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What do neuropsychological tests assess?

Alfredo Ardila[a,b] and Feggy Ostrosky[c]

[a]Institute of Linguistics and Intercultural Communication, Sechenov University, Moscow, Russia; [b]Doctoral Program, Albizu University, Miami, FL, USA; [c]Department of Psychology, National Autonomous University of Mexico, Mexico, Mexico

ABSTRACT

Background. Contemporary neuroimaging techniques, particularly fMRI and PET, have demonstrated that cognitive abilities do not strictly depend on specific brain areas, but rather on complex brain circuits or systems.

Methods. Using PubMed and Google Scholar databases, a search for functional studies (fMRI and PET) during the performance of several neuropsychological tests was done. The pattern of brain activity found during the solution of some executive functions, language, memory, calculation, and visuospatial/visuoconstructive abilities is reviewed.

Results. Brain activity supporting the performance in these tests is usually quite extended, and involves not only those brain areas traditionally assumed in neuropsychology, but also other cortical and sometimes subcortical regions.

Conclusions. Most neuropsychological tests are simultaneously evaluating different cognitive abilities associated with the activity of diverse brain areas. "Cognitive/anatomical" correlations could only be established for some relatively simple functions. This change in the understanding about the brain organization of cognition has not been reflected in the interpretation of the neuropsychological tests yet. The interpretation of neuropsychological tests should be based not only in clinical observations but also in functional studies. This is a necessary further step in clinical neuropsychology.

KEYWORDS

Cognitive assessment; fMRI; intellectual tests; neuropsychology

Introduction

Neuropsychological tests were developed from clinical observations, which demonstrated certain cognitive abilities as impaired in cases of focal brain pathologies. For instance, executive functions are impaired in cases of prefrontal damage (e.g., Robbins, 1996), naming is impaired associated with left temporal lesions (e.g., Raymer, Rothi, & Hillis, 2002), and mathematical abilities are disturbed in cases of left posterior parietal damage (e.g., Takayama, Sugishita, Akiguchi, & Kimura, 1994). Departing from these observations, it seems evident to conclude that the prefrontal cortex represents the neuroanatomical substrate of executive function, the left temporal lobe is the neuroanatomical substrate of naming, and the left posterior parietal lobe is the substrate of mathematical abilities. Underlying these conclusions there is the implicit assumption that cognitive abilities can be localized in discrete brain areas (Table 1). This is probably a relatively simplistic idea. As a matter of fact, simple motor and sensory abilities indeed are related to the activity of very specific brain areas (primary motor and sensory areas), but not so with cognitive functions (e.g., Lerch et al., 2017); cognitive functions represent complex functional systems (Luria, 1980) and depend on extended brain circuits.

Toward the end of the 20th and the beginning of the 21st century, a new approach to study the brain's organization of cognition appeared: contemporary neuroimaging techniques, particularly fMRI and PET. These techniques have demonstrated that cognitive abilities do not strictly depend on specific brain areas, but rather they depend on complex brain circuits or systems (e.g., Cabeza & Kingstone, 2006). For instance, executive functions depend on a complex brain system, including not only the frontal lobes, but also the parietal regions, the supplementary motor area, and even subcortical structures (e.g., Ardila & Bernal, 2007; Niendam et al., 2012). Naming represents a complex ability depending upon an extensive circuit, partially different according to the naming characteristics. This circuit includes a diversity of brain areas, not only the temporal, but also the frontal, the parietal, and even the supplementary motor area is involved (e.g., Liljeström et al., 2008). Mathematical abilities represent a multi-component ability, requiring the involvement of multiple brain areas, including Broca's area, prefrontal cortex, inferior and superior parietal lobe, and even the lingual and fusiform gyri (e.g., Rickard et al., 2000).

Thus, neuroimaging studies usually demonstrate a pattern of activation extending beyond those brain areas assumed from the clinical perspective, to be involved in a particular type of cognition. For some neuropsychological tests, however, clinical evidence and functional evidence are quite coincidental. As an example of coincidence from the clinical

CONTACT Alfredo Ardila ardilaalfredo@gmail.com Albizu University, 12230 NW 8th Street, Miami, FL 33182.
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Table 1. Brain areas activated when performing some cognitive tests/tasks.

Domain	test/task	fMRI activation
Executive functions	*WCST*	Lateral prefrontal cortex (bilateral)
		Anterior cingulate cortex
		Inferior and superior parietal lobule
		Ventrolateral prefrontal cortex
		Temporo-parietal area
		Striatum
		Thalamus
	Tower of Hanoi	Left and right prefrontal cortices
		Right superior parietal
		Left inferior frontal gyrus
Language	*Prelexical speech perception*	Superior temporal gyri (bilateral)
	Meaningful speech	Middle and inferior temporal cortex.
	Semantic retrieval	Left angular gyrus and pars orbitalis activation
	Sentence comprehension	Bilateral superior temporal sulci.
	Speech production	Left middle and inferior frontal cortex
		Left anterior insula
		Left putamen
		Pre-SMA, SMA, and motor cortex.
Memory	*Working: n-back task*	Parietal and cingulate cortices
		Insula
		Claustrum
		Cerebellum
		Prefrontal cortex
	Autobiographical	Posterior visual areas (precuneus)
Calculation	*Diverse*	Left posterior parietal lobe
		Intraparietal sulcus
		Inferior frontal lobe
		Dorsolateral prefrontal cortex
		Inferior and superior parietal areas
		Lingual and fusiform gyri
		Occipito-temporal cortices
Visuospatial and visuo-constructive	*Draw-a-clock test*	Posterior parietal cortex bilaterally
		Dorsal premotor area also bilaterally
		Left supplementary motor area
		Left ventral prefrontal cortex
		Left precentral gyrus
		Bilateral cerebellum

and neuroimaging perspectives, in neuropsychology it is assumed that verbal fluency tests are tapping a lexical knowledge ability (depending on the left temporal lobe), and also an executive function ability (depending on the left prefrontal cortex) (Henry & Crawford, 2004). Neuroimaging studies are in general coincidental with these assumptions (Costafreda et al., 2006), even though, the specific pattern of activation may depend on the conditions of the verbal fluency test (Vitali et al., 2005).

Consequently, during the last decades, neuroimaging investigations have demonstrated convincingly that specific cognitive functions are supported by multiple brain regions that comprise functional network systems (Gratton, Nomura, Pérez, & D'Esposito, 2012; Power, Schlaggar, Lessov-Schlaggar, & Petersen, 2013). The cognitive and behavioral consequences of disrupting hypothesized functional networks have also been analyzed by different authors (Carter et al., 2010; Corbetta et al., 2015; He et al., 2007; Nomura et al., 2010; Seeley et al., 2007; Sestieri, Corbetta, Romani, & Shulman, 2011).

Some specific brain networks have been proposed to be crucial in cognition. For example, it has been suggested that three intrinsic connectivity networks (ICNs) may be especially important when studying psychiatric and cognitively impaired patients in task-free resting-state contexts. ICNs consist of structurally and functionally connected brain areas as identified during rest (Menon, 2011). (1) First, the default mode network (DMN), with the medial PFC (including the ventromedial prefrontal cortex [vmPFC] and ventral anterior cingulate cortex [vACC]), hippocampus, and posterior cingulate cortex (PCC)/precuneus as its core nodes, has been associated with task-independent internally focused thought, and autobiographical memory (Greicius, Krasnow, Reiss, & Menon, 2003). (2) The salience network [SN], with the dorsal anterior cingulate cortex [dACC], anterior insula [AI], and amygdala as its core nodes, is involved in detection of and directing attention to biologically salient stimuli in the environment. Finally, (3) the central executive network [CEN] consists of the dorsolateral prefrontal cortex and lateral parietal regions, and is associated with memory processes and goal-directed behavior, such as decision-making and planning (Seeley et al., 2007). Typically, the DMN is activated during rest and disengaged during task performance (Greicius et al., 2003). It has been suggested that the SN (especially the AI) mediates between the DMN and CEN, determining whether one should focus on external, biologically relevant information, or can engage in internally focused thought (Sridharan, Levitin, & Menon, 2008).

In this paper, the current evidence of neurological systems involved in some major cognitive tests will be reviewed. The following five domains will be considered: executive functions, language, memory, calculation abilities,

and finally visuospatial and visuo-constructive abilities. In each domain, only those tests clearly analyzed from the neuroimaging perspective will be selected. Unfortunately, for many neuropsychology tests, no fMRI or any other functional information is available. Finally, some general conclusions will be presented.

Methods

The pattern of brain activity found during the performance of some executive functions, language, memory, calculation, and visuospatial/visuoconstructive abilities was reviewed. Although "calculation" does not necessarily represents a basic cognitive domain, it was entered in this paper because it can be regarded as a particularly complex type of cognition, including not only numerical abilities, but also language, memory, executive functions, and other abilities (Ardila & Rosselli, 2002; Cappelletti & Cipolotti, 2010).

The following procedure was used in selecting the studies reviewed in this paper:

- Two databases were used: Google Scholar and PubMed. Initially the search was done in Google Scholar and later it was repeated using PubMed.
- Considering that functional studies have been developed only during the late 20th and early 21st century, no time limit was used.
- Several neuropsychological domains were reviewed: executive functions, language, memory, calculation, and visuospatial/visuoconstructive abilities. These areas were selected because – excepting calculation – they represent basic neuropsychological domains.
- For executive functions a search was performed for the following two tests: Wisconsin Card Sorting Test (WCST), and Tower of Hanoi. There is a diversity of tests assessing executive functions (e.g., Category Test, n-back working memory test, Stroop test, diverse controlled attention tests, Similarities, Matrix Reasoning, solving numerical problems, phonological verbal fluency, etc.). These two test were selected because they represent widely used concept formation (WCST), and non-verbal problem solving/planning (Tower of Hanoi) tests. The search words were "fMRI" and "WCST"; "fMRI" and "Tower of Hanoi".
- The same procedure was repeated using "PET". For instance, "Wisconsin Card Sorting Test" and "PET".
- For the WCST not only a significant number of articles was found, but also an extensive review paper (Nyhus & Barceló, 2009) and a meta-analysis (Buchsbaum, Greer, Chang, & Berman, 2005). In the current paper, the analysis of the brain areas involved in the WCST solution was based in these two major integrative papers.
- For the Tower of Hanoi only two papers were found, both using fMRI. None was found using PET.
- Language is a complex domain and many papers were found approaching different language abilities: naming, understanding, repetition, etc. Two major review papers (Price, 2010, 2012) based in both fMRI and PET, as well as a meta-analytic study (Ardila, Bernal, & Rosselli, 2016) were used to describe the brain areas involved in language.
- Considering the complexity of memory, only two types of memory were analyzed: working memory and autobiographical memory. Only one working memory test was selected – the n-back working memory task – because there is an extensive and up-dated meta-analysis of this test (Yaple, Stevens, & Arsalidou, 2019). A recent paper examining autobiographical memory was also included (Mazzoni et al., 2019).
- When using the words "calculation" and "fMRI" 21 papers were found. When using "calculation" and "PET" 16 paper were retrieved. Four illustrative studies are described. Nonetheless, "calculation" is not always considered as an independent cognitive domain. It was included in the current paper as an illustration of a complex type of cognition, involving both verbal and non-verbal abilities.
- As an example of visuo-spatial and visuo-construtive abilities, the "Draw-A-Clock Test" was selected. A single paper has specifically analyzed the brain activity using fMRI when drawing a clock. Two PET studies were also found, but they referred to Alzheimer's disease, not to normal population.

Executive functions

The Wisconsin Card Sorting Test (WCST) and the Tower of Hanoi are regarded as two major executive functions tests.

Wcst

The WCST represents one of the most popular neuropsychological tests. It was created by Grant and Berg (1948) as a procedure to assess abstraction and concept formation abilities, and during the following years it was frequently used in cognitive psychology research. Later, Milner (1963) began to use it with brain damaged patients as an instrument to evaluate prefrontal dysfunction. Heaton (1981; Heaton, Chelune, Talley, Kay, & Curtis, 1993) developed a shortened version that is currently the most frequent version used in neuropsychological assessment (Lezak, Howieson, Loring, & Fischer, 2004).

It is usually accepted that the WCST performance is impaired in cases of frontal lobe pathology (e.g., Goldstein, Obrzut, John, Ledakis, & Armstrong, 2004; Stuss et al., 2000). Nonetheless, there are reports indicating that the WCST performance is also affected by non-prefrontal lesions (e.g., Mukhopadhyay et al., 2007; Van den Broek, Bradshaw, & Szabadi, 1993), indicating that the WCST is not only sensitive to prefrontal pathology, but can also be impaired in non-frontal pathology.

Many neuroimaging studies have analyzed the pattern of brain activation when answering the WCST (for an extensive review, see Nyhus & Barceló, 2009). Usually, an increase in activity is found in the prefrontal cortex, particularly the dorsal prefrontal area (e.g., González-Hernández et al., 2002;

Monchi, Petrides, Petre, Worsley, & Dagher, 2001) and sporadically in the ventrolateral prefrontal cortex (Lie, Specht, Marshall, & Fink, 2006) either left (e.g., Konishi, Jimura, Asari, & Miyashita, 2003) or right (e.g., Rogers, Andrews, Grasby, Brooks, & Robbins, 2000). Nonetheless, brain activation when answering the WCST is not limited to the frontal lobes. Activation of the following brain areas have been reported: inferior parietal lobe (e.g., Gonzalez-Hernandez et al., 2003), visual cortex (e.g., Rogers et al., 2000), temporo-parietal area (Barceló, Escera, Corral, & Periañez, 2006), and even the thalamus (e.g., Monchi et al., 2001).

Buchsbaum et al. (2005) developed a meta-analysis of neuroimaging studies of the WCST. Results revealed an extensive frontoparietal activation pattern. Answering the WCST was associated with extensive bilateral clusters of activity particularly in the lateral prefrontal cortex, anterior cingulate cortex, and inferior parietal lobule. Lie et al. (2006) used fMRI to decompose the neural processes underlying the WCST. They observed an extensive neural network underlying WCST performance, including frontoparietal regions and the striatum. Further analysis disclosed that, within this network, right ventrolateral prefrontal cortex was related to simple working memory operations, whereas right dorsolateral prefrontal cortex related to more complex/manipulative working memory operations. The rostral anterior cingulate cortex and the temporoparietal junction bilaterally represented an attentional network for error detection. Non-frontal activations were also found related to the cerebellum, and superior parietal cortex.

After reviewing a significant number of functional studies, Nyhus & Barceló (2009) concluded that neuroimagining research demonstrate activation in an extensive brain circuit when solving the WCST. A significant activation is observed not only in frontal but also in non-frontal areas. Consequently, the WCST can be considered as a multifactorial test, based in the activity of an extensive neural network (Stuss et al., 2000).

Tower of Hanoi

The Tower of Hanoi is frequently considered as a test especially sensitive to frontal lobe pathology (Goel & Grafman, 1995; Roberts, Hager, & Heron, 1994). From the functional point of view, two major papers have analyzed the pattern of brain activation during the solution of the Tower of Hanoi.

Newman, Carpenter, Varma, & Just (2003) using a graded fMRI paradigm compared the brain activation during the solution of the Tower of Hanoi with varying levels of difficulty: easy (1 and 2 moves), moderate (3 and 4 moves) and difficult (5 and 6 moves). fMRI analyses focused on measuring the modulation of the volume of activation from four regions of interest (ROIs): left and right superior parietal and dorsolateral prefrontal cortex. It was found that: (1) both the left and right prefrontal cortices were equally involved during the solution of moderate and difficult problems, while the activation on the right prefrontal area was differentially attenuated during the solution of the easy problems. (2) The level of activation observed in the right prefrontal cortex was significantly correlated with individual differences in working memory. (3) Different patterns of functional connectivity were observed in the left and right prefrontal cortices. Analysis of the parietal lobe activity also demonstrated left/right differences; only the left superior parietal region revealed an effect of difficulty. The authors suggested that: (1) the right prefrontal area probably participates in the generation of a plan, whereas the left prefrontal area may be especially involved in plan execution; and (2) the right superior parietal region is more involved in attention processes while the left homolog is more of a visuo-spatial workspace.

Fincham, Carter, Van Veen, Stenger, & Anderson (2002) used an adaptation of the Tower of Hanoi and recorded fMRI activity. Participants were trained in applying a specific strategy to an isomorph of the five-disk Tower of Hanoi task. After training, participants solved novel problems during event-related functional MRI. The procedure used is described in the following way: "Anatomical scans (36 slices) were acquired by using a standard T1-weighted pulse sequence, with the middle of the 15th slice from the bottom through the AC-PC line. Data from individual subjects were subjected to a between-block subtractive mean normalization. Images were then coregistered to a common reference structural MRI scan by means of a 12-parameter automatic algorithm AIR and smoothed with an 8-mm full-width half-maximum three-dimensional Gaussian filter to accommodate individual differences in anatomy" (page 3348). Regions showing the parametric relationship comprised a frontoparietal system and include right dorsolateral prefrontal cortex [Brodmann area (BA 9)], bilateral parietal (BA 40/7), and bilateral premotor (BA 6) areas. Regions preferentially engaged only during goal-intensive processing include left inferior frontal gyrus (BA 44).

The conclusion is evident: the Tower of Hanoi is not only a test supported by prefrontal activity, but also the parietal lobe activity. In other words, it is not only a frontal but also parietal lobe test. It is not just an executive test (planning, anticipating, etc.), but also a visuo-spatial, attentional, and even verbally mediated test.

Language

Several papers have integrated the fMRI information about the brain areas involved in language (e.g., Ardila et al., 2016; Price, 2010, 2012). Different levels of the language can be distinguished: phonetic, phonemic, lexical, semantic, grammatical, and pragmatic. Also, different linguistic abilities or operations included in neuropsychological tests can be recognized, usually: comprehension, production, repetition, and naming. Thus, language is a particularly complex type of cognition, and language assessment requires diverse strategies.

Price (2010) reviewed 100 fMRI studies of speech comprehension and production, published in 2009. It was found that activation is reported for a diversity of language abilities levels. First, prelexical speech perception resulted in bilateral activation of the superior temporal gyri; where meaningful speech was associated with an increase in activity in middle

and inferior temporal cortex. Furthermore, semantic retrieval was related with the left angular gyrus and pars orbitalis activation; and sentence comprehension resulted in an increased activity in bilateral superior temporal sulci. Interestingly, speech production activates the same brain regions found in speech comprehension. Activation of those brain regions were found in: word retrieval observed in left middle frontal cortex, articulatory planning found in the left anterior insula, and the initiation and execution of speech several brain areas were also activated including left putamen, pre-SMA, SMA, and motor cortex.

In a later paper, Price (2012) presents a summary of the PET and MRI research developed during the last decades, approaching speech perception, speech production and reading. The conclusions of many hundreds of studies were considered, grouped according to the type of processing, and reported in the order that they were published. The author presents an anatomical model summarizing the language areas and the most consistent functions that have been assigned to them. He also makes a further distinction between processes that are localized to specific brain areas (sensory and motor processing) and processes based in multiple functions.

Some general conclusions found in this extensive review paper include: speech comprehension, where many left hemisphere areas participate in accessing semantics from auditory speech and other stimuli, including the anterior temporal areas, posterior temporal areas, ventral inferior frontal areas dorsal superior frontal. The angular gyri (participate in cross-modal integration of semantic features while more medial parietal areas (precuneus and posterior cingulate) are more involved for narrative than single word comprehension. Covert articulatory planning has been associated with activation in the ventral pars opercularis and the ventral premotor cortex. Covert articulation also activates areas that are engaged by other motor modalities (e.g., fingers); for example, the left dorsal pars opercularis associated with motor sequencing and the bilateral premotor cortex. Producing the sounds of speech involves more than sensorimotor activity in the pre- and post-central regions that control the orofacial muscles. It also involves activation related to laryngeal activity, phonation and the voluntary control of breathing.

Ardila et al. (2016) departing from several meta-analytic studies of fMRI proposed here that there are two different language networks in the brain: (1) a language reception/understanding system involved in word recognition (Brodmann area –BA21, BA22, BA41 and BA42), and language associations (associating words with other information: BA20, BA38, BA39, BA40); (2) a language production system (BA44, BA45, and also BA46, BA47, partially BA6-mainly its mesial supplementary motor area-and extending toward the basal ganglia and the thalamus). Additionally, they proposed that the insula (BA13) plays a certain coordinating role in interconnecting these two brain language systems.

The general conclusion is that both language understanding and language production are based in an extensive brain system extending far beyond the classical language areas.

Memory

Memory represents a particularly complex cognitive domain. Only two types of memory will be analyzed: working memory and autobiographical memory.

Working memory

Working memory is a fundamental cognitive ability that holds and manipulates information in mind for a short period of time. One of the most popular measures of working memory is the n-back task (Kirchner, 1958). Numerous fMRI studies have analyzed the n-back task. Behavioral meta-analysis on n-back performance across the lifespan documents significant age-related changes (Bopp & Verhaeghen, 2018). Yaple et al. (2019), presents a meta-analysis that examined concordance and age-related changes across the healthy adult lifespan in brain areas engaged when performing the n-back task. Three age-groups were included: young (23.57 ± 5.63 years), middle-aged (38.13 ± 5.63 years) and older (66.86 ± 5.70 years) adults. Findings showed that the three groups share concordance in the engagement of parietal and cingulate cortices, which have been consistently identified as core areas involved in working memory; as well as the insula, claustrum, and cerebellum, which have not been highlighted as areas involved in working memory. Critically, prefrontal cortex engagement is concordant for young, to a lesser degree for middle-aged adults, and absent in older adults, suggesting a gradual linear decline in concordance of prefrontal cortex engagement.

Autobiographical memory

Regarding memory for personal events, in general, only a handful of events are remembered in detail for each year of life. Two recent case reports, described two people with the exceptional ability to remember in detail almost every day of their life (Parker, Cahill, & McGaugh, 2006; Ally, Hussey, & Donahue, 2013). This rare skill has been called hypermnesia or highly superior autobiographical memory.

Mazzoni et al. (2019), examined functional brain activation in a single case of highly superior autobiographical memory. Results showed that initial access was very fast, did not activate the hippocampus, and involved activation of predominantly posterior visual areas, including the precuneus. These areas typically become active during later stages of elaboration of personal memories rather than during initial access. Elaboration involved a balanced bilateral activation of most of the autobiographical network areas, rather than the more typical shifts observed in people without highly superior autobiographical memory.

Calculation abilities

Calculation is a complex multifactor cognitive domain, including both verbal and spatial abilities. There is a diversity of tests used in the evaluation of calculation abilities,

even though there is not a "standardized" and widely accepted calculation ability neuropsychology test.

Since the initial observations about arithmetical disturbances associated with brain pathology (Henschen, 1920) calculations abilities, have been related to the activity of the left posterior parietal lobe (Takayama et al., 1994). Primary acalculia has been reported associated with left posterior parietal damage (Ardila & Rosselli, 2002; Boller & Grafman, 1983, 1985). Furthermore, it has been pointed out that the intraparietal sulcus represents the crucial area in mathematical knowledge (Dehaene, Molko, Cohen, & Wilson, 2004). This brain area has been observed systematically activated in diverse numerical tests and could represent a core area for the representation of quantities.

Diverse functional studies have approached the analysis of the brain organization of numerical abilities. Rickard et al. (2000) used three different tasks in eight college students while fMRI was recorded: simple arithmetic, numerical magnitude judgment, and a perceptual-motor control task. The procedure used is described in the following way: "MRI images were obtained using a 1.5 T GE Signa (General Electric, Milwaukee, WI, USA) with gradient head coils designed for echo plannar imaging (EPI). An interleaved multislice gradient echo EPI scanning sequence was used to produce 18 axial sections, each 5 or 6 mm thick (depending on the size of the subject's head), with a 64 64 matrix and a 24 cm ®eld of view (repetition time (TR) = 3000 ms, echo time (TE) = 40 ms, \bar ip angle = 908)" (page 317). For the arithmetic task the following brain areas were activated: Brodmann area (BA)44, dorsolateral prefrontal cortex (BA9 and BA10), inferior and superior parietal areas, and lingual and fusiform gyri. Activation was more evident on the left hemisphere for all subjects, but only at BA44 and the parietal cortices. No activation was observed in the arithmetic task in several other areas supposedly involved in arithmetic, including the angular and supramarginal gyri and the basal ganglia. Areas activated by the magnitude task were more variable, but in five subjects included bilateral inferior parietal cortex.

The brain representation of mathematical expressions was analyzed by Maruyama, Pallier, Jobert, Sigman, & Dehaene (2012). They used fMRI and magneto-encephalography (MEG) in adult subjects while they viewed simple strings ranging from randomly arranged characters to mathematical expressions. Bilateral occipito-temporal cortices and right parietal and precentral cortices appeared as the primary nodes for mathematical syntax. A small increase in activation with increasing expression complexity was observed in several areas including the left inferior frontal gyrus and the posterior superior temporal sulcus. The authors suggested that mathematical syntax, although arising historically from language competence becomes "compiled" into visuo-spatial areas in well-trained mathematics students. This proposal is congruent with the idea that mathematical abilities are both, verbal and nonverbal. The involvement of each one may depend on the level of complexity of the arithmetical task.

Amalric and Dehaene (2016) analyzed the brain networks for advanced mathematics in expert mathematicians. The authors scanned professional mathematicians and not experts in mathematics of equal academic level as they evaluated the truth of advanced mathematical and nonmathematical statements. In the first group, mathematical statements, whether in algebra, analysis, topology or geometry, activated bilaterally a specific set of frontal, intraparietal, and ventrolateral temporal regions. These activations spared brain areas related to language. Mathematical judgments were related to the amplification of brain activity at sites that were activated by numbers and formulas in the second group of participants. The results interpreted suggest that high-level mathematical expertise and basic number sense share common roots in a particular nonlinguistic brain network.

The question of complex arithmetic learning was approached by Delazer et al. (2003). Thirteen participants were trained on a set of 18 complex multiplication problems. In a later fMRI session, trained and untrained problems (similar in the level of difficulty to the trained problems) were presented. Left hemispheric activations were dominant in the two contrasts between untrained and trained condition. This observation suggests that arithmetic learning processes are predominantly supported by the left hemisphere. Contrasting the two conditions, the left intraparietal sulcus and the inferior parietal lobule presented significant activations. Another significant activation was observed in the left inferior frontal gyrus. Contrasting trained versus untrained conditions a significant focus of activation was also found in the left angular gyrus. The authors concluded that the left angular gyrus is not only involved in arithmetic tasks requiring simple fact retrieval, but may show significant activations as a result of relatively short training of complex calculation.

Taking together these studies, it can be concluded that arithmetical abilities are based on an extensive brain network, including not only the left parietal lobe, but also the frontal and temporal. Seemingly, the left posterior parietal lobe, and particularly, the intraparietal sulcus represent a major hub for controlling the brain activity involved in solving mathematical operations. Indeed, calculation abilities represent a multifactor skill, including verbal, spatial, memory, body knowledge, and executive function abilities (Ardila & Rosselli, 2002). In addition to the primary acalculia (primary defect in the ability to use the numerical system), a diversity of disturbances associated with language, spatial abilities, and executive functions have been described. It is not surprising that arithmetical difficulties represent an early sign of cognitive decline (Girelli & Delazer, 2001; Rosselli et al., 1998).

Visuospatial and Visuo-Constructive abilities

Only one test will be reviewed: Draw-a-clock test. It will be enough to illustrate the complexity of the brain activity supporting visuospatial and visuo-constructive abilities.

Draw-A-Clock test

The clock-drawing test has become a popular test for screening for cognitive impairment and visuospatial abilities

spatial (Agrell & Dehlin, 1998). It was initially used to assess visuo-constructive abilities (Freedman, Leach, & Kaplan, 1994), but it has been observed to be sensitive to executive dysfunctions (Royall, Cordes, & Polk, 1998).

A single paper has specifically analyzed the brain activity using fMRI when drawing a clock. Ino, Asada, Ito, Kimura, & Fukuyama (2003) selected 18 right-handed volunteers. Participants were required to draw the hands of a clock corresponded to the time presented acoustically. In a control task, participants drew horizontal and vertical lines after reciting silently the numerals of three figures presented acoustically. When comparing the experimental and the control conditions, some specific areas related to clock drawing were found, including the posterior parietal cortex bilaterally but with right dominance, dorsal premotor area also bilaterally, left supplementary motor area, left ventral prefrontal cortex, left precentral gyrus, and bilateral cerebellum. The authors proposed that there was a major brain circuit involved in clock drawing, involving specially the posterior parietal cortex and the dorsal premotor area; these two areas were strongly activated in all the participants.

It is evident that the clock-drawing test involves the participation of multiple brain areas, some of them related with spatial knowledge (right parietal), numerical understanding (left parietal), motor control of the right hand (left precentral gyrus, left supplementary motor area, and cerebellum), and executive functions (left ventral prefrontal cortex). It is understandable that it is impaired in cases of parietal and frontal pathology. It may be considered both, as a visuoconstructive and a visuospatial test, as well as an executive task.

Discussion

Initial neuropsychological tests were developed during the early 20th century and were mostly targeting aphasia assessment (Head, 1926). However, most of the currently used neuropsychological tests (e.g., Boston Diagnostic Aphasia Examination, Wisconsin Card Sorting Test, Rey-Osterrieth Complex Figure, Stroop test, etc.) as well as some major neuropsychological assessment test batteries (e.g., Hastead-Reitan Neuropsychological Battery, Luria-Nebraska Neuropsychological Battery) were developed during the middle 20th century (1930s–1980s). These neuropsychological tests and batteries were created departing from clinical observations of patients with focal brain pathologies, and attempted to correlate certain cognitive disturbances with specific brain-damaged areas. Thus, they implicitly assumed that cognitive abilities could be related to specific brain regions; in other words, they implicitly contained a "localizationist" interpretation of the brain organization of cognition.

The introduction of contemporary neuroimaging techniques, especially fMRI and PET, in a significant extend led to a re-interpretation of the question about the brain organization of cognition. It was observed that the areas involved in any type of cognition were notoriously more extended than it had been assumed departing from clinical observations (e.g., Cabeza & Kingstone, 2006). Evidently, cognitive processes were related not with specific brain areas, but rather with extended brain circuits or systems. However, this change in the interpretation about the brain organization of cognition, has not been reflected in the interpretation of the neuropsychological tests yet. This is a necessary further step in clinical neuropsychology.

These observations have significant clinical implications. The interpretation of neuropsychological tests should consider that quite frequently a test is simultaneously assessing different cognitive abilities, and hence, low scores may be due to different fundamental deficits. It becomes advisable to use different tests to evaluate a particular ability; and, by the same token, it may be problematic to assume an impairment based on a single test.

Conclusions

Departing from the above observations, the following conclusions can be proposed:

1. Cognitive domains (e.g., executive functions, language, etc.) are based on extended brain systems, including not only those brain areas traditionally assumed to support that cognitive domain (e.g., the prefrontal cortex for executive functions, the perisylvian area of the left hemisphere for language, etc.) but usually some other cortical and sometimes subcortical areas.
2. Most neuropsychological tests are simultaneously assessing several cognitive abilities. For instance, it can be assumed that the Boston Naming Test (Kaplan & Goodglass, 1983) requires not only some lexical knowledge (vocabulary retrieval), but also visuoperceptual, and attention abilities. These three abilities are associated with different brain areas and systems.
3. "Cognitive/anatomical" correlations could potentially be established for some relatively simple functions, such as phoneme discrimination. Complex functions, such as language understanding, memory, or executive functions depend upon extensive brain systems involving diverse cortical and frequently also subcortical brain regions.
4. The interpretation of neuropsychological tests should be based not only in clinical observations but also in functional studies.

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