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Perspective

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The brain's action-mode network

Nico U. F. Dosenbach[1,2,3,4,5,6] ✉, Marcus E. Raichle[1,2,4,5,7] & Evan M. Gordon[2]

Abstract

The brain is always intrinsically active, using energy at high rates while cycling through global functional modes. Awake brain modes are tied to corresponding behavioural states. During goal-directed behaviour, the brain enters an action-mode of function. In the action-mode, arousal is heightened, attention is focused externally and action plans are created, converted to goal-directed movements and continuously updated on the basis of relevant feedback, such as pain. Here, we synthesize classical and recent human and animal evidence that the action-mode of the brain is created and maintained by an action-mode network (AMN), which we had previously identified and named the cingulo-opercular network on the basis of its anatomy. We discuss how rather than continuing to name this network anatomically, annotating it functionally as controlling the action-mode of the brain increases its distinctiveness from spatially adjacent networks and accounts for the large variety of the associated functions of an AMN, such as increasing arousal, processing of instructional cues, task general initiation transients, sustained goal maintenance, action planning, sympathetic drive for controlling physiology and internal organs (connectivity to adrenal medulla), and action-relevant bottom–up signals such as physical pain, errors and viscerosensation. In the functional mode continuum of the awake brain, the AMN-generated action-mode sits opposite the default-mode for self-referential, emotional and memory processing, with the default-mode network and AMN counterbalancing each other as yin and yang.

Sections

[1]Department of Neurology, Washington University School of Medicine, St. Louis, MO, USA. [2]Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, MO, USA. [3]Department of Pediatrics, Washington University School of Medicine, St. Louis, MO, USA. [4]Department of Psychological & Brain Sciences, Washington University, St. Louis, MO, USA. [5]Department of Biomedical Engineering, Washington University, St. Louis, MO, USA. [6]Department of Neurosurgery, Washington University School of Medicine, St. Louis, MO, USA. [7]Department of Neuroscience, Washington University School of Medicine, St. Louis, MO, USA. ✉e-mail: ndosenbach@wustl.edu

Introduction

At rest, in the absence of externally oriented, purposeful behaviour, the brain enters the default-mode[1,2], during which it engages in self-referential and emotional processing and recollects prior experiences[3]. Default-mode processing is supported by a dedicated set of brain regions, the default-mode network (DMN)[4,5]. To engage with the environment through goal-directed behaviour, the brain transitions to an action-mode, which is characterized by attenuation of default processes[1,2,6,7], heightened alertness[8,9], extrinsic focus[7,10–13], voluntary purposeful movement[14] and processing of action-relevant feedback, such as physical pain[15] and task errors[16]. Recent studies[17–19] have provided evidence that this action-mode is supported by a circuit we previously identified in 2007 using resting-state functional connectivity (RSFC) and task functional MRI (fMRI), and which we named the cingulo-opercular network (CON) based on its anatomical distribution in the dorsal anterior cingulate cortex (dACC) and anterior insula[7,12,13] (Fig. 1a).

Given our initial limited understanding of CON function, we thus shied away from giving it a functionally descriptive name[7,12,13]. Since then, other functional networks have been described and labelled[19–27], but often inconsistently. Some networks were given multiple names, by different groups, whereas some names are incorrectly applied to multiple distinct networks[28,29]. Anatomical names (such as CON) have worsened the confusion because distinct networks are often found adjacent to each other across multiple lobes of the cerebral cortex[21]. For example, the salience network[22] shares a similar cingulo-opercular anatomical pattern (dACC, anterior insula) with the CON, contributing to frequent and ongoing confusion between the two networks (Box 1). Because the number of networks has expanded, researchers often cannot be certain which one is being discussed from the manuscript text alone without scrutinizing the figures[28]. Thus, ascribing intuitive, unique and easy-to-remember names to functional networks for consistent identification has become urgent.

A well-chosen, functionally descriptive name such as DMN can be specific and informative and, by becoming widely adopted, enable effective science[3]. The functional ascription of a network should accurately distinguish it from all others, but it should not be so narrow that it cannot accommodate additional subfunctions that tend to be discovered in the future. Identifying a name that satisfies these criteria requires sufficient understanding of the distinctive core function of a network, which has yet to be achieved for some of the best documented ones, such as the fronto-parietal network (FPN)[12,30]. Building on lessons learned from the naming success of DMN and the confusion surrounding anatomical labels, the present work synthesizes older evidence with new findings, forcing a functional renaming of the CON into the action-mode network (AMN).

Originally, we had conceptualized the CON as an executive control circuit characterized by task initiation and goal maintenance signals[7,31], which was difficult to reconcile at the time with its many other functions suggested by other research teams[14,22,32–34]. Fortunately, recent human[15,17–19,35–37] and animal data[38–41] shed new light on CON function, which have allowed us to reconcile what previously seemed contradictory. In this Perspective, we review and synthesize a wide range of human (RSFC, task fMRI, lesions, stimulation, electrophysiology), non-human primate (imaging, electrophysiology) and rodent (imaging, electrophysiology, optogenetics) evidence for the involvement of CON in supporting action-mode functions and, thus, reconceptualize it using its functionally derived name, the AMN. First, we discuss how renaming the CON to AMN (Box 1) reduces confusion by articulating its functional distinctiveness from spatially adjacent networks, including the salience, language and fronto-parietal networks. Next, we overview evolving work that substantiates the functional role of the AMN in controlling the action-mode. Last, we synthesize the action-mode of brain function and the regions of the AMN supporting it, elucidating how the action-mode and default-mode are counterbalanced, as evidenced by the push–pull relationship of the AMN with the DMN (Table 1).

Functional network origins

The default-mode network

A 1997 meta-analysis of nine PET studies[1] provided the data for a breakthrough realization: relative to the true resting-state metabolic baseline, a set of brain regions, including the ventromedial prefrontal cortex and precuneus (Fig. 1b), deactivated during goal-directed, outwardly oriented tasks[2,42]. These data sparked the proposal of an organized default-mode of brain function, supported by these brain regions, that is temporarily attenuated during specific goal-directed behaviours[2]. Subsequently, the earliest RSFC studies have identified the same set of task-attenuated brain regions as a coherent network[4,5], fittingly naming it the DMN. Later studies have revealed that the DMN also includes the anterior and middle hippocampus[43] and is active during self-referential memory encoding and retrieval[3,44]. A defining feature of the DMN is its anticorrelation with brain regions commonly activated during allocentric (outwardly oriented), goal-directed tasks[5] (Fig. 1b).

The cingulo-opercular network

Motivated by the PET meta-analyses[1,6] that identified the default-mode of the brain and the network that implements it, a 2006 fMRI study[45] has characterized a set of brain regions with the opposite activation pattern (which we subsequently anatomically named the CON[7]; Fig. 1). Across goal-directed tasks, the dACC, anterior insula (frontal operculum), anterior prefrontal cortex (aPFC) and supramarginal gyrus (SMG) exhibited executive control signals, including transient action initiation[7,31], sustained goal maintenance[7,45] and error-feedback[7,13,16]. Initial RSFC analyses[12,13] have shown that this set of regions also form a coherent functional network. Improved functional connectivity methodology has later revealed that the CON also includes regions in the SMA and lateral premotor cortex; middle and posterior insula; and pars marginalis of the cingulate sulcus, lateral cerebellum, central thalamus and anterior putamen[20,21,46–49] (Fig. 1a).

The original description limited the CON to the dACC, frontal operculum[7], aPFC and SMG[12,13], and it thus partially overlapped with the RSFC-defined task-positive network[5]. Despite strong evidence for the importance of the CON in task execution, it initially seemed most appropriate to give it an anatomically descriptive name[12,13]. Hesitancy existed to assign a functionally descriptive label such as 'executive control network' because other studies examining these brain regions had reported other signals, including salience[22] (Box 1), conflict monitoring[32], pain[33] and motor control (pre-supplementary motor area)[14,34]. Whether these various functions were in overlapping or spatially adjacent brain regions was unclear because the available data had relatively low spatial specificity. At the time, pain and motor signals seemed difficult to square with the conceptualization of the CON as a higher-order top–down control network. We hoped that future work would either reconcile seemingly disparate signals (action control, arousal, pain, motor) under a superseding functional category (Box 2) or subdivide cingulo-opercular regions into distinct functional networks (Box 1), or both.

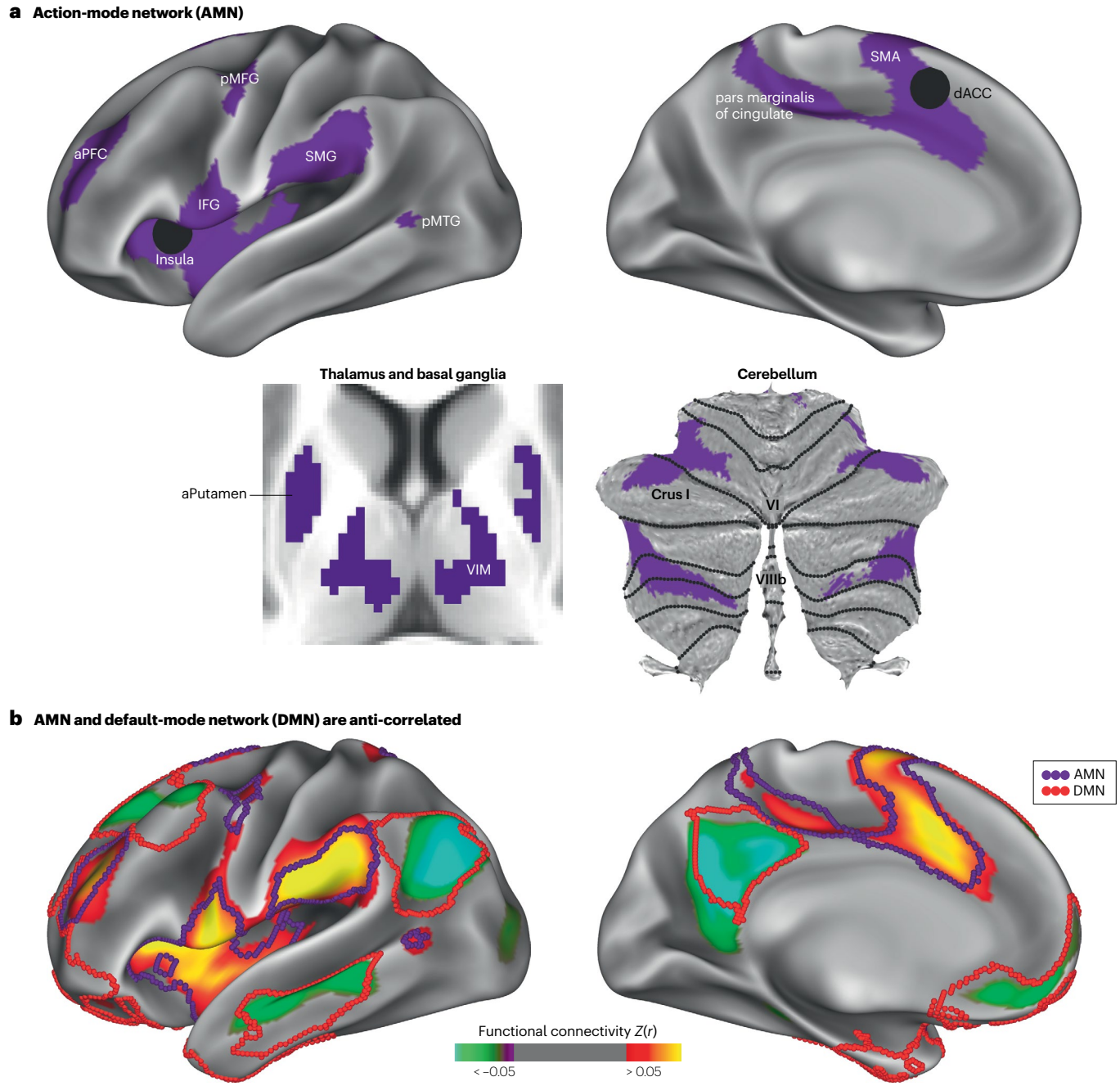
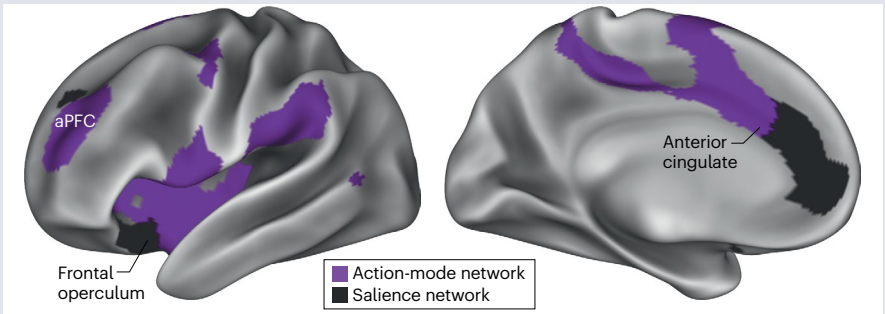


Fig. 1 | Action-mode network. a, The action-mode network (AMN; purple), which we had previously labelled the cingulo-opercular network (CON) because of the prominence of the dorsal anterior cingulate cortex (dACC) and anterior insula (frontal operculum), is also represented in many other cortical and subcortical locations, including the supplementary motor area (SMA), anterior prefrontal cortex (aPFC), supramarginal gyrus (SMG), inferior frontal gyrus (IFG), posterior middle frontal gyrus (pMFG), pars marginalis of the cingulate gyrus, posterior middle temporal gyrus (pMTG), anterior putamen (aPutamen), thalamus (anterior nucleus, centromedian, ventral intermediate (VIM)), and the cerebellum. Black circles indicate core AMN regions first described as the CON in 2006 (ref. 7). **b**, The AMN and default-mode network (DMN) are strongly anticorrelated[5,12]. The AMN regions visualized on the functional connectivity map that have the strongest negative correlations (blue-green) overlap almost perfectly with the DMN. The networks (AMN and DMN) and functional connectivity maps are derived from Adolescent Brain Cognitive Development (ABCD) Study data (see ref. 150 for imaging acquisition details), processed as previously published[147,151]. We derived the AMN and DMN from the group-averaged ABCD functional connectivity matrix following ref. 152, using the Infomap algorithm for community detection[153]. Averaging all columns within the group-averaged functional connectivity matrix corresponding to AMN vertices and/or voxels computed the functional connectivity of the AMN, as in refs. 19,43,55. We used Connectome Workbench V1.5 to visualize the resultant AMN functional connectivity map[148].

Box 1 | Differentiating the cingulo-opercular action-mode and salience networks



In 2007, coinciding with the identification of the cingulo-opercular network (CON; retrospectively functionally annotated as the AMN in the following discussion), Seeley et al.[22] described the salience network based on resting-state functional connectivity (RSFC) and task functional MRI (fMRI) data. Like the AMN, the salience network is most prominently represented in the anterior insula (frontal operculum) and anterior cingulate. Thus, initial uncertainty existed about whether the AMN and salience networks are distinct or merely different labels for the same cingulo-opercular circuit. Improved methods for dividing the whole brain into non-overlapping functional networks using resting-state fMRI data[20,21] made it clear that the AMN and salience were distinct, despite being spatially adjacent (see the figure) — a position upheld by the researchers who first reported these networks[65]. Specifically, the AMN lies more posterior along the cingulate than the salience network and is more superior in the anterior insula (frontal operculum; see the figure, bottom). The AMN also extends into the middle and posterior insula, whereas the salience network does not (see the figure, top). Along the midline, the AMN extends dorsally to premotor and motor regions, whereas the salience network extends to the DMN ventrally (compare figure with Fig. 1b). In the striatum, the salience network has a critical node in the ventral striatum which includes the nucleus accumbens (not shown in figure)[57], which is being evaluated as a deep brain stimulation target in addiction[155–157], whereas the anterior putamen is part of the AMN (Fig. 1a).

Functionally, the action-mode and salience networks both seem important for allostasis, namely anticipating and meeting the requirements for maintaining physiological homeostasis. A defining function of the salience network appears to be the processing and/or prediction of positive (reward) and negative (errors) events, mediated by dopamine signalling, with a focus on social and emotional stimuli[65]. A recent precision functional mapping study, which has used repeated RSFC scans of the same individuals, has revealed that an enlarged salience network in the prefrontal cortex corresponds to an increased risk of depression[75]. In contradistinction, the AMN includes overtly pre-motor (dACC, pre-SMA) and embodied functions, including viscerosensory and visceromotor (middle insula)[158–160] and physical pain processing (posterior insula)[160,161]. The physical adjacency of the salience network to the AMN in the cortex[21], striatum[57] and red nucleus[134] hints at the possibility that its allostatic salience signals could bias adjacent action-mode processes and vice versa[162,163]. Despite their clear and striking differences, the AMN and salience networks are occasionally still confused, misnamed or mistakenly treated as one entity[28]. The AMN and salience network in the figure are derived from Adolescent Brain Cognitive Development (ABCD) Study data (see ref. 150 for imaging acquisition details) and processed as previously published[147,151]. We derived the networks from the group-averaged ABCD functional connectivity matrix following ref. 152, using the Infomap algorithm for community detection[153]. We used Connectome Workbench V1.5 to visualize the networks[148].

aPFC, anterior prefrontal cortex.

Confusion of association cortex network names

Following recognition of the DMN[2,4,5], multiple different research groups have proposed various higher-order cognitive networks within the non-DMN parts of association cortex[12,22–24,50–52]. For largely methodological and data quality reasons, it was initially almost impossible to be confident about whether any given pair of separately named networks might be representing the same brain structure using different names or whether a single network named by one group might converge with several separable networks named by another group. Finally, Yeo et al.[20] and Power et al.[21] published back-to-back functional parcellations in 2011 that used two different advanced network identification methods and two different datasets but converged onto very similar network divisions (Fig. 2). Although these studies have clarified that association cortex outside the DMN is divided into a series of distinct parallel functional networks, much of the confusion surrounding network names persisted.

We now focus on how applying the functional annotation of action-mode to the specific network depicted in Fig. 1a, which is identifiable in every individual, given sufficient fMRI data quality and quantity[19,43,47,48,53–64], clarifies network naming. Thus, in subsequent references to this specific network, we no longer use its original anatomically based name of CON[12,13] but instead use its functionally annotated name of AMN. The salience network[22,65] is clearly a separate entity, but it has a similar cingulo-opercular spatial pattern and has been frequently confused with the AMN (Box 1). The clarified action-mode versus salience functional annotation will help alleviate the prior confusion fuelled by these networks' close spatial adjacency in the anterior cingulate and frontal operculum. Several other previously named networks exhibit partial anatomical overlap and some functional similarity with the AMN, but they extend well beyond the clear anatomical boundaries of the AMN. The cognitive control network[51] is similar in proposed function to our original conceptualization of the AMN (limited to the dACC, frontal operculum, aPFC and SMG) but extends into lateral frontal and parietal regions that are less action-oriented and are clearly separable with RSFC. Defined based on task fMRI contrasts, the multiple-demand system[66] similarly combines the AMN with parts of other fronto-parietal networks. Although the presence of multiple

demands does increase activity in certain AMN nodes, multi-tasking is not required for entering the goal-directed mode. The extrinsic mode network[67,68] is also more extensive than the AMN, extending into fronto-parietal and salience networks.

Yeo et al.[20] and Power et al.[21] have both identified networks that were spatially consistent with the AMN (Fig. 2) but gave them different labels. Yeo et al. have labelled the AMN the ventral-attention network (VAN), positing that it was a previously identified system for bottom–up attentional capture[69]. Reflecting on the inherent difficulties with network annotation based solely on anatomy, Yeo et al. have discussed that this VAN could also be the CON, salience network or both[20]. Power et al. have labelled Yeo's VAN as the CON[21] (Fig. 2), but contributing further confusion, Power et al.'s networks also included a VAN that is a different network than Yeo's VAN. The network referred to as VAN by Power et al. overlaps strongly with language-driven task fMRI activity[25,70] and should be referred to as the language network[27,71]. The language network sits adjacent to the AMN in frontal and superior temporal cortex, but the two are clearly distinct networks[25,27,70,72]. Other higher-order networks with a more fronto-parietal distribution, referred to variably as executive control network[22], central executive network[24], dorsal attention network[23] and FPN[12,30], are more obviously spatially distinct, but a detailed discussion of them is beyond the scope of this article.

The new functional AMN name more clearly distinguishes it from the fronto-parietal, salience and language networks and, thus, eliminates some of the prior naming confusion. Below, we discuss the recent research advances that sufficiently clarified the function of the AMN to beyond the threshold for this naming upgrade. The case for permanently discontinuing the use of CON or other names in favour of AMN is based on animal and human studies using a wide range of experimental approaches.

Evolving evidence for AMN function

AMN is important for motor plasticity

Precision functional mapping (PFM) uses repeated sampling of individuals to improve the signal-to-noise ratio of fMRI data, while improving spatial precision by eschewing group-averaging of data[54,62,73]. PFM, for the first time, enabled the accurate identification of the AMN in individuals[53,54,62], allowing for within-person longitudinal studies and experimental manipulations[17,74,75]. Within-participant motor plasticity studies have revealed that casting-induced disuse of the dominant arm and hand for 2 weeks induced large, replicable functional connectivity changes not only in primary motor cortex but also in the AMN[17,18,35,76], such that connectivity strengthened between the disused upper extremity-specific motor cortex and the AMN. Unaffected other networks important for higher-order motor control suggested a greater and more specific role of the AMN in motor behaviour than previously thought.

Realizing that the AMN is central to rapid motor circuit plasticity led to a re-evaluation of the concept of executive control and its interdependence with goal-directed movement. In retrospect, ample evidence always existed for the involvement of the AMN in pre-motor processes, but, beholden to a false dichotomy between movement and cognition, our research group had ignored it in favour of more abstract functional ascriptions such as executive control. In non-human primates, the cingulate motor areas are critical for hierarchical motor planning, in which goals and intentions are translated to progressively more concrete action plans[14,34,77]; their human homologues are probably located in the dACC portion of the AMN. The output projections of the non-human primate cingulate motor areas are thought to primarily target the SMA, which is also within the human AMN[14,34,77]. The posterior middle frontal gyrus regions of the AMN are typically interspersed between the eye movement controlling frontal and supplementary eye fields, and in macaques, this region has classically been referred to as lateral premotor cortex[78]. In subcortex, the AMN includes the anterior putamen, which is known to receive projections from premotor areas in macaques[79]. Motor nuclei in the central thalamus[48] are also strongly functionally connected to the AMN (Fig. 1a). Regions of the vermis and the lateral anterior and posterior cerebellum[47], with suspected motor control roles, are also part of the AMN.

AMN is interconnected with the somato-cognitive action network

A breakthrough in understanding the function of the AMN came with the recent discovery of the somato-cognitive action network (SCAN), which integrates whole-body physiology, as well as smooth and skeletal muscle movement, with behavioural goals[19]. In the motor circuits of the brain, two parallel systems intertwine in an integrate–isolate pattern: effector-specific regions for isolating fine motor control of the foot, hand and mouth, and the SCAN for integrated action execution. The SCAN's inter-effector nodes not only alternate with effector-specific foot, hand and mouth regions in primary motor cortex but also strongly connect with AMN regions (in SMA and dACC). In addition, the SCAN includes the centromedian nucleus (CM) of the thalamus, the dorsal posterior putamen, and crus VI and VIIIa of the cerebellum (paravermian), all regions wherein the SCAN and the AMN are spatially adjacent. SCAN inter-effectors lack movement specificity[19,37,80] and co-activate during action planning (coordination of hands and feet) and axial body movement (such as of the abdomen or eyebrows)[19]. In macaques, direct cortical stimulation of the SCAN is thought to evoke complex actions[81–85], and animal studies have demonstrated its connectivity to internal organs such as the adrenal medulla[86,87], stomach[88], kidney[89] and heart[90]. Deep brain stimulation (DBS) targets in individuals with Parkinson disease, namely the subthalamic nucleus (STN), globus pallidus pars interna (GPi) and ventral intermediate thalamus (VIM), are part of the SCAN[19,36]. The STN, GPi and VIM show hyperconnectivity to cortical SCAN nodes in individuals with Parkinson disease, which is reduced by successful DBS[36].

A hallmark feature of the SCAN is its strong and specific connectivity to the AMN. The strongest SCAN–AMN inter-connectivity is found

Table 1 | Action-mode versus default-mode functional networks

Functional name	Anatomical name	Global mode	Functional MRI activations	Behavioural state	Attentional focus	Physiology and body	Intrinsic activity	Energy use
Action-mode network	Cingulo-opercular network[12]	Action[39]	Task-positive[7]	Goal-directed[136]	Allocentric[67]	Strive and survive[86]	Ongoing[5]	High[100]
Default-mode network	Medial fronto-parietal network[29]	Default[2]	Task-negative[1]	Rest[4]	Egocentric[3]	Rest and digest[92]	Ongoing[5]	High[100]

Box 2 | Inside–out functional annotation of the action-mode network

Initial failures to recognize the overarching action-mode function of the cingulo-opercular network (CON) were rooted in the 'outside–in' approach to studying the brain[164]. The outside–in approach, which involves searching for the neural correlates (such as task fMRI activations) of a pre-defined psychological concept (such as conflict monitoring), has long been dominant in cognitive neuroscience[32]. Each separate study using this approach typically succeeds in identifying specific brain regions and networks that exhibit signals associated with the psychological concept of interest. However, reconciling findings across studies can be difficult when a single psychological concept (such as cognitive control) is supported by multiple distinct networks, or when multiple psychological concepts map to the same brain region. A striking example of the latter is provided by the dorsal anterior cingulate cortex, anterior insula (frontal operculum) and other regions of the CON, wherein many different types of signals overlap, including executive control[7,12,13,66,165], action initiation[7,14,31], arousal[8,9,92], motor control[34], cognitive conflict[32], error[16] and pain monitoring[15,130] (but not salience[22,65]; see Box 1). Out of all these possibilities, which is the correct functional annotation for the CON? Could it be all of them?

Trying to parcellate the brain according to psychological concepts that are not derived from neurobiology is fraught with difficulty and uncertainty because the various concepts being tested may not be separately represented in the brain with the same divisions as conceived by psychology. An alternative way to examine brain representations of behaviour is the 'inside–out' approach[164], which starts with brain properties (inside) and works towards understanding how they give rise to behaviours (outside). Instead of trying to localize brain networks for executive control or arousal based on task fMRI contrasts, it starts with an RSFC-defined intrinsic network[20,21] (such as the CON) and subsequently seeks to identify its core functions (such as the action-mode), which may or may not yet have names.

Searching for the behavioural correlates of the CON revealed that its seemingly diverse set of functions (arousal, executive control, movement, pain and so on) share the common denominator of being required for typical goal-directed behaviour. Furthermore, both RSFC (anti-correlations; Fig. 1b) and task fMRI data activation patterns (task-positive) suggest that the function of the CON is diametrically opposed to the inwardly oriented DMN. Thus, the term action-mode provides an informative functional label for renaming the CON the action-mode network (AMN) because it encompasses the foundational role of the AMN underlying ethologically relevant goal-directed behaviour and articulates the default-mode's yin-yang relationship with it.

along the dorsal midline in the SMA and posterior dACC, which control voluntary action[14]. The special relationship to the SCAN prompted us to reassess the AMN's arousal[8,9,91,92], pain[15], viscerosensation[93,94] and viscerocontrol signals[90], which we had previously been unable to reconcile with its role in top–down executive control. The SCAN discovery suggested that rather than limiting the role of the AMN in goal-directed behaviour to executive and motor control, that role could be extended to include setting the proper conditions for successful activity, by affecting arousal, body physiology and physical pain processing. In this action-centred framework[19,85,95], the SCAN functions as the actuator of the AMN, implementing goal-directed actions via coordinated skeletal and smooth muscle movement and hormone release (increased sympathetic tone).

Evidence synthesis: action-mode is implemented by the AMN

An action-mode of brain function

The brain accounts for over 20% of human energy expenditure at rest, even though it constitutes only 2% of human body weight[96–98]. Over 90% of this energy supports the intrinsic activity of the brain, which is independent of specific behavioural demands[99,100]. The energy usage of the brain only increases by ~5% over baseline in regions specifically associated with a task (for example, effector-specific motor cortex during a hand movement)[100], in contrast to skeletal muscle which can increase its energy demands by up to 1,800% with exercise[101]. Thus, the brain is always using energy at very high rates because intrinsic brain activity never ceases. What is the purpose of all of this energetically demanding intrinsic activity?

From an evolutionary perspective, the purpose of a nervous system is goal-directed behaviour, typically expressed as safely moving to explore and exploit one's environment[102–104]. Organisms that cannot actively move, such as plants, corals or polyps, do not have brains[105]. Cisek argues that "all aspects of brain function, including thoughts and feelings, must ultimately serve overt action or they would not have been supported by natural selection"[102]. However, in practice, awake animals are not always behaviourally striving, but often spend time resting[38] — a very distinct pattern of behaviour that must be just as critical for survival. Thus, awake behavioural states range from high-arousal, goal-directed to low-arousal, resting states[40] (Table 1). Humans may also spend time in an intermediate medium-arousal behavioural state, linked to abstract thinking and possibly the FPN, but relatively decoupled from both imminent goal-directed action and self-referential processes[106–110].

In simpler, phylogenetically less refined animals, the moving-to-resting behavioural state spectrum maps closely onto the basic functional division of the brain into action and default modes[38,40,102,103]. In the behavioural resting state, the brain enters its default-mode to maintain and update itself through intrinsic processes. When an animal is actively behaving, its brain transitions to the action-mode to achieve allostasis[40,101,111,112] through interaction with the extrinsic environment. The equilibrium between action-mode and default-mode balances current behavioural needs against improved future behaviour readiness and quality. In higher, phylogenetically more refined animals, the default-mode also includes remembering and egocentric imagining, whereas the action-mode also includes decision-making, planning and action-preparation (pre-motor) processes. The default-mode of the brain has been well substantiated, but what about evidence for the action-mode that it seems to alternate with?

In humans, physiological and neuroimaging work strongly supports the existence of an action-mode of function. Initiation of goal-directed behaviour coincides with physiological alertness markers driven by greater sympathetic tone, such as pupillary constriction[91],

brain-wide EEG[113] and fMRI signal changes[7,31,45]. These neurophysiological markers of the action-mode also correlate with improved performance on cognitive and motor tasks[40,113–116]. Physical pain, perhaps the most salient physiological feedback signal, also increases arousal and can interrupt the default in favour of the action-mode[117].

Electrophysiology and imaging studies in rodents also support the existence of an action-mode of brain function. In these studies, the action-mode is most clearly indexed by movement signals[38–40]. During action periods of mouse decision-making, global cortical representation of task engagement is encoded in the activity dynamics of cells and superficial neuropil across the majority of dorsal cortex[39]. Electrophysiological recordings across 267 mouse brain regions during decision tasks have shown that neural responses correlated with task-related motor action almost everywhere in the brain, whereas neural responses to sensory stimuli were restricted to sensory regions[118]. This suggests that neural representations of movement may be linked to a brain-wide change in neural processing during action periods of goal-directed behaviour.

In addition to alternations between extended periods (minutes, hours) of goal-directed behaviour and rest, more rapid arousal fluctuations, on the timescale of seconds (infraslow; 0.01–0.2 Hz), drive cycling along the brain mode continuum between action-mode and default-mode in both humans[119] and mice[120]. These arousal fluctuations are related to variance in goal-directed behavioural performance[121–124], as variability in EEG[123], magnetoencephalogram[125] and event-related fMRI task activations[115] has been linked to intrinsic infraslow fluctuations driving brain-mode alternations. Such mode-related alternations in turn are related to spontaneous changes in arousal at rest[119,120]. In mice, cortex-wide functional networks are embedded within a canonical arousal cycle indexed by increased pupil diameter and locomotion and changes in hippocampal activity[120]. In humans, analyses of the coherence between arousal (pupillometry, vital signs) and RSFC data have revealed that global waves, which are part of the RSFC signal and contribute to the division of the brain into distinct functional networks, are time-locked to spontaneous arousal fluctuations[119]. These arousal-locked global waves are phase shifted across functional networks, such that the AMN is maximally offset from the DMN, sitting at opposite ends of the action-mode to default-mode along the brain-mode continuum[119,126]. Furthermore, infraslow fluctuations can modulate the amplitude of higher-frequency brain activity (1–40 Hz), via phase-amplitude coupling[123,127]. Because the infraslow (0.01–0.2 Hz) fluctuations in spontaneous brain activity are coupled to arousal and performance variability, they may confer a long-term memory and/or skill encoding benefit to offset potential online performance decrements owing to brain mode cycling. The infraslow changes in brain-mode are themselves embedded within blocked, even lower-frequency, brain-mode changes tied to tasks humans are consciously aware of (for example, 'I am reading a manuscript').

The action-mode network

Just as the default-mode of the brain is controlled by the DMN, the action-mode is controlled by a specific set of brain regions in the AMN (Fig. 1). In mice, a region in anterolateral premotor cortex seems critical for entering the action-mode of the brain because optogenetic inhibition abolished both the cortex-wide response to task-initiation cues and the voluntary behaviour[39]. In macaques, neural activity consistent with the initiation and maintenance of the action-mode of the brain has been recorded from the prefrontal cortex across a variety of different tasks[128], and fMRI has revealed that anterior cingulate cortex translates choice values into action[129]. In humans, the cingulo-opercular task-positive regions (Box 2) control the action-mode.

The AMN combines functions for achieving behavioural goals through bodies successfully interacting with the environment. The AMN initiates, maintains and controls a domain-general action-mode of brain function in which many specific behaviours may be performed, from complex mental tasks to physical actions, wherein AMN regions implement all the shared common processes these actions require.

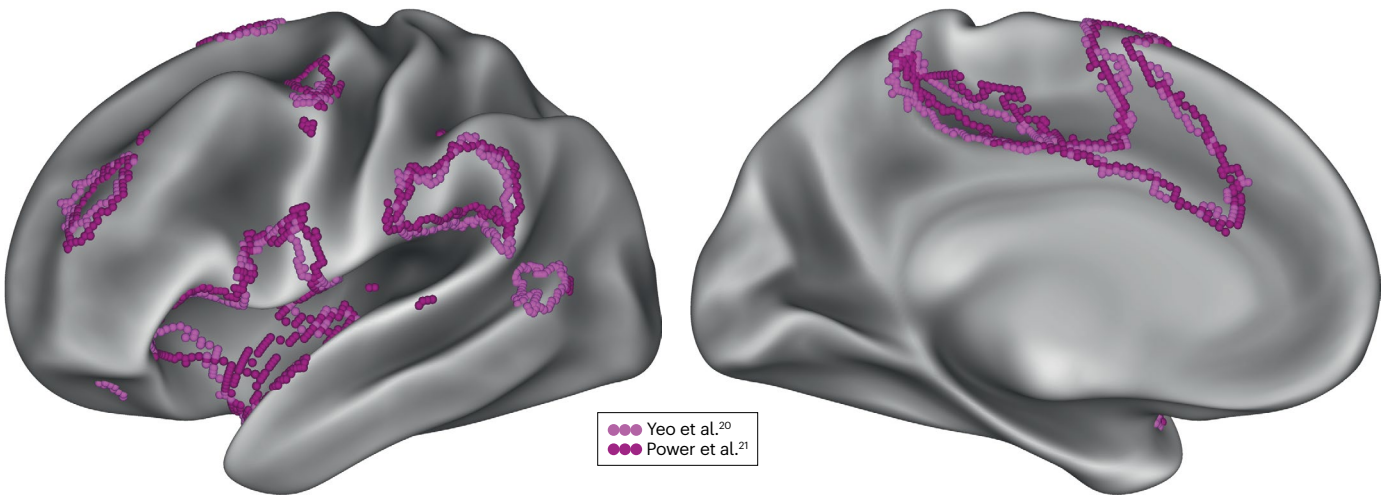


Fig. 2 | Action-mode network (AMN) anatomy is consistent across datasets and analysis pipelines. A pair of back-to-back landmark studies in 2011 by Yeo et al.[20] and Power et al.[21] have subdivided the brain into its canonical functional networks in a data-driven, inside–out (see Box 2) manner[154], using different resting-state functional connectivity datasets, image processing pipelines and network identification algorithms. These studies have shown high consistency in functional network anatomy, but not in their names. Power et al. referred to the AMN anatomically as the cingulo-opercular network (CON). Yeo et al. settled on referring to the AMN functionally as the ventral attention network (VAN), but they discussed the possibility that this network could also correspond to the CON, the salience network or the combination of both (compare with Box 1 figure). The AMN outlines for each study are available for downloading as part of Connectome Workbench V1.5 (https://balsa.wustl.edu/study/kN3mg)[149].

Subsumed by the action-mode are functions conceptualized as planning, decision-making, alertness, goal maintenance, sustained extrinsic attention, planning or initialization of motor output, and feedback processing (pain, physiological and body states, motor and cognitive errors)[7–9,12–16,31,46,66,130,131].

The AMN is critical for initiating and maintaining higher-arousal states. It shows very large activity onset and offset transients required for moving out of and into rest periods[7,31,132], with AMN regions sustaining goal maintenance signals throughout task periods[7]. Activity in central thalamic nuclei (CM, ventroposterolateral), which are part of both the AMN and SCAN, precedes all other brain regions when arousing from sleep, and dACC regions of the AMN are the first cortical areas to become active in the arousal cascade of the brain[133]. The AMN may extend even deeper into the brainstem, to the substantia nigra, STN, red nucleus[134], dentate nucleus, locus coeruleus and the vagus nerve nuclei, but to know conclusively, better imaging methods are needed.

Alteration of or damage to the AMN prevents or disrupts goal-directed behaviour. For example, lesions within the AMN caused apathy and abulia[135,136] and decreased spontaneous self-initiated activity[137]. These individuals with AMN lesions could perform activities when specifically instructed, but they did not become active voluntarily. Similarly, epileptic seizures in the pars marginalis of the cingulate caused a loss of the sense of bodily agency[41,138,139], such that individuals with epilepsy were consciously aware of their own self and they were aware that they were moving, but they did not feel that they were the agent or cause of their own activity. The apparent efficacy of DBS targeting the CM of the thalamus in reducing seizures[140,141] may be attributable to the CM's place in the AMN and SCAN circuitry that regulates cortical arousal via changes in the cortical excitatory-to-inhibitory ratio[142]. By contrast, human direct electrocortical stimulation of AMN regions in the anterior cingulate reliably induced a sense of determination to persevere and continue despite adversity[143].

The AMN also has a key role in processing physically painful stimuli. The dACC and the anterior insula are the brain regions activated during application of painful stimuli[15,144]. This pattern is generally consistent across both somatic and visceral pain[145] and is separate from negative affect or social pain[144], which is more closely associated with the salience network. Within the AMN, distinct subnetworks related to the cognitive (decision-making; dACC), motor (action; SMA) and bottom–up (feedback; insula) components of the action-mode are identifiable[46]. However, the overarching structure of the AMN is that of a vertically integrated system that encompasses the cortex, cerebellum, striatum, thalamus and brainstem nuclei, which as a whole generate the cognitive, motor and sensory functions required for executing and updating actions quickly and safely.

Importantly, the AMN is the functional network most anticorrelated with the DMN[5,46]. Thus, the AMN counterbalances the DMN, and its activity is amplified during goal-directed extrinsic activity when DMN activity is attenuated, independent of the specific task demands[7,13].

Conclusion: the brain is for action

The evolutionary origins of the basic circuitry of the AMN are probably more distant than those of other association brain systems[146] because animals in the human lineage were behaving before they developed the rich inner life thought to be supported by the DMN[103]. The neuroanatomy of the AMN, including its representation in the SMA, striatum and cerebellum, as well as its strong connection to the SCAN in primary motor cortex, betrays its roots as a system for moving the body to achieve behavioural goals. The AMN seems to derive from simpler control systems for movement of the body (skeletal muscles) and movement within the body (smooth muscles).

Through phylogenetic refinement, the human AMN, like the rest of our brain, has become capable of extremely abstract processing. It no longer produces only physical movement, but also complex cognition. However, the principal differentiator of the AMN from all other higher-order functional brain networks, such as the salience, language and fronto-parietal networks, is that it remains closest to the original biological reason for using a brain: goal-directed movement, also known as action. Thus, the complex processing of the AMN is best conceptualized as cognition for action, which complements the self-referential thought supported by the DMN.

Data availability

The data used to generate the functional connectivity and network maps in Fig. 1 and Box 1 were released as part of Feczko et al.[147] and are available for download at https://nda.nih.gov/edit_collection.html?id=3165. The network outlines shown in Fig. 2 were released as part of Connectome Workbench[148] V1.5 and are available for download at https://balsa.wustl.edu/study/kN3mg (ref. 149).

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N.U.F.D. has a financial interest in Turing Medical Inc. and may benefit financially if the company is successful in marketing FIRMM motion monitoring software products. N.U.F.D. and E.M.G. may receive royalty income based on technology developed at Washington University School of Medicine and Oregon Health and Sciences University and licensed to Turing Medical Inc. N.U.F.D. is a co-founder of Turing Medical Inc. These potential conflicts of interest have been reviewed and are managed by Washington University School of Medicine. The other authors declare no competing interests.

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