Opinion

Is it time to put rest to rest?

Emily S. Finn1,2,@,*

The so-called resting state, in which participants lie quietly with no particular inputs or outputs, represented a paradigm shift from conventional task-based studies in human neuroimaging. Our foray into rest was fruitful from both a scientific and methodological perspective, but at this point, how much more can we learn from rest on its own? While rest still dominates in many subfields, data from tasks have empirically demonstrated benefits, as well as the potential to provide insights about the mind in addition to the brain. I argue that we can accelerate progress in human neuroscience by de-emphasizing rest in favor of more grounded experiments, including promising integrated designs that respect the prominence of self-generated activity while offering enhanced control and interpretability.

From task, to rest, to a third wave in human neuroimaging

The phenomenon of so-called resting-state activity in the human brain has revolutionized how we acquire and analyze neuroimaging data and yielded breakthroughs in our understanding of brain function. Since structured activity in the absence of any explicit task was first described more than two decades ago, studying the brain at rest has elucidated principles of macroscale brain organization, shed light on the balance between spontaneous and evoked activity, and revealed the extent to which behaviorally relevant patterns of brain function are trait- versus state-like, among other discoveries. But at this point, how much more do we have to learn from rest alone?

Here, I argue that just as rest represented a paradigm shift from the first wave of traditional task-based approaches, the time is now ripe for another shift– this time toward a third wave of paradigms that marry the broadened perspective and methodological toolkit we gleaned from our foray into rest with the enhanced control and interpretability afforded by tasks. First, I critically re-examine common uses of rest and argue that moving toward task-based acquisitions (broadly defined) will accelerate progress in areas that have been dominated by rest in recent years, including characterizing brain functional organization and brain–behavior relationships. Next, I elaborate on another point in favor of task data, namely that these data can speak to brain–mind relationships in addition to, and in combination with, these two goals. Finally, I consider the most promising modern task paradigms, including integrated designs that blend the best of both the resting-state and task-based worlds.

Re-examining the supposed advantages of rest

After a somewhat slow start [1–3], resting-state (see Glossary) acquisitions, in which subjects lie quietly with no externally imposed task or stimulation, have captured an impressive share of the human neuroimaging market. An online search via dimensions.ai revealed that in 2008, the term resting state appeared in roughly 4% of all scholarly sources containing the term fMRI in the title or abstract (85/2132), while in 2020 this was up to 33% (1620/4962). Rest is convenient to collect and easy to share, making it an attractive option, especially in the age of large-scale data collection and discovery science. Compared to the highly constrained task paradigms that dominated the first wave of neuroimaging, rest has many touted benefits. But do these hold up to scrutiny?

Highlights

Studying brain function at rest -- that is, absent any experimenter-imposed task -- has grown immensely popular over the last few decades and now accounts for a large share of human neuroimaging research.

While resting-state research gave us new analysis methods and a broadened perspective on brain functional architecture, it suffers from fundamental limitations that place a ceiling on the insights we can draw from it.

Data acquired during tasks have empirical benefits, including enhanced interpretability and sensitivity to brain–behavior relationships.

At this point, progress in human neuroscience is most likely to come from third-wave paradigms that reintroduce task-like manipulations and/or pair imaging data with additional measurements, providing more anchor points for understanding the brain and mind.

1Department of Psychological and Brain Sciences, Dartmouth College, Hanover, NH 03755, USA
2https://thefinnlab.github.io
*Correspondence: emily.s.finn@dartmouth.edu (E.S. Finn).
@Twitter: @esfinn (E.S. Finn).
Rest data are not unique in how they can be analyzed

First, it is important to acknowledge that a major benefit of the resting-state second wave was that it broke us out of the traditional analysis mode, which was dominated by task design and the general linear model, and spurred us to develop more powerful ways to find structure in our high-dimensional neuroimaging data. Many would agree that the most popular family of approaches, functional connectivity, has revolutionized how we think about the brain [4]. As it turns out, evoked activity that is precisely locked to task timings is only the tip of the iceberg for the signals we record (Figure 1). The explosion of methods for characterizing the remainder of the variance has opened up new fields within neuroscience and yielded fundamental insights into brain organization and the neural code.

But although it took the blank slate of rest to inspire these creative tools, rest is by no means the only type of data on which we can use them. Most functional connectivity techniques can be just as validly applied to data acquired during a task. In fact, task-based connectivity is in many cases more meaningful and informative than resting-state connectivity (see the following sections for specific examples, and Box 1 for considerations when using task data in functional connectivity analyses). While rest is sometimes considered uniquely valuable for multimodal and cross-species work, see Box 2 for a critical re-examination of this perspective.

Thus, a desire to use functional connectivity is no longer, and has never been, a good reason to scan at rest. It is unfortunate that terms like 'resting-state networks' have become ingrained in our vocabulary when we have known from the beginning that these networks are just as present and identifiable during tasks, if not more so. Simply calling them 'functional networks' would be more accurate and appropriate, and might help promote the collective acknowledgment that structured brain dynamics, and the tools used to characterize them, extend to almost any observable brain state.

Does rest provide unique insights into functional organization?

One way that rest data are commonly used is to map the functional organization of the brain. Regions with coherent signal fluctuations are grouped into networks whose topographical

![First wave: task paradigms](image1)

![Second wave: resting state](image2)

![Third wave: integrated designs](image3)

Figure 1. From task, to rest, to a third wave in human neuroimaging. The first wave of functional neuroimaging consisted largely of investigators (represented by the boat) using highly controlled task paradigms (represented by the boxcar, denoting task on–task off periods) to attempt to isolate specific cognitive processes. While this approach could generate and localize small ripples in brain activity, ultimately, it ignored a large fraction of variance that arose from task-unrelated, seemingly spontaneous signals. In the second wave, investigators (represented by the submarine) dove headlong into the depths to characterize the spatiotemporal structure of this resting-state activity. However, because we had little to anchor our observations to, it was difficult to interpret these signals. The third wave calls for us to partially resurface and regain some experimental control, while still respecting the importance of self-generated activity in dynamic patterns of brain function.
Box 1. Functional connectivity on task-based data

Some have raised concerns that task-induced coactivations lead to spurious correlations in functional connectivity analyses [115]. One proposed solution is to regress the task design (i.e., stimulus onsets) and calculate functional connectivity on the residuals of this regression [116,117]. Depending on the task, this approach might be more or less feasible; for example, it might be straightforward to model blocks in a finger-tapping task, but in a working memory task where the bulk of the processing happens between external cues (and likely with dynamics that are not well modeled by a simple boxcar), it is harder to see how one could plausibly remove all or even most task-related signal variance. Many tasks, even simple ones, have anticipatory, attentional, and learning and/or adaptation effects that are not captured by a typical design matrix, even if the shape of the hemodynamic response is allowed to vary across brain regions, trials, and individuals [115,118,119] (which is rarely done in practice). Despite all of this, empirically, it seems that using residualized versus nonresidualized task connectivity often does not substantially alter the pattern of observed results [21,34,120]. If or how task-evoked signals are handled should depend on the ultimate goal of the study, but should not be used as a reason to avoid tasks in research using functional connectivity tools.

This issue may be another point in favor of naturalistic paradigms (e.g., movie watching or story listening). Thanks to a shared, time-locked stimulus across subjects, one can take the group-average time course as an index of task-evoked activity. This, being a full data-driven, largely model-free approach, likely captures much more of the task-related variance than any classic forward model (i.e., design matrix). Investigators concerned with removing as much of the task-evoked signal as possible could regress this average time course from each voxel or spatial region and use the residuals for functional connectivity analyses.

properties, internal (within-network) dynamics, and external (between-network) dynamics can be further studied. Rest was critical to our initial discoveries of this macroscale network architecture, and many researchers continue to believe that rest is the best state in which to characterize functional organization. Is this true?

One assumption, which was especially common in earlier days of resting-state research but in some subfields persists, explicitly or implicitly, is that rest is a neutral backdrop, offering a view of brain functional organization that is unbiased by the influence of externally imposed tasks (here I refer to bias at the relatively abstract level of cognitive state; see Box 1 for a discussion.

Box 2. Advantages of task for multimodal and cross-species work

For multimodal or high-resolution acquisitions, tasks provide a ground truth that enables averaging across runs or sessions, and helps parse signal into meaningful and nonmeaningful components. Whereas combining rest acquisitions is nearly always limited to spatial summary statistics that collapse across time in some way (since time is not commensurate across rest sessions), task paradigms allow for combining data across sessions while retaining information in the temporal domain. Averaging can take place over individual trials in more traditional paradigms, or entire time courses in naturalistic paradigms. In multimodal imaging [e.g., combinations of functional magnetic resonance imaging (fMRI), electroencephalography, magnetoencephalography, intracranial recordings, etc.], this permits a pseudo-simultaneous acquisition when a shared, time-locked stimulus across subjects, one can take the group-average time course as an index of task-evoked acquisition. This, being a full data-driven, largely model-free approach, likely captures much more of the task-related variance than any classic forward model (i.e., design matrix). Investigators concerned with removing as much of the task-evoked signal as possible could regress this average time course from each voxel or spatial region and use the residuals for functional connectivity analyses.

Should rest continue to play a role in cross-species comparisons? If resting-state activity is substantially influenced by ongoing cognition, and the mental contents of rest for humans and nonhumans are different, scanning at rest could obscure rather than reveal links across species. If resting-state activity is not strongly influenced by ongoing cognition, and instead mostly reflects basic physiology, then the choice of paradigm should not matter much (and would be more reason to take advantage of the increased quality of task data in humans). Despite the challenges of awake imaging in nonhuman primates, these animals can successfully perform many tasks inside and outside the scanner, including movie watching [121,122]. Just as in humans, functional organization in nonhuman primates is broadly similar between rest and naturalistic viewing [123], but the latter affords the opportunity to link observed activity patterns to a ground-truth stimulus, and opens the door to interspecies correlation [124]. There is ever some evidence that similar to humans, movie-watching reduces head motion relative to awake rest in nonhuman primates [123], so investigators might choose these paradigms for purely practical reasons. Phenomena like replay that have been detected across species are good candidates for study at rest, but only in conjunction with task data to characterize sequence-related activity in the first place [88]. Thus, overall, task data offer several advantages over rest for cross-species work.
of bias from task-evoked activity at the level of the measured signal). However, the idea that rest is a passive state has long been problematic [5–7]. In fact, rest is its own task that varies in unobserved and uncontrolled ways across sessions, individuals, and populations. Again, this is by no means a new argument [8,9]. Nevertheless, it bears repeating, especially with the rise of large-scale imaging efforts. From a theoretical perspective, then, rest is just as biased as any other task state, and it is biased in ways that may be less easily measured or mitigated.

Empirically, does rest outperform other acquisition states for characterizing functional organization? On the one hand, functional organization shows a degree of stability such that major networks can be mapped in both groups and individuals across many distinct acquisition states [10–14]. On the other hand, network topography reconfigures to a substantial extent as subjects engage in various activities [12,15], including considerable individual-task interactions [10,16,17]. Thus, no single acquisition state can give us a full picture of brain functional organization. In theory, then, rest is no better or worse than any other task. Yet in practice, it is often easy to treat rest as though it reflects the true underlying functional topography (compare how often the word intrinsic appears alongside descriptions of rest-derived activity patterns, whereas one rarely sees this term in conjunction with task-derived results). This assumption can muddy our interpretations and suggest a degree of stability and generalizability that is not there. A growing body of work finds that minute for minute, estimates of functional connectivity derived from one or a combination of task states are often more stable, generalizable, heritable, and meaningful (in the sense of relationships with behavior) than estimates derived from rest alone [18–21]. In one recent study, rest was a particularly poor proxy for latent (i.e., model-based average) functional organization compared with other tasks [19]. Thus, rest may in fact yield the more biased picture.

Perhaps we should flip the typical perspective – that is, that rest gives intrinsic information, while tasks give state-level information – on its head: rest may be best for studying states rather than traits, while combining data across task paradigms may bring us closest to identifying a generalized functional architecture. However, using rest acquisitions as a window into states is likely to be most useful if we combine rest acquisitions with other explanatory variables that we can measure or, ideally, manipulate. I discuss this further in the final section.

Is rest the best state to reveal brain–behavior relationships?

A second way that rest data are often used is to relate patterns of functional brain organization to phenotypic measures acquired outside the scanner (e.g., age [22,23], cognitive ability [11], personality [24,25], and symptom scores [26]), and to build models that predict these measures from functional connectivity in new subjects. Most studies to date have focused on trait-like between-subject differences, though the approach can also be applied to within-subject changes [27]. While several papers that initially popularized this approach used rest data [11,22], recent work is converging on the fact that task data is, in many cases, much more sensitive and powerful for this purpose.

In one-to-one comparisons, tasks typically yield better predictions of behavior than does rest [20,28–30]. The difference is striking: for predicting the same target behaviors in the same participants, using certain tasks can increase explained variance more than threefold [28,29]. Tasks increase sensitivity to meaningful between-subject variability not only in healthy young adults, but also in developmental [28,31], aging [32], and clinical populations [33–35]. While tailoring the task to the target behavior, akin to a stress test, may afford some of the best accuracy [31,36], even in-scanner tasks that are seemingly unrelated to the target behavior yield better predictions than does rest (e.g., predicting fluid intelligence using data from a finger-tapping task). Tasks also enable evoked activity-based, rather than connectivity-based, predictions, which may be not only
more accurate in some cases [37], but also more interpretable. Analogous to how functional organization is better estimated from several task states than from rest alone, behavior prediction models trained on data from a combination of tasks (sometimes including rest) consistently outperform models trained on a matched amount of rest data alone [19,20].

Why the advantage for task data? Better data quality may be a factor: people generally move less [38] and have an easier time staying awake during certain tasks; this effect may be even more pronounced for hard-to-scan populations (e.g., children [39,40], or patients with psychiatric illness [38]). On a cognitive level, tasks also perturb ongoing neural activity in differential ways across individuals [41]. One interpretation is that tasks act as a sort of lens through which we can project subjects to constrain overall variability (i.e., reduce noise) while preserving meaningful differences. We do not yet fully understand how and why tasks enhance behaviorally relevant variability. But given the evidence to date, the practical view should favor task over rest for brain-behavior predictive modeling.

Can rest further our understanding of brain–mind relationships?

What has rest taught us about the mind? In contrast to the goals discussed previously, many researchers may not consider understanding the mind a major aim of resting-state work. However, whether or not this goal is explicitly stated, rest data are often interpreted in light of assumed mental processes (though see [42] for a counter-perspective). This is at best an inefficient and at worst a misleading way to understand how the brain gives rise to the mind.

Although they have separate origins, resting-state research and the concepts of the default mode and default-mode network are now tightly intertwined [43]. Though it took some time for rest to be widely accepted as a highly active state in its own right rather than a passive baseline [2,5–7], most researchers now recognize that resting-state signals reflect a mix of intrinsic functional organization and the mentation people do when left to their own devices, namely self-referential thinking: reflecting on the past, planning for the future, and ruminating on social relationships. However, these activities are not inherently at odds with experimenter-imposed paradigms. In other words, default-mode regions are only less active during a task if you are not using the right task [6]. Furthermore, is it meaningful to treat this collection of activities as a monolith? If we replace rest with intrinsic activity [44] (or self-referential processes, mind wandering, daydreaming, etc.), are we content to map that term onto a summary of resting activity patterns and leave it at that? Probably not; we would presumably like to draw more specific links between brain and mind. But this requires a more fine-grained window into what the contents of the mind are at any given moment, which in turn requires some kind of experimental control, whether pre hoc (via experimental instructions, as in tasks), in the moment (via experience sampling), or post hoc (via retrospection).

If the primary goal of a given study is to map functional brain topography without directly linking features of that topography to ongoing cognition, rest yields maps that are to some degree stable and sensitive to out-of-scanner behavior (though perhaps less so than maps derived from more controlled task states, as discussed in the previous two sections). However, there are two potential issues with using rest in this way. First, like any other acquisition state, rest can easily invite reverse inference: reasoning backward from a map of brain regions to infer the involvement of specific mental processes commonly ascribed to those regions, without directly manipulating those processes [45]. For example, aberrant resting-state connectivity in psychiatric patients in the default-mode network is often interpreted as mechanically linked to hyper- or hypoactive self-referential processes, such as rumination or social cognition [46–48]; resting connectivity differences in the frontoparietal network are sometimes interpreted as mechanistically linked to
executive function [49,50]; and reduced connectivity between visual and prefrontal regions in dyslexia has been interpreted as mechanistically linked to failures of attention to visual stimuli [51]. However, without directly manipulating or measuring these processes during the experiment itself, such interpretations are not necessarily warranted. Just because an individual or group shows, for example, less coherent activity in a network at rest, does not mean they cannot coherently activate that network when cognition requires it. Furthermore, how do we know if differences at rest reflect intrinsic endophenotypes, or if certain people simply tend to engage in different mental activities while in the scanner? Either is interesting, but pure rest affords us no way to tease apart these possibilities.

Second, even resisting the temptation of reverse inference, as a field, what can we learn from topographic maps derived solely from rest data? What does it mean that certain networks occupy more, or different, real estate in some individuals than others? What are the consequences of these differences for the mind and its functions? Encouragingly, recent work has shown, for example, that resting-state spatial topography of cortical networks predicts individual cognitive and affective phenotypes [52], and that total cortical representation of the executive function network at rest is associated with both age and executive performance [53]. But while these studies reinforce the value of topographical approaches, they do not necessarily reinforce the value of rest per se: it is possible – perhaps even likely given the evidence outlined in the previous section – that applying the same tools to data acquired during task would have yielded just as robust, if not more robust, relationships with behavior. Furthermore, by relating brain measures derived from an unconstrained cognitive state (i.e., rest) to cognitive measures acquired outside the scanner, these studies can establish only very indirect associations between topography and cognitive phenotypes. They cannot, for example, inform theories of cognition by characterizing interactions between the spatial extent of a region or network and its functional properties during cognition itself (e.g., the strength of activations or multivariate representations in that region), or suggest any compensatory mechanisms or alternative strategies that may be at play within or across individuals. To this end, other recent work has used dense sampling approaches that combine rest with hypothesis-driven task paradigms to probe the function of specific territories in individual subjects [14,54], finding evidence for individually distinct, topographically interdigitated networks that subserve dissociable cognitive functions (i.e., language [14], episodic projection, and theory of mind [54]). These exciting studies are beginning to bridge brain and mind in individuals, although again, the specific value of rest for this work is unclear because these networks seem to be just as easily delineated during task [14]. In short, while these are promising avenues of inquiry, the same conclusions might have been reached (perhaps even more efficiently, or with stronger possible interpretations) by foregoing rest and using one or a combination of tasks instead. The trade-off between acquisition types will be increasingly consequential as we scale these paradigms to larger data collection efforts, balancing the need for more subjects with the need for adequate data per subject. These efforts will be necessary to understand the consequences of topographical differences for behavior within and across individuals.

The third wave: integrated designs

The irony of calling for a pendulum swing back to task-based paradigms, the bread-and-butter of human functional neuroimaging since the early 1990s, is not lost on me. (The phrase ‘take to task’ comes to mind.) However, we do not return to the same tasks with the same analysis approaches geared toward isolating single functions and single regions; rather, we move forward into a third wave armed with a new suite of tools and a broader perspective on brain functional organization (Figure 1). Third-wave designs can involve using rest-inspired analyses on data from traditional tasks to gain fresh insights into the systems-level architecture supporting those tasks, as described at the end of the preceding section. There also exist several promising avenues that
blend the best of both the resting-state and task-based worlds into integrated experimental designs (Figure 2). I outline some of these in the following sections.

**Introspection and annotated rest**

One way to understand what people are doing during rest is simply to ask them [55–57]. Having participants provide first-person reports of their mental experiences, either retrospectively or in real-time, gives us anchor points for resting-state activity which can increase the interpretability of within-subject dynamics and/or between-subject differences [58].

How frequently these reports should be made, and what format they should take, are open questions and depend on specific research goals [55]. While retrospective reports are less disruptive in the moment, they do not allow for mapping between instantaneous thoughts and instantaneous brain activity patterns; however, they may still be useful for capturing broad differences (e.g., across development, in certain patient populations). In-the-moment thought probes, which sample experiences at regular, random, or adaptive intervals, allow for a more granular mapping between thoughts and brain activity [59]. In both cases, reports are surface level in

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**Third wave: integrated designs**

Annotated rest: Task-signature echoes:

Naturalistic tasks: State-informed approaches: e.g., state-triggered paradigms

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**Figure 2. Third-wave integrated designs that blend task- and rest-inspired approaches.** In the third wave, we have an opportunity to draw from the best of both worlds during acquisition and analysis. Four families of integrated designs are depicted. Annotated rest refers to acquiring introspection data — that is, first-person reports of ongoing mental experiences during or after the scan — that can be linked to spatiotemporal features of brain activity. Naturalistic tasks (e.g., movie watching and story listening) are richer, more dynamic, and in some ways more ecologically valid than traditional tasks. These paradigms thus create stronger yet more organic ripples, bringing surface-level and deeper phenomena closer together. In task–signature echoes, activity patterns are characterized using data with a known task manipulation, and then rest data are mined to see if echoes of these signatures can be detected at rest, suggesting a kind of replay, reinstatement, or engagement in similar mental activities. Finally, in state-informed approaches, experimenters monitor brain state (either post hoc, or online using real-time neuroimaging), and deliver tasks at certain intervals to causally test the role of ongoing activity in shaping perception and behavior toward an external stimulus.
the sense that subjects can only report experiences they are conscious of, and they depend on subjects’ capacity for accurate introspection, which may vary across individuals and populations (but can also be trained to some degree). We also risk altering the system by measuring the system. Yet even if the ultimate goal is to understand how trains of thought arise organically, injecting some declarative measures is likely the best way forward.

Movies and stories as drivers of cognition

So-called naturalistic paradigms, such as watching movies or listening to stories, are often much more engaging than traditional tasks, thereby driving brain activity in a way that is at once stronger and potentially closer to freeform cognition [60]. These stimuli possess features at every rung of the perceptual hierarchy, from low-level audiovisual (light and/or sound), to mid-level categories (faces, scenes), to high-level (language, affect), yielding multiplexed neural responses that are rich in both shared [61] and idiosyncratic [62,63] components.

Naturalistic paradigms may be a good replacement for rest when study goals are open ended. Logistically, these paradigms are relatively easy to acquire: in their minimal form they require only basic presentation equipment and a way to synchronize onset time with the scanner; no complex task timing, logging, participant training, or behavior recording is needed. Thus, the barrier to entry is low for researchers and clinicians accustomed to acquiring rest and for scan centers participating in large-scale data collection efforts. Of course, these paradigms require researchers to choose a specific stimulus or set of stimuli; this choice should be informed by the research questions, planned analyses, and populations under study (see [61,64,65] for theoretical and practical guidance on stimulus selection). Data acquired during these paradigms are flexibly analyzed using tools developed for traditional task data (e.g., model-based regression) as well as those developed for rest (e.g., functional connectivity). As with traditional tasks, major functional networks and reliable brain states [66,67] are readily identified during naturalistic stimulation, if the goal is to interrogate systems-level organization. Individual differences in functional connectivity are often more stable during movie watching than during rest [68,69], and better predict behavior [30].

At the same time, the presence of a time-locked stimulus shared across participants opens the door to a unique set of tools, namely intersubject correlation and related approaches [70,71]. These analyses are especially powerful because they require few assumptions about the structure of either the stimulus (i.e., which features are important) or the neural response (i.e., the hemodynamic response function), and thus can recover maximal stimulus-driven signal. Intersubject correlation is a natural denoiser in that nearly all noise arises from artifacts within brains, so by looking across brains – that is, using one brain as the model for another – the observed signal variance is almost guaranteed to be neuronal in origin [71–73]. Note that these approaches are not necessarily limited to capturing activity that is shared across all subjects; they can also capture activity patterns that are more stereotyped in certain subjects than others [63,74], which can, in turn, be related to state- or trait-related behaviors, including clinical phenotypes [75–81].

Echoes of task signatures at rest

Another type of integrated design involves using task paradigms to learn signatures of brain activity that correspond to particular mental states or activities, then searching for echoes of these same signatures in unstructured rest. As proof-of-concept with robustly observable phenomena, two recent studies learned signatures of body movements and arousal level, respectively, from task or multimodal imaging data, and found that recapitations of these signatures could classify similar events or fluctuations during rest [82–84]. First characterizing, and then detecting echoes
of, more nuanced cognitive states – for example, what a participant is thinking about – is more challenging, but there has been some progress here too [85, 86]. For example, in another recent study [87], researchers developed an unsupervised method to map dynamic functional connectivity onto distinct cognitive states, validated this method using task data with known state transitions, then applied this same method (but not necessarily the same states) to rest. The phenomena of **replay** and **reactivation** have been studied using this approach as well, with reports that fast, stereotyped patterns of neural activity in response to sequences are also detected at rest [88–91], where they support planning [92] and predict memory performance [93].

A directed thought may diverge in some ways from the same self-generated thought – in other words, being instructed to think of a positive memory may not be exactly the same, either phenomenologically or neurally, as having one come to mind spontaneously. Still, leveraging task paradigms with known ground truths to create a dictionary of states that can then serve as templates for rest may shed some initial light on the brain–mind relationship during unconstrained cognition. With this approach, we can draw on tools for large-scale meta-analysis [94, 95] as well as reuse existing data from both task-based and rest designs, making it an efficient way to accelerate discovery and develop hypotheses for new experiments.

**State-informed paradigms**

The echo-detection approaches outlined previously go from task to rest. We can also flip the direction and go from rest to task, to ask how ongoing activity affects perception and behavior for an extrinsic stimulus.

There is a rich literature on how prestimulus brain activity predicts trial-wise accuracy and reaction time on sensory tasks [96–101]. More recent work has begun to use predefined signatures of arousal [82] in a prospective design to directly test their relevance for behavior and has reported slower reaction times and more frequent misses when stimuli are presented during a low arousal state [102]. Some studies have gone beyond unidimensional performance measures to explore not just how attentive someone is at a given moment, but what they are likely to be most attentive to, finding category-specific signatures that bias detection of, for example, faces versus objects [103, 104], or prime subsequent self-referential [105] or social [106] processing. A compelling next step is to search for ever more nuanced signatures of how upcoming stimuli will be perceived, even within categories. For example, can prestimulus brain activity predict whether an ambiguous social stimulus will be perceived as positive, neutral, or negative?

A powerful extension to this framework is to close the loop by using **real-time neuroimaging** for state-triggered paradigms [107, 108]. In these adaptive experiments, participants’ brain activity is monitored for when they enter a specific state, which then triggers a task event for which processing should be facilitated or inhibited (or otherwise affected) by that state. This approach relies on similar technology as neurofeedback, but does not necessarily involve neurofeedback that the participant is consciously aware of. States could be predefined (i.e., supervised), learned bottom-up through initially random trial-and-error (i.e., unsupervised), or some combination, and they might be defined with respect to univariate activity, multivariate activity [109], and/or functional connectivity [110–112]. Along with brain stimulation techniques, these designs can get us closer to learning causal relationships between moment-to-moment resting brain activity and behavior.

**Concluding remarks**

In certain circumstances, rest may still be an appropriate, or perhaps the only, choice. For example, in very young infants, comatose patients, or subjects in altered states of consciousness, resting-state acquisitions may be the most flexible and feasible. Still, experimenters should
carefully examine their assumptions in choosing acquisition states, even for these special cases. For example, movies or spoken language can reveal time-locked brain activity in otherwise unresponsive individuals [113,114], potentially providing deeper clues into residual cognition than rest alone.

While rest likely still has a place, the choice to collect resting-state data should be deliberate in the same way that the choice of any other task is deliberate – driven by where it can add true value, and not just be an easy default (see Outstanding questions). Big-data consortia should consider reducing the amount of rest they acquire in favor of task paradigms that are more sensitive to behavior; naturalistic paradigms may be particularly good candidates. Investigators designing smaller-scale experiments should question if and why rest suits their research goals, and if they do move forward with rest, collect additional data whenever possible (e.g., introspection) to boost explanatory power. If human neuroimaging is to continue to advance either basic science or translational tools, the next wave of progress will most likely come from a pivot toward more precise and interpretabel designs.

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