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Review article

The search for the number form area: A functional neuroimaging meta-analysis

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ABSTRACT

Recent studies report a putative "number form area" (NFA) in the inferior temporal gyrus (ITG) suggested to be specialized for Arabic numeral processing. However, a number of earlier studies report no such NFA. The reasons for such discrepancies across studies are unclear. To examine evidence for a convergent NFA across studies, we conducted two activation likelihood estimation meta-analyses on 31 and a subset of 20 neuroimaging studies that have contrasted digits with other meaningful symbols. Results suggest the potential existence of an NFA in the right ITG, in addition to a 'symbolic number processing network' comprising bilateral parietal regions, and right-lateralized superior and inferior frontal regions. Critically, convergent localization for the NFA was only evident when contrasts were appropriately controlled for task demands, and does not appear to depend on employing methods designed to overcome fMRI signal dropout in the ITG. Importantly, only five studies had foci within the identified ITG NFA cluster boundary, indicating that more empirical evidence is necessary to determine the true functional specialization and regional specificity of the putative NFA.

1. Introduction

Numbers are one of the most ubiquitous written symbol systems in the modern world. Relative to the 200,000 years of existence of modern humans, the oldest written numeration systems are only approximately 5500 years old (Chrisomalis, 2010). The modern-day digits '0' to '9' of the Hindu-Arabic numeral system are an even more recent invention that were introduced to the Western world as late as the 12th century, and adopted worldwide only several centuries later (Chrisomalis, 2010; Smith and Karpinski, 1911). Despite their relative youth, numbers and the fields of study they enable have allowed the development of astonishing advances in human civilization, from medicine to computing to space travel. The last twenty years have seen a tremendous growth in research on numerical cognition, aimed at understanding how the human brain processes numbers in different formats (i.e., nonsymbolic and symbolic), the quantities they represent, and the mathematical science they support. At the same time, a significant body of research suggests that efficient Arabic numeral processing is an important predictor of children's mathematical skills (Bugden and Ansari, 2011; Defever et al., 2011; Holloway and Ansari, 2009; Lonnemann et al., 2011; Mundy and Gilmore, 2009). However, despite their evident importance, little is known about how the human brain comes to instantiate Arabic numerals as symbols of numerical information. While a number of neuroimaging studies have employed Arabic numerals as stimuli, there is little to no consensus regarding the existence of a neural network specific to the processing of symbolic numbers. A deeper understanding of the 'symbolic number processing network' in typically developing adults is a crucial first step towards understanding its typical and atypical development, and the role it plays in the development of symbolic mathematical skills. The present *meta*-analysis therefore investigates whether across studies and task contexts, there exist common neurocognitive mechanisms that are specialized for Arabic numeral processing, and if so, where those mechanisms are located.

Guiding a substantial amount of research in numerical cognition over the past two decades is the Triple-Code Model (Dehaene, 1992; Dehaene and Cohen, 1995). The neuropsychology-based model posits that numbers are processed in three distinct representations. First, a visual "Arabic number form" code that represents numbers visuospatially as an ordered string of Arabic digits (e.g., '27' as '2' '7' instead of '7' '2'), and is assumed to be subserved by specialized visual object recognition regions in the bilateral ventral occipitotemporal cortex (vOTC; see Fig. 1). Second, a "verbal word frame" code that represents numbers as syntactically structured sequences of words (e.g., 'twenty-seven' or '2 tens 7 ones'), as well as a verbally learned count sequence and arithmetic facts. The verbal code is assumed to be subserved by the

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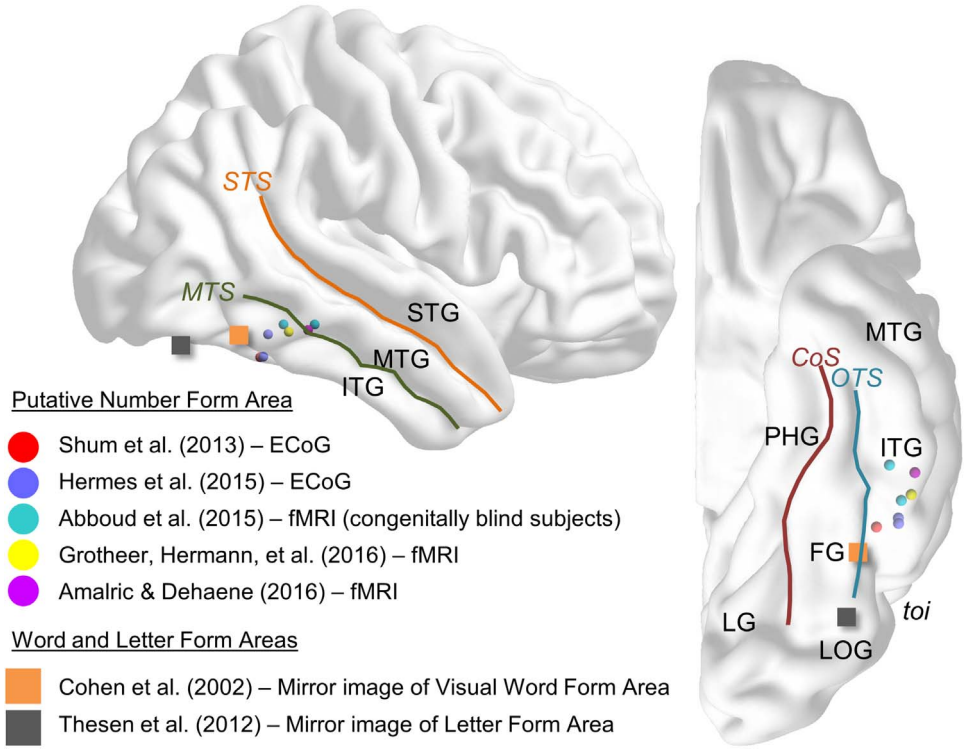

Fig. 1. Anatomy of the lateral temporal and ventral occipitotemporal cortices in the right hemisphere, and illustrations of the putative number form area, as well as mirrored locations of the left-hemispheric visual word form and letter form areas. STG: Superior temporal gyrus. MTG: Middle temporal gyrus. ITG: Inferior temporal gyrus. *STS*: Superior temporal sulcus. *MTS*: Middle temporal sulcus. *OTS*: Occipitotemporal sulcus. *CoS*: Collateral sulcus. *toi*: Temporo-occipital incisure. FG: Fusiform gyrus. PHG: Parahippocampal gyrus. LG: Lingual gyrus. LOG: Lateral occipital gyrus. ECoG: Electrocorticography. fMRI: Functional magnetic resonance imaging. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

left-hemispheric perisylvian language regions extending to the temporoparietal junction, comprising the angular and supramarginal gyri (Dehaene, 1992; Dehaene and Cohen, 1995; Dehaene et al., 2003). Third, an "analogue magnitude" code that allows us to represent, estimate, compare, and manipulate nonsymbolic numerical magnitudes, is assumed to be subserved by the bilateral intraparietal sulci (Dehaene, 1992; Dehaene and Cohen, 1995; Dehaene et al., 2003).

A considerable proportion of numerical cognition research has focused on the magnitude and verbal codes, finding consistent empirical support for neural circuits underlying those two representational codes (for reviews and meta-analyses, see Ansari, 2008; Arsalidou and Taylor, 2011; Cohen Kadosh et al., 2008; Dehaene et al., 2003; Houdé et al., 2010; Kaufmann et al., 2011; Moeller et al., 2015; Sokolowski et al., 2017; Zamarian et al., 2009). In contrast, there has been a paucity of research investigating the visual "Arabic number form" code. Hence, little is currently known about the neural mechanisms that enable the processing of Arabic numerals as visual objects and symbols of numerical magnitude that we use effortlessly to compare and order quantities, and perform arithmetic with.

The proposition of an "Arabic number form" code suggests the existence of a putative 'number form area' (NFA) in a region of the vOTC that is specialized for the processing of Arabic numerals (i.e., it is engaged by Arabic numerals more than other learned written symbols and novel written characters). Such localization for an NFA would be logical, given that there are regions in the human vOTC thought to have evolved for the processing of highly frequent visual stimuli, such as faces and body parts (Kanwisher, 2010). Indeed, there is a large body of evidence for category specificity in the vOTC for visual categories such as faces (Kanwisher et al., 1997) and body parts (Downing et al., 2001), and such functionally specialized regions have also been observed in non-human primates (Tsao et al., 2003; Yovel and Freiwald, 2013). In contrast, relative to the pace of neural evolution in hominids, the 'recent' cultural invention of writing and reading provides insufficient time for specific brain regions to become specialized for visual symbol recognition through the process of natural selection. Nonetheless, the discovery of a putative "visual word form area" (VWFA; see Fig. 1) in the left mid-fusiform gyrus (FG), which has a preferential response to visually presented words versus pseudowords (Cohen et al., 2000, 2002; McCandliss et al., 2003; for a review, see Dehaene and Cohen, 2011) – as well as a less-discussed, and more posteriorly localized "letter form area" (Thesen et al., 2012) – suggests that ontogenetic experience is sufficient to drive specific brain regions to become progressively specialized for processing visual symbols (Dehaene and Cohen, 2007; Kanwisher, 2010). Apart from the broader question of modularity in the brain (Karmiloff-Smith, 2015), the existence of the VWFA has been controversial (see Cohen and Dehaene, 2004; Dehaene and Cohen, 2011; Price and Devlin, 2003, 2011; for the discussion). Moreover, there is increasing evidence that orthographic processing subserved by the VWFA is dependent on higher-level language representations based in left-hemispheric perisylvian language regions (Bouhali et al., 2014; Saygin et al., 2016). This suggests that the VWFA may not be as functionally independent as other category-specific vOTC regions such as the "fusiform face area". As Arabic numerals are also a recent invention relative to the evolution of the human brain, the possibility of an NFA, and its role as an independent functional module ought to be questioned (for a recent discussion see Merkley et al., 2016).

If an NFA does exist, to what extent is the NFA spatially distinct from the VWFA? Neuropsychological evidence thus far has been mixed in its support for distinct visual symbol processing regions. Starrfelt and Behrmann (2011) reviewed neuropsychological studies conducted on pure alexia (i.e., an impaired ability to read but not write) since 1892, and found no consistent evidence for a strong dissociation between number- and letter-reading impairment due to temporal lobe (mainly left) lesions. However, they noted that it could be due to a lack of detailed reporting of assessment methods and findings in many studies,