV negative (HIV−) control group (Chang et al., 2004; Chang et al., 2001; Ernst et al., 2002), results that were interpreted in the context of compensatory activation induced by dysfunction of frontostriatal circuits in HIV+ individuals.

Recent neuroimaging studies have reported increased signal change in a cognitively intact HIV+ group compared to the HIV− group in lateral frontal and posterior parietal areas (Castelo, Sherman, Courtney, Melrose, & Stern, 2006). These findings also support the idea that HIV-related brain changes extend beyond the frontostriatal circuits to their parietal projections. Neuropsychological studies of cognition in HIV have shown that asymptomatic HIV+ individuals exhibit cognitive deficits consistent with dysfunction of frontostriatal circuits (Bogdanova, Diaz-Santos, & Cronin-Golomb, 2007; Castelo, Courtney, Melrose, & Stern, 2007; Heaton et al., 1995) and parietal cortical areas (Bogdanova &

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Cronin-Golomb, 2005; Olesen, Schendan, Amick, & Cronin-Golomb, 2007).

Neuropsychological measures of number processing, according to neuroimaging studies, have been linked to bilateral fronto-parietal cortico-subcortical circuits (reviewed in Dehaene, Piazza, Pinel, & Cohen, 2003; Hubbard, Piazza, Pinel, & Dehaene, 2005), including parietal areas that are important for visuospatial processing (Dehaene, Spelke, Pinel, Stanescu, & Tsivkin, 1999). Deficits in number processing and spatial function arise from changes in the cortico-striato-thalamic circuit that includes the basal ganglia, which are subject to pathology early in the course of HIV, and their cortical projection areas, the dorsolateral prefrontal cortex (DLPFC) and the posterior parietal lobes. There has been a recent surge of interest in number processing studies in healthy adults (Gobel, Calabria, Farne, & Rossetti, 2006; Izard & Dehaene, 2008; Longo & Lourenco, 2007) and neglect patients (Cappelletti, Freeman, & Cipolotti, 2007; Doricchi, Guariglia, Gasparini, & Tomaiuolo, 2005; Priftis, Zorzi, Meneghello, Marenzi, & Umilta, 2006; Zorzi, Priftis, Meneghello, Marenzi, & Umilta, 2006), significantly extending our understanding of numerical cognition, in particular mental number line and spatial representation of a number. To our knowledge, there are no published studies assessing numerical cognition in HIV.

In the present study, we used a series of neuropsychological measures to investigate numerical and visuospatial processing in the early asymptomatic stage of HIV. This study examined the relation between numerical distance estimation and spatial orientation in asymptomatic HIV+ individuals.

1.1. Mental number line

Galton (1880) first introduced the concept of the spatial representation of numbers similar to a mental number line. Since then, there have been many behavioral, neuroimaging and lesion studies investigating the mechanisms underlying numerical processing and the abstract concept of a mental number line.

Luria (1945, 1962) demonstrated that lesions to the parietal area lead to number processing deficits based on a disorder of spatial synthesis, or a disturbance of the category of direction of space. When parietal systems of the brain are damaged, the spatial reference system, essential for calculation, is lost. Impairment of the spatial coordinate system with respect to numbers is manifested in the deterioration of a number's decimal structure. With respect to calculation, the impairment of the spatial coordinate system is demonstrated by spatial errors on a mental number line. According to Luria's model, we can expect that parietal lesions would lead to the impairment of the concept of number as well as a specific spatial impairment in number processing.

Restle (1970) suggested that the representation of numbers could be spatially organized along a mental number line, a concept that recently has been expanded and popularized by Dehaene. Dehaene's triple-code model (Dehaene & Cohen, 1997) postulates that a magnitude code is subserved by the parietal lobes, and that numbers are represented as a distribution of activation on an oriented number line. Recent reports suggest that number magnitudes are represented spatially along a continuous analogue mental line, with smaller numbers located to the left and larger numbers to the right of the line (reviewed in Hubbard et al., 2005).

The left-to-right orientation of the mental number line is currently a subject of investigation in the numerical cognition literature. Dehaene, Bossini, and Giraux (1993), and Dehaene, Dupoux, and Mehler (1990) demonstrated the SNARC effect (Spatial Numerical Association of Response Codes), the observation that individuals respond to smaller numbers faster with their left hand, and to larger numbers faster with their right hand. This phenomenon was observed even on a task that did not require processing the magnitude of the number stimuli, such as indicating whether the number was even or odd. The SNARC effect provides further evidence for the spatial nature of mental number representation and suggests left-to-right number organization on a horizontally oriented mental number line.

1.2. Neural mechanisms for mental number line

While exact neural mechanisms involved in number line processing remain unknown, some studies suggest that mental number line orientation relies mostly on parietal areas (Hubbard et al., 2005), whereas others suggest that mental number line orientation relies on spatial working memory mechanisms involving frontal areas (Doricchi et al., 2005). Several studies indicate that numerical quantity judgments, used in mental number bisection tasks, involve activation of the intraparietal sulcus (horizontal segment) bilaterally, the left precentral gyrus, and prefrontal areas (Dehaene, Molko, Cohen, & Wilson, 2004; Dehaene et al., 2003; Walsh, 2003). Repetitive transcranial magnetic stimulation (rTMS) studies provide further insight into the mechanisms of mental number line processing. Gobel et al. (2006) used rTMS over parietal and occipital areas in healthy individuals during a mental number bisection task. Performance during control trials was similar to performance reported in physical line bisection where participants underestimated the midpoint of the numerical interval (that is, exhibited leftward bias). rTMS over the right posterior parietal cortex produced a significant rightward shift of the perceived midpoint of the numerical interval, simulating 'spatial' neglect in healthy subjects. rTMS over the occipital cortex did not produce any effect on bisection performance. The study provided further evidence for spatial representation of a mental number line and for the involvement of the right posterior parietal cortex in the spatial representation of numbers.

1.3. Physical line orientation

Right posterior parietal cortex has been implicated in physical line bisection, a task frequently used in numerical cognition studies. Neuroimaging (Fink et al., 2000) and patient (Doricchi & Angelelli, 1999) studies showed that physical line bisection is associated with processing by the inferior and superior parietal lobes. Additionally, a neuroimaging (fMRI) study of physical line bisection judgment (Landmark task) indicated that processing horizontal and vertical physical lines activates anatomical networks in the right inferior parietal cortex (Fink, Marshall, Weiss, & Zilles, 2001). The study reported no significant interaction between the physical line bisection judgment task and stimulus orientation, suggesting that the activation of inferior parietal cortex during the Landmark task reflects visuospatial judgment irrespective of line orientation.

1.4. Relation between spatial and numerical cognition

The studies of the SNARC effect provided evidence for spatial-numerical interactions (reviewed in Hubbard et al., 2005). Moreover, Caessens, Hommel, Reynvoet, & van der Goten (2004) demonstrated that the SNARC effect or spatial–numerical interaction occurs regardless of input or output modality. This study measured the spatial–numerical interaction without using visual digit presentation. Participants were presented with visual stimuli (arrows, then colors) and were asked to respond verbally with 'one' or 'two'. The automatic activation of numerical information interfered with participants' responses to the orientation of an arrow.

Lesion studies provide additional evidence for the close relation between spatial and numerical domains (Roux, Boetto, Sacko,