Broad domain generality in focal regions of frontal and parietal cortex

Evelina Fedorenko, John Duncan, and Nancy Kanwisher

A striking feature of the human brain is that it contains cortical regions specialized for particular mental tasks, from perceiving visual motion, to recognizing faces, understanding language, and thinking about others’ thoughts. However, an equally striking feature of human cognition is our ability to solve novel problems. Unlike brain regions that respond selectively to specific kinds of information content, a number of frontal and parietal regions are thought to be domain- and process-general: that is, active during a wide variety of demanding cognitive tasks. However, most previous evidence for this functional generality in humans comes from methods that overestimate activation overlap across tasks. Here we present functional MRI evidence from single-subject analyses for broad functional generality of a specific set of brain regions: the same sets of voxels are engaged across tasks ranging from arithmetic to storing information in working memory, to inhibiting irrelevant information. These regions have a specific topography, often lying directly adjacent to domain-specific regions. Thus, in addition to domain-specific brain regions tailored to solve particular problems of longstanding importance to our species, the human brain also contains a set of functionally general regions that plausibly endow us with the cognitive flexibility necessary to solve novel problems.

Multiple-demand system | cognitive control

However, although the neurophysiological evidence from non-human primates is tantalizing, it is not obvious that similar functional generality would be present in humans. Indeed, previous work has established that larger brains are associated with greater functional differentiation of brain regions (e.g., refs. 13–15; see ref. 16 for a recent discussion). At present, most evidence in humans comes from studies that rely on traditional group analyses (e.g., refs. 17–19) or metaanalyses of activation peaks pooled across studies (e.g., refs. 20–25). These methods have been shown to overestimate activation overlap across tasks because of inter-subject variability in neuroanatomy (e.g., refs. 26–28). In particular, a group analysis can reveal overlapping activations for two tasks even when these tasks activate distinct, nonoverlapping brain regions in each subject. To overcome these problems, we have designed a method that has specif

Based on previous neuroimaging data, a plausible neural substrate for cognitive flexibility is provided by a specific set of frontal and parietal brain regions—the degree of functional specialization present in the human brain. Prior work has discovered several highly specialized components dedicated to particular mental functions, like face recognition or motion perception. However, our cognitive versatility suggests the additional existence of more general-purpose machinery. Building on prior neuroimaging evidence, along with neurophysiological evidence from non-human primates, we searched for such domain-general brain regions in humans. Seven diverse demanding cognitive tasks produced overlapping activation at the individual-subject level in a number of frontal and parietal brain regions. Thus, human cognition arises from hardware that includes not only specialized components, but also very general-purpose ones that plausibly enable us to solve novel problems.

Significance

One of the oldest debates in cognitive neuroscience concerns the degree of functional specialization present in the human brain. Prior work has discovered several highly specialized components dedicated to particular mental functions, like face recognition or motion perception. However, our cognitive versatility suggests the additional existence of more general-purpose machinery. Building on prior neuroimaging evidence, along with neurophysiological evidence from non-human primates, we searched for such domain-general brain regions in humans. Seven diverse demanding cognitive tasks produced overlapping activation at the individual-subject level in a number of frontal and parietal brain regions. Thus, human cognition arises from hardware that includes not only specialized components, but also very general-purpose ones that plausibly enable us to solve novel problems.

Author contributions: E.F., J.D., and N.K. designed research; E.F. performed research; E.F. analyzed data; and E.F., J.D., and N.K. wrote the paper.

The authors declare no conflict of interest.

Frequently available online through the PNAS open access option.

1To whom correspondence may be addressed. E-mail: evelina9@mit.edu, john.duncan@mrc-cbu.cam.ac.uk, or nkg@mit.edu.

This article contains supporting information online at www.pnas.orglookup/suppl/doi/10.1073/pnas.1315235110/-/DCSupplemental.

www.pnas.org/cgi/doi/10.1073/pnas.1315235110

PNAS Early Edition | 1 of 6
on these initial results to test for the existence of functionally general brain regions more stringently and comprehensively.

To this end, we test the engagement of the MD regions in seven diverse tasks (Fig. 1). Each task has a difficult condition and an easier control condition. To test for activation overlap among these tasks, we first used one contrast as a “localizer” to identify regions in each subject individually that are sensitive to cognitive demand, and then we measured the responses of these functional regions of interest (fROIs) to the other tasks.

The tasks were chosen to vary along several dimensions. First, the tasks differed in the kinds of representations they involved: four tasks [the localizer task, verbal working memory (WM), verbal multisource interference task (vMSTT), and Stroop] used verbal representations, two tasks [math and MSTT] used Arabic numerals, and the spatial WM task used spatial locations. Second, the tasks differed in the kinds of cognitive processes they taxed most strongly: the localizer task required participants to read sequences of nonwords or sentences and to respond to a memory probe at the end of each; WM tasks required keeping sets/sequences of elements in memory for a brief period; the math task required manipulating representations and storing/updating intermediate results; and the two MSIT tasks and Stroop required inhibiting a prepotent response and selecting a task-relevant response. Finally, six tasks required a manual response (a button press), and one task (Stroop) required a vocal response.

Note that these tasks were not designed to be directly comparable to one another, even though they have all been shown to produce behavioral difficulty effects with the hard condition, leading to lower accuracies and longer reaction times (2, 27). As a result, differences among tasks in the magnitude of the overall response or in the size of the hard > easy effect may be hard to interpret. In the present study, we focus on whether a given brain region does or does not show a significantly greater response during the hard compared with the easy condition of each task. Furthermore, these tasks were not designed to test any particular hypotheses about specific functions of any of the MD brain regions (although in the Discussion we briefly relate these data to some existing proposals). What is important about this set of tasks is their diversity in terms of the representations they involve and the mental processes they engage, which provides the critical test of whether the MD regions get engaged by a variety of cognitive tasks.

Results
Consistent with previous findings, traditional group analyses revealed several regions in the frontal and parietal cortices that are robustly activated by the hard > easy contrast across tasks (SI Text, Figs. S1 and S2, and Table S1). In Fig. 2 we show the aggregate representation of these activation maps, highlighting that they contain stable features. In particular, we see activation in the premotor regions of the precentral gyrus, going as far inferiorly as the posterior parts of the inferior frontal gyrus and the nearby anterior insula/frontal operculum, along the middle frontal gyrus, and in and around the intraparietal sulcus. On the dorsomedial frontal surface, we see activation in the SMA and preSMA, and in some of the tasks we additionally observe activation in anterior/mid cingulate cortex (ACC). Furthermore, consistent with previous findings, we see activation in the inferior posterior temporal and adjacent occipital regions, presumably because of the attentional enhancement of visual representations in the more difficult conditions. Finally, we observe activity in the cerebellum, consistent with work implicating some regions of the cerebellum in high-level cognitive functions (e.g., refs. 33–35).

These results are broadly consistent with prior work, but like the prior work leave open the important possibility that activations for different tasks do not in fact overlap at the critical level of individual subjects. In the present paper we test this hypothesis, focusing on the frontal and parietal regions. To do so, we first defined fROIs in each subject by intersecting that subject’s localizer activation (thresholded at $P < 0.001$, uncorrected) with a set of key anatomical ROIs previously implicated (e.g., ref. 20) in domain-general functions (see SI Text and Fig. S3 for a demonstration that similar results obtain when different tasks are used as localizers). The fROI definition procedure adopted here is similar to the group-constrained subject-specific approach recently introduced by Fedorenko et al. (27; see also ref. 36), except that anatomical parcels are used instead of group-level functional parcels to constrain the selection of subject-specific voxels. [A complementary analysis using the group-constrained subject-specific method on the whole brain (27, 36) found the same pattern of results, with no new frontal/parietal functionally general regions.] For all regions, fROIs could be defined in at least 70% of the subjects (and for 11 of 18 regions fROIs could be defined in >80% of the subjects; see Table S2 for details).

Fig. 3 shows the response profiles of the individually defined fROIs across hard and easy conditions for each of the seven tasks (see Table S3 for the statistics). The responses to the localizer task conditions are estimated using independent data (a left-out run not used for fROI definition). Most of the regions show reliable hard > easy effects for all (or six of seven) tasks. Furthermore, at least half of the voxels in these fROIs on average show individually significant hard > easy effects within individual subjects for the other six tasks (Fig. S4). These regions include parts of the precentral gyrus bilaterally, the opercular part of the inferior frontal gyrus (IFG) bilaterally, the right middle frontal gyrus, the SMA bilaterally, the inferior and superior parietal cortex bilaterally, and the insula bilaterally. Three of the regions—the orbital parts of the middle frontal gyrus in the left hemisphere and, to some extent, in the right hemisphere, and the left ACC—show weaker results, with significant hard > easy effects for fewer tasks.

Is this pattern of increased response to greater difficulty across tasks restricted to these regions, or does the brain as a whole show the same pattern? As discussed next, functionally general responses demonstrated above appear to be spatially restricted to the MD system. First, (2; see also 37–38) showed that brain regions sensitive to linguistic stimuli—responding more strongly...
to meaningful and structured stimuli, like sentences, than to various degraded versions of those stimuli (e.g., lists of unconnected words or nonwords)—respond weakly or not at all during the same demanding cognitive tasks examined here. These regions instead appear to require a particular type of stimulus (language) to drive them, much as many high-level visual regions require specific visual information (e.g., ref. 1). Language-responsive regions thus show a very different profile of response from the MD regions identified here, despite often lying immediately adjacent to the MD cortex (30; see Fig. S5 for sample activation maps showing both contrasts).

Second, to test the idea that any large anatomical region—like the ones used in the current analysis—contains a substantial number of voxels that respond more to difficult conditions than to easier conditions across tasks, we performed an analysis using four control regions: bilateral superior and middle temporal pole regions, which have been implicated in a wide range of mental processes (e.g., ref. 39) but are not considered to be part of the MD system. The analysis procedures were identical to those used above, and the results are shown in Fig. S6. Although in each region a little less than half of the subjects have a few localizer-responsive voxels (seven voxels per region per subject on average), (i) the nonwords > sentences effect does not replicate in a left-out run (ts < 1.5), and (ii) these voxels do not show the hard > easy effect for any of the other six tasks (ts < 1.5). These results indicate that it is not the case that any large anatomical region contains voxels with the properties of the MD system. (Note that these results are not simply a result of signal dropout in the temporal poles. For example, the language-responsive portions of the same regions—that is, regions defined by the sentences > nonwords contrast—show highly robust and replicable responses in the left-out run: ts > 3.8, Ps < 0.0005.)

Finally, in addition to the language-responsive regions and regions in the temporal poles discussed above, a set of brain regions that have become known as the “default mode network” (e.g., ref. 40) show a response profile that is essentially the opposite of that exhibited by the regions of the MD system. These regions—which include parts of the medial temporal lobe, parts of the medial prefrontal cortex, the posterior cingulate cortex, and the precuneus—deactivate in response to demanding cognitive tasks.

In summary, the activations reported here and in previous studies—greater responses to more cognitively demanding conditions—albeit extensive, are spatially restricted to a specific set of brain regions: the MD system.

**Discussion**

Using the most stringent method currently available for human fMRI (activation overlap within individual subjects), we found that brain regions throughout the MD system respond across a wide range of demanding cognitive tasks. These results extend previous conclusions about the MD system in three key respects. First, almost all prior claims of functional generality were based on group analyses (e.g., refs. 17–19) or meta-analyses of activation peaks pooled across studies (e.g., refs. 20–25), where apparent activation overlap could have resulted spuriously from data in which each subject individually shows functional segregation (e.g., ref. 28). Extending previous reports focusing on selected parts of the MD system (30–32), the present data show that activation overlap is not an artifact of group averaging, but is present within individual subjects. Second, by testing a large number of tasks varying in both the content and operations invoked, we demonstrate broader functional generality of the MD response than previously shown. Finally, the present study characterizes the spatial topography of the MD system (Fig. 2) and its regional specificity (Figs. S5 and S6), in which abutting regions often show strikingly different profiles.

Taken together, these results provide both the strongest evidence to date for the existence of the MD system in humans, and a richer anatomical and functional characterization of that system. More generally, the present data show that the strikingly domain-specific brain regions that have been characterized over the last 15 y (e.g., ref. 1) are complemented by an extensive system of brain regions exhibiting the diametrically opposite property of broad functional generality.

In the present paper we have focused on the similarity in the functional profiles among the regions of the MD system. However, data in which some functional differentiation exists among these regions, and it remains an important goal for future research to identify such dissociations. We briefly mention a number of recent proposals here. Some proposals have attempted to...
link particular MD regions to specific cognitive functions. For example, Aron et al. (41) have argued for the specific role of the right IFG in inhibitory control (see ref. 42 for a similar proposal with respect to the left IFG). Others (43–45) have argued for a distinction between the ACC, critical in detecting conflict, and the lateral prefrontal cortex, responding to the ACC signal with strengthened cognitive control (cf. 46–47). Still others (48; see 49 and 50 for a related proposal) have hypothesized that an anterior–posterior gradient exists on the lateral surface of the frontal lobes, with the more anterior regions supporting more hierarchically complex operations. A few studies have reported differences between frontal and parietal regions (e.g., refs. 51–55), including differences in the timing of neural activity (e.g., refs. 56 and 57), or between the left and right hemisphere MD regions (e.g., refs. 58–61). Already existing, but often hidden in the variety of methodologies used for the existence of subnetworks within the broader MD system, with the number and functional interpretation of these subnetworks varying across proposals (e.g., refs. 6, 62–70). For example, Dosenbach et al. (62) have proposed that the MD system includes two subsystems: one subserving transient control and the other subserving more sustained control processes. Based on resting-state correlation analyses, Power et al. (66) identified three subnetworks in the cortices previously linked to cognitive control: the dorsal attention network, the fronto-parietal task control network, and the cingulo-opercular (ventral) network (use a combination of two or more MD tasks for localization purposes, to identify the most robust and stable MD voxels.)

Of course, even at the single-subject level, the resolution of fMRI does not come close to that of single-cell recordings in nonhuman primates. Nevertheless, complementing our results, several studies have used multivoxel pattern analyses (86) to show that MD regions code many specific properties of attended stimuli, responses and tasks in the fine-grained patterns of spatial activity (e.g., refs. 32, 87–93). Such results dovetail with analogous findings of widespread, adaptive coding of task-relevant information in single neurons of frontal and parietal cortex (8, 12).

Ever since Gall, Flourens, and Broca, neuroscientists have debated whether the human brain is made up of highly specialized components, each conducting a very specific function, or whether instead each brain region is broadly engaged in a wide range of cognitive tasks. Careful individual-subject–based analyses of fMRI data over the last 15 y have revealed a high degree of functional specificity for at least a few regions of the human brain (1). Here we use similar individual-subject–based analyses of fMRI data to provide strong evidence for the functional generality of a set of regions in the frontal and parietal lobes that are broadly engaged in a wide range of tasks, from mental arithmetic, to holding information in working memory, to filtering and suppressing task-irrelevant information. The evidence presented here for the broad functional generality of these regions comes together with prior evidence for the extreme domain-specificity of other brain regions to paint a rich and fascinating picture of the functional architecture of the human brain: Human cognition is accomplished by the joint efforts of both highly specialized and very general-purpose cognitive and neural mechanisms.

**Materials and Methods**

**Participants.** Forty right-handed participants (28 females) from the Massachusetts Institute of Technology (MIT) and the surrounding community were paid for their participation. All subjects were native speakers of English between the ages of 18 and 50, had normal or corrected-to-normal vision, and were naive as to the purposes of the study. All participants gave informed consent in accordance with the requirements of Internal Review Board at MIT.

**Design.** The tasks included reading sequences of nonwords and sentences and performing a memory-probe task after each (the localizer task), and one or more of the following: an arithmetic task, a spatial and a verbal WM task, two versions of the MSIT (84), and the classic Stroop task (Fig. 1). Each task used a blocked design and included a harder and an easier condition. We used the nonwords > sentences contrast as the localizer contrast because it was present in each of the 40 participants (but see SI Text and Fig. S3 for a demonstration that the results are similar when other contrasts are used as localizers).
Procedure. Each participant was run on the localizer manipulation, and between 13 and 16 participants performed each of the other tasks. In the localizer manipulation, the sequence (A–p) of word pairs presented was pseudo-randomized (no exactly repeating sequence of 100 mm2 and matrix size 96 mm × 96 mm, TR = 2000 ms, and TE = 30 ms. The first 10 s of each run were excluded to allow for steady-state magnetization.

Statistical Analyses. MRI data were analyzed using SPM5 (www.fil.ion.ucl.ac.uk/spm) and custom Matlab scripts (available from http://web.mit.edu/evelina9/ wwwfundoc.html and www.nitrc.org/projects/spm_ss). Each subject’s data were motion-corrected and then normalized in a common brain space (the Montreal Neurological Institute template) and resampled into 2-mm isotropic voxels. Data were then smoothed using a 4-mm Gaussian filter and high-pass filtered (at 200 s). For the individual-subject fROI analyses, we used the wfu_pickatlas tool (95) to create anatomical ROI masks for brain regions within which MD activity has been previously reported (Fig. 3). (For the ACC region, we edited the mask manually to restrict the region to the dorsal part of the anterior cingulate.) We then intersected each anatomical ROI with each subject’s activation map for the localizer contrast (thresholded at P < 0.001, uncorrected), to define each subject’s ROIs. (No spatial contiguity constraints were imposed on these fROIs: any voxel that passed the specified threshold and fell within the boundaries of the anatomical parcel was included in the ROI definition. However, visual examination of the resulting fROIs revealed that for most subjects and regions a fROI took the form of a set of contiguous voxels with occasional small noncontiguous sets nearby.) These regions were defined in each hemisphere separately, for a total of 18 fROIs. To estimate the responses of these fROIs to various conditions, we averaged the responses across the voxels in each individual fROI and then averaged these values across subjects for each region. To estimate the responses to the localizer conditions, we used all but the first run to define the fROIs and the first run to estimate the responses, so that the data used to estimate the effects were always independent of the data used for ROI definition (e.g., refs. 96 and 97).

ACKNOWLEDGMENTS. We thank Michael Behr and Eyal Dechter for help with the experimental scripts and with running the participants; Afonso Nistico-Castañon for help with analyses; Daniel Mitchell for help with creating the interior cingulate control condition; Charles Triantafyllou, Steve Shannon, and Sheeba Arnold for technical support; members of the N.K. laboratory, Saxe laboratory, and Gibson laboratory for helpful discussions; Alex Kell and Jason Fischer for comments on earlier drafts of the manuscript; and the Athinoula A. Martinos Imaging Center at McGovern Institute for Brain Research, Massachusetts Institute of Technology. This research was supported by Eunice Kennedy Shriver National Institute of Child Health and Human Development Award K99HD-057522 (to E.F.); a grant from the Ellison Medical Foundation to N.K. (to N.K. and P. Golland); and by the Medical Research Council (United Kingdom) Intramural Program A060_SPQ10.


