

and so virtually every molecular tool required for genetics has been developed for use in this system, for example: gene knock-outs and knock-ins; insertional mutagenesis (REMI); cell-type-specific or inducible expression systems; replicative and integrative plasmids. Cell biological tools such as protein tagging, organelle markers, and immunostaining are also available. All strains generated can be easily frozen down in liquid nitrogen for long-term storage.

What resources are there? Since the completion of the genome in 2005, it has become easy to search for gene homologues in *Dicty*. The genome is very simple to browse thanks to dictyBase, a website that provides access to all sorts of information from movies, to techniques, to mutant phenotypes, to gene expression data. The stock centre is another fantastic resource: a central repository where wild-type strains, mutants, cDNA libraries and constructs are maintained and available to order.

Anything else? *Dicty* is being used to study so much more than has been possible to mention here! Many other researchers have taken advantage of *Dicty*'s genetic tractability and conserved machinery to investigate other biological processes such as histone modification, DNA repair pathways, mitochondrial diseases and nuclear architecture.

Others are interested in *Dicty* biology itself and how Dictyosteliida do things such as sexual reproduction; how this is achieved in lower eukaryotes can tell us much about evolution of such fundamental processes.

Where can I find out more?

<http://dictybase.org/>

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Primer

Dreaming and offline memory processing

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The activities of the mind and brain never cease. Although many of our waking hours are spent processing sensory input and executing behavioral responses, moments of unoccupied rest free us to wander through thoughts of the past and future, create daydreams, and imagine fictitious scenarios. During sleep, when attention to sensory input is at a minimum, the mind continues to process information, using memory fragments to create the images, thoughts, and narratives that we commonly call 'dreaming'. Far from being a random or meaningless distraction, spontaneous cognition during states of sleep and resting wakefulness appears to serve important functions related to processing past memories and planning for the future. From single-cell recordings in rodents to behavioral studies in humans, recent studies in the neurosciences suggest a new conception of dreaming as part of a continuum of adaptive cognitive processing occurring across the full range of mind/brain states.

Models of the dreaming process

Once regarded as messages from gods or portents of the future, supernatural explanations of dreaming had largely given way to psychological approaches by the late 19th century. Yet for many decades to come, concepts of dreaming continued to be dominated by the presumption that these seemingly bizarre nocturnal experiences originated in mechanisms disparate from those supporting normal waking cognition. With the publication of *The Interpretation of Dreams* in 1900, Freud famously popularized the notion that dream content cannot be taken at face value, instead originating in complex psychological mechanisms entirely dissimilar from those generating the thoughts, feelings, and reminiscences of our typical waking experience. Although the Freudian notion that

dreams communicate a 'hidden meaning' disguised in symbolic language has become entrenched in popular folk psychology, there is scant empirical evidence to support this view. Grounded in the neurosciences, modern models of dreaming have instead focused on understanding the observable neural and psychological mechanisms that produce dream cognition.

In direct opposition to psychoanalytic dream theory, Hobson and McCarley first presented their 'activation-synthesis' hypothesis in 1977, a highly influential neuroscientific account of dreaming that rejected the notion of dreams originating from a 'meaning' in need of deciphering. The key tenet of Hobson's distinctly anti-Freudian theory was that dreams originate from neural signals in the brainstem generated during rapid eye movement (REM) sleep. According to the activation-synthesis model, dreaming is experienced when the sleeping brain attempts to make some sense of this chaotic input into its higher-level cortical circuitry. Indeed, intermittent bursts of brainstem activity are a prominent feature of REM sleep, a phase during which dreaming is particularly likely to occur. Yet, since the late 1960s, it has been increasingly recognized that dreaming also occurs in the absence of REM, and is reported even from the deepest stages of 'slow wave' sleep. The clear presence of dreaming in non-rapid eye movement (NREM) sleep, sometimes as vivid, bizarre, and story-like as REM dreaming, presents a problem for models proposing REM-specific physiology as the exclusive origin of dream experience.

Most recently, developments in the cognitive neuroscience of memory have led to a new brain-based framework for understanding dreaming, in which dream experience is viewed as one of several forms of spontaneous offline cognition involving the reactivation and processing of memory during resting states. There is now substantial empirical evidence to suggest that, during sleep, the neural-level 'replay' of recent experience plays a critical role in the consolidation and evolution of memory, helping us to process our past experiences and prepare for future events. Here, we will review evidence that the activity of memory systems in the sleeping brain contributes to the conscious

experience of ‘dreaming’, a mental state that shares many features with thought, imagery, and daydreaming during wakefulness.

Offline reactivation of memory during sleep and quiet wakefulness

Recent work in the neuroscience of memory has been particularly enlightening for thinking about the neural basis of dream experience. Perhaps of greatest importance is evidence from divergent methodologies that describe the neural ‘reactivation’ of recent experiences during quiet wakefulness and sleep. Multi-unit recordings in animals have shown that sequences of network activity first seen when a rodent is exploring its environment are again reiterated when animals rest or fall asleep. First observed within the hippocampal memory system, this reactivation effect has now been demonstrated to simultaneously occur in several cortical areas as well. In sleep, memory reactivation has most often been observed during NREM sleep immediately after exploration/learning, with the strength of the reactivation effect decaying substantially across the first hour of post-training rest. Analogous results have been obtained in humans, with imaging studies demonstrating that activity in brain regions engaged during a learning task is elevated during post-training sleep, relative to participants who did not engage in learning. This offline reactivation of newly acquired information is thought to play a role in stabilizing labile memory traces into a more permanent form of long-term storage, while integrating new experience into existing cortical knowledge structures (‘memory consolidation’).

Is the so-called ‘replay’ of memory in the sleeping brain related to the conscious experience of dreaming? Recent evidence from a variety of sources suggests that the answer is ‘yes’. Particularly during early-night NREM sleep — when memory reactivation in animals is at its strongest — dream content is very likely to reflect recent learning experiences. Work from our laboratory and others has experimentally demonstrated this ‘cognitive-level memory reactivation’ by observing the impact of highly engaging or emotional learning tasks on the content of

thought and imagery in subsequent periods of sleep. The impact of such experiences on dream content is often dramatic: after extensively playing the downhill skiing arcade game *Alpine Racer II*, a third of participants’ sleep onset dreams contained task-related thought or imagery, for example “I keep seeing all the places where I fall — like, hit the walls. It’s kind of annoying; and then my legs fly up in the air”.

Non-experimental approaches also clearly indicate that recent experience is frequently represented in dreams. For example, in an analysis comparing hundreds of dream reports with possible memory sources from a diary of waking events, 51% of dreams contained at least one feature bearing strong, direct similarity to a recent waking experience. Interestingly, however, it was rare for a dream experience to *exactly replicate* any particular waking event, occurring in only about 2% of all reports. Instead, *elements* of a waking experience, perhaps a character or theme, are typically integrated into the dream, but without replicating the original context in which these elements were embedded. As an example, take the following dream report, presented together with a waking memory source:

Waking memory source: “When I left Starbucks [at the end of my shift], we had so many leftover pastries and muffins to throw away or take home. I couldn’t decide which muffins to take and which to toss...”

Corresponding dream report: “My dad and I leave to go shopping. We go from room to room, store to store. One of the stores is filled with muffins, muffins, muffins from floor to ceiling, all different kinds, I can’t decide which one I want...”

A substantial body of human behavioral data demonstrates that post-learning sleep actually enhances memory for newly learned information, relative to equivalent periods of wakefulness. Offline ‘reactivation’ of memory in the sleeping brain may be a critical aspect of this sleep-dependent memory processing. For example, systems-level memory reactivation in humans, as indexed by functional neuroimaging, predicts overnight memory enhancement observed at a subsequent retest. Furthermore, several experiments demonstrate that delivering learning-related sensory

cues to sleeping subjects — for example, sounds or smells present during encoding — enhances later memory performance, presumably by inducing reactivation of the learning experience during sleep.

Critically for our purposes here, recent work in our laboratory has established cognitive-level reactivation of memory traces as a predictor of sleep-dependent performance enhancement, thus linking sleep-dependent memory processing to human dreaming. Following training on a virtual maze navigation task, participants either lay down for a 90-minute nap, or else remained awake. As expected, post-learning sleep enhanced navigation performance. But in addition to measuring performance, memory reactivation was indexed by collecting verbal reports of participants’ mental experience during the nap, and examining these reports for content directly related to the maze task performed just prior to sleep. Those participants reporting task-related dreams exhibited strongly enhanced memory for the maze environment at subsequent retest.

Taken together, these findings suggest that dream experience is a reflection of mnemonic processes in the sleeping brain. But we are not suggesting that mechanisms of memory consolidation alone can provide a complete account of mental experience in any state of consciousness. Nor do we propose that dreaming of a learning task *causes* improved memory. More likely is a scenario in which neural-level mechanisms of memory reactivation support sleep-dependent memory consolidation and performance improvement, while simultaneously contributing to dream construction. It is worth noting that the type of memory reactivation described in rodent models cannot be the only neural mechanism involved in dreaming, as individual ‘reactivation’ events seen during NREM sleep occur on a very fast timescale, during bursts of activity which last only a fraction of a second. In contrast, dream scenarios may focus on a single mnemonic theme for extended periods of time. Thus, it is most realistic to view memory reactivation as one of possibly many *contributors* to the dream construction process. As in our waking hours, the complex nature of mental experience during sleep is the product of an active cortex continuing

its interpretive functions during periods of reduced sensory input, as the brain engages in a variety of offline cognitive processes. Indeed, we will conclude this primer by describing how the study of offline forms of cognition across states of consciousness may serve to further elucidate both the neural basis of dream experience, and the nature of waking cognition.

The 'default' mode of brain function

Traditionally, cognitive neuroscience has focused on understanding the activities of the mind and brain in response to external inputs. However, recent years have brought renewed attention to the importance of spontaneous brain activity occurring during periods of rest, sleep, and other offline states, when the processing of sensory input is reduced to a minimum. Research on the 'default' mode of brain function, in particular, has fruitfully explored the role that resting brain states may play in the processing of new memories, in theory of mind, and in anticipation of the future. Attention was first drawn to default-network activity in the 1990s, when imaging researchers noticed a consistent network of brain regions in which activity *increased* during baseline resting conditions, and *decreased* when subjects attended to an experimental task. This network of rest-active areas — including medial temporal, medial prefrontal, midline, and parietal regions (reviewed in Buckner *et al.* 2008) — has reminded the neuroscience community that in rest, as in sleep, the brain continues to process information and to generate conscious experience.

Default mode brain function shares features with sleep and dreaming which suggest resting wakefulness as a practical model for investigating neurophysiological relationships between memory systems and subjective experience across states of consciousness. Fundamentally, resting wakefulness and sleep share a dramatically reduced attention to sensory input. In sleep, inhibition at the level of the thalamus dramatically increases sensory thresholds and effectively blocks input from the outside world — this inhibition has long been thought to facilitate the emergence of dream imagery. In waking rest, we likewise turn our attention away from the environment and towards *internally* generated thought and imagery. During

wakefulness, the prevalence of daydream-like 'stimulus-independent thought' varies reciprocally with sensory demands, increasing with interstimulus interval in signal detection tasks.

Most recently, Buckner *et al.* (2008) have reported that default network activity is enhanced under conditions of reduced sensory monitoring that increase the incidence of stimulus-independent thought. Furthermore, individuals reporting more task-irrelevant thoughts of the past and future during a resting condition exhibited increased functional connectivity between medial temporal lobe structures and other components of the default network. In pathological conditions as well, reduction of sensory input produces imagery and hallucination — for example, in Charles Bonnet syndrome or during periods of extended visual deprivation. Thus, reduction of sensory processing alone may partially account for the emergence of spontaneous mental experience during both resting wakefulness and sleep, with the generation of this mentation in both of these states being related to activity in default-network structures.

The content of thought and imagery during resting wakefulness also shares many features with dream experience. Although reports of daydreaming are typically shorter and less fantastical than REM-stage dreaming, at times these experiences can be highly visually vivid and bizarre. Conversely, dream reports from early-night sleep often consist of unremarkable reminiscences and musings indistinguishable from waking thought. More specifically, both waking daydreams and nocturnal dream experiences contain a mélange of fragments from recent and remote episodic memory. Thus, far from being an obscure symbolic language in need of interpretation, both waking thoughts and dream experiences are transparently centered on people, activities, and ideas experienced in daily life.

Of course, not all dreaming can be characterized as a simple recombination of discrete waking events — spontaneous cognition in both sleep and waking synthesizes novel content by interleaving memory elements with related concepts, images, emotions, and themes. The resulting experiences are replete

with objects, events, and narratives never encountered in waking life. During wakefulness, this process of constructing novel scenes and scenarios from mnemonic content has been studied in the context of 'future projection', scene construction, and the generally 'constructive' nature of memory.

The default mode brain state also shows striking neurophysiological similarities with sleep. The pattern of regional brain activation that defines the 'default mode' during resting wakefulness overlaps substantially with patterns of preserved brain activity identified in imaging studies of sleep. Perhaps most notably for our purposes here, regional activity in memory-related areas of the medial prefrontal cortex and medial temporal lobe is relatively preserved throughout all stages of sleep, even in the face of dramatically decreased overall cerebral blood flow during NREM stages. These same areas are critical components of the resting state default network. Certainly, patterns of brain activation are not identical during quiet wakefulness and sleep — for example, some parietal regions identified as key components of the default network show distinct deactivation during sleep.

There are neurochemical similarities too. During early-night NREM sleep — when neural-level reactivation of memory is prominent in rodents and when 'cognitive-level replay' of recent learning experience is particularly evident in dreaming — acetylcholine levels are at a minimum. Similarly, during quiet wakefulness, acetylcholine is reduced to about 60% of active waking levels. The decreased acetylcholine levels characteristic of these states are thought to promote the consolidation phase of episodic memory by supporting information flow from the hippocampus out through the entorhinal cortex. Note, however, that decreased acetylcholine cannot be taken as a precondition for the emergence of spontaneous offline cognition, as acetylcholine levels during REM sleep dreaming actually exceed those in wakefulness. Different neurochemical conditions in REM sleep *versus* NREM and quiet waking may support different forms of memory processing in these states. Indeed, REM and NREM sleep have been implicated in the consolidation of different forms of memory, while REM

and NREM dream experiences tend to incorporate different types of memory source.

Finally, during both quiet wakefulness and NREM sleep, the medial temporal electroencephalogram (EEG) is characterized by hippocampal 'sharp-wave ripple' events, brief (~100 ms) population bursts associated with high-frequency (>100 Hz) 'ripple' oscillations. In sleep and waking rest, the reactivation of memory traces in rodents occurs during these sharp-wave ripple events. These electrophysiological events are thought to support hippocampal-cortical communication involved in consolidation of memory. Taken together, these observations indicate that memory-related activity — which represents a prominent feature of the default state — is relatively preserved during sleep (at least during NREM), further suggesting that mnemonic processing contributes similarly to the generation of dreams during sleep, and daydreams during relaxed wakefulness.

Although the functional significance of default-network activity remains a topic of debate, several proposed functions for resting brain activity overlap with those ascribed to sleep states. Most relevant for the present discussion is the notion that memory consolidation occurs during offline resting wakefulness, as well as during sleep. As mentioned above, it is well-established that sleep following learning leads to an enhancement of memory, relative to an equivalent period of active wakefulness. However, several recent studies indicate that, for certain types of learning task, a period of quiet wakefulness may also be beneficial for memory retention. Although there is scant evidence addressing the question of whether default-network activity is involved in memory consolidation, the strong activity of memory-related networks during the default state, in concert with the mnemonic contents of daydreaming, support such a hypothesis.

Recently, default-mode brain activity has also been conceptualized as a vehicle for 'future-projection', in which past experience is used to construct stimulations of possible future events. This description of cognition during the default state — in which fragments of past experience are recombined into novel scenarios —

is formally identical to the description of the incorporation of memory fragments into dreams described above. Thus, default network brain activity appears to share meaningful features with the neurophysiology of sleep, and supports a form of mental experience similar to dreaming ('daydreaming'), in which memory consolidation processes involving the reactivation and recombination of memory fragments contribute to the content of concomitant mental experience.

In summary, research on the default mode suggests that we must abandon the entrenched view of dreaming as an unintelligible and mysterious phenomenon relying on entirely unknown brain processes and serving little or no function. Instead, dreaming is more accurately seen as part of a continuum of subjective experience spanning states of sleep and wakefulness, and serving mnemonic functions related to the evolution of memories, including both the consolidation of existing memory and the simulation of possible future events.

A new model of dreaming

Of course, it has been recognized for many decades that elements from recent and long-past memories form much of the content of dream experience. Indeed, analysis of dream content led several theorists to postulate a role for dreaming in processing past experience and planning for the future, prior to much of the neuroscientific evidence reviewed above. Current work on future projection during the default state echoes, for example, the work of Antti Revonsuo exploring dream cognition as a vehicle for 'threat simulation', in which emotionally laden scenarios are played out during sleep, in preparation for future experience. In studies dating back to the 1960s, dream researchers John Antrobus and David Foulkes proposed influential models of dreaming-as-cognition, which viewed subjective experience during sleep as an extension of, rather than a departure from, the activities of the brain during wakefulness. It is only recently, however, that empirical evidence to support a detailed brain-based model of dreaming cognition has been available, with science now in a position to answer questions about the nature and function of

dream experience that seemed intractable only a few decades earlier.

These observations lead us to a view of dreaming as of the product of a mind that is constantly encoding and processing information about the world. When sensory input is at a minimum, newly formed memory traces are stabilized during offline states of quiet wakefulness and sleep, through the repeated reactivation of experience-related activity patterns. During sleep, this reactivation of memory traces contributes to the imagery, thought, and narrative of dreaming. During wakefulness, memory reactivation and consolidation constitute one important function of the default network state, contributing to the thought and imagery characteristic of 'daydreaming'.

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Further reading

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