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Relationship between dreaming and memory reconsolidation

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ABSTRACT

Dreaming is a ubiquitous phenomenon in human beings and has been discussed, researched, and hypothesized since a long time. The substrate, physiological mechanism, and function of dreaming have been explained by many scientists from the neurological, psychiatric, psychological, and philosophical perspective. With the development of scientific technology, many theories of dreaming have been established. In the present review, we first summarize the different theories of dreaming; furthermore, we introduce memory consolidation and reconsolidation. Lastly, we propose that memory might be associated with memory reconsolidation and list the explanations.

1 Introduction

Dreaming is a ubiquitous phenomenon in human beings that has been discussed and recorded for a long time. During the century-long epoch of experimental science focusing on dreaming research, quite a few theories have been proposed by different academic groups. However, the mechanism and function of dreams is still unknown, and whether dreaming is related to cognition, consciousness, and other neuropsychiatric disorders is still controversial.

2 Different theories of dreaming

As dreaming is elusive, quite a few basic unanswered questions in contemporary dream research studies still exist. When dreams happen, how long each dream lasts, how many dreams occur every night, how dreams can be controlled, and whether a dream can be recalled entirely or partly are still unknown. Especially with respect to the research studies that focused on the dream content, researchers could do nothing more than record dreamers' subjective

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descriptions of their randomly appearing episodes. This might partly explain the many controversial theories on the mechanism and function of dreaming as well as the distinct perspectives from which dreaming should be studied.

2.1 The threat simulation theory

The Finnish psychologist Antti Revonsuo recently proposed a hypothesis called threat simulation theory, which explains the fearful characteristics of dream content [1, 2]. According to this theory, dreams serve as virtual training places to improve threat avoidance or threat fighting ability. The theory postulates that such nocturnal training makes the dreamer more efficient at resolving future threatening situations during wakefulness.

2.2 The psychoanalytic theory

This theory was developed by the neurologist Sigmund Freud [3] in the beginning of the twentieth century and proposes answers to the questions raised earlier. Indeed, his theory of the human mind comprises hypotheses about the rules of selection and organization of the representations that constitute dreams. For Freud, the dream is a highly meaningful mental product that is the outcome of particular mental processes under the circumstances of sleep. The meaning of the dream is not apparent in the “manifest content”, which is the dream as recalled by the dreamer, but is to be found in the “latent dream thoughts”, some of which are unconscious; the latent thoughts have to be uncovered by processes of association to the manifest elements of the dream, as the latent dream thoughts are transformed into the manifest dream by what are called primary process mechanisms, a primitive form of thinking that is predominant in dreams. Primary process mechanisms include condensation, the combining or fusing of two or more elements into a single one, and displacement, a shifting of emphasis from one element to a

different one. The primary process mechanisms also subserve the need for disguise, or censorship, of the conflicted wishes to avoid arousing excessive anxiety and disturbing sleep.

2.3 Activation-input-modulation model

Hobson and associates have been major contributors to the understanding of the sites and neurochemical interactions in the brain stem (pontine especially) that are involved in the generation of rapid-eye movement (REM) sleep [4]. In the activation portion of the model, the authors view the brain stem as providing random, direct stimulation of the forebrain such as the oculomotor, vestibular, and motor systems, accounting for the prominence of visual and movement elements in dreams. The forebrain is seen as attempting to synthesize the information that has been generated, perhaps by a process in which “best fits to the relative inchoate and incomplete data are called up from memory, the access to which is facilitated during dreaming sleep”. The forebrain may be making the best of a bad job in producing even partially coherent dream imagery from the relatively noisy signals sent up to it by the brainstem [5]. The formal qualities of dreams are directly derived in this model from the properties of the brainstem stimulation. Dreams in this view are not essentially meaningful, although some meaning may accrue secondarily in the efforts of the forebrain to make sense of its physiologically determined stimulation.

The activation-input-modulation (AIM) mode utilizes a three-dimensional space concept for explaining in neurobiological terms the entire spectrum of brain-mind states on the basis of the variables of activation (level of brain activation), input source (external sensory versus internally generated), and modulation (neuromodulatory balance between aminergic and cholinergic influences, thought to affect the mode of cognitive

functioning). The REM sleep, when most dreaming events occur, is thus seen as involving a high level of activation (hence the intense mental activity), internal rather than external input, and aminergic demodulation (related to the diminution of such qualities as logic, orientational stability, self-reflective awareness, and memory).

2.4 Memory consolidation

Currently, a new hypothesis in cognitive neuroscience tried to credit sleep and dreaming with a role in memory consolidation. [6]. At first, decreased performance during the post-training day in sleep-deprived subjects suggested that the replay of brain activity at night contributes to memory consolidation [7]. Only recently, however, have experimental results in humans argued in favor of a role of dreaming *per se* in memory consolidation.

Memory consolidation is believed to involve the integration of multiple experiences and the extraction of generalities. During dreaming, the intermingling of memory fragments into novel and sometimes bizarre combinations could reflect this adaptive process. However, the two types of hypothesis, namely “continuity hypothesis” and “discontinuity hypothesis”, are conflicting. They both support the memory consolidation function of dreams, although some interesting phenomena exist during dreaming. For example, discontinuity could present, in extreme cases, as dissociation in waking or bizarreness in dreams [8]. REM dreams are especially typically bizarre [9], featuring sudden changes and eliciting feelings of strangeness, curiosity, or mystique upon awakening. Another example is an array of literatures concerning negative emotions in dreams, such as anger, worry, sadness, and fear. This could be explained by “boundary conditions”, that is, memory should not be exactly the same when reactivation, otherwise memory could not be consolidated [10]. This negative valence dreams are

not similar to the waking world. This phenomenon could also be explained by the theory of Hughes that states that, “the more bizarre, dramatic and absurd is the cue, the more resilient is the memory to which the cue has been associated” [11].

2.5 Neurocognitive theory of dreaming

Domhoff and his colleagues proposed that dreaming is what occurs when the mature brain is adequately activated and disconnected from external stimuli without self-reflection [12]. This theory was supported by the similarities between mind wandering and dreaming [13].

Research focused on the specific nature of the thinking supported by the default network has revealed two subsystems within it, the dorsal medial subsystem activated by instructions to think about the present situation or a present mental state and medial temporal subsystem is activated by thinking about personal situations and decisions in the future [14]. The former activation and latter deactivation could explain why dreaming as intensified mind wandering is often focused on the dreamers’ concerns about their relationships with significant others, regrets about the past, and worries about anxiety-arousing future events [15]. This phenomenon is also found in mind wandering.

In their opinion, dreams probably have no function, but they do have coherence and meaning, which is often conflated with function. Dreaming might be a by-product of the evolution of sleep and consciousness. The neural substrate for dreaming is a subsystem of the default network [16].

3 The phenomenology of dreams

The level and nature of our conscious experience varies dramatically in sleep. During slow-wave sleep (SWS) early in the night, consciousness can nearly vanish despite persistent neural activity

in the thalamocortical system [17]. Subjects awakened from REM sleep, report “typical”, full-fledged dreams, which are vivid, sensorimotor hallucinatory experiences that follow a narrative structure [5].

4 The source of the dream content

Despite the hypotheses based on oversimplified approaches to dream analysis (e.g., the continuity hypothesis versus the discontinuity hypothesis), psychological studies demonstrated that dream content had some precise phenomenological characteristics [18]. For example, visual imagery occurs more frequently in dreams than imagery of other senses (audition, olfaction, touch, and taste). The dream drama is mostly lived by the dreamer from a first-person perspective; some elements of real-life events previously experienced by the dreamer often contribute to the scene of the dream. Most often, the dream sequence is not within the dreamer’s voluntary control (i.e., the dreamer may be convinced during the dream that the dream’s story is really happening). Temporal and spatial incoherencies can occur in the dream story; the dream report is often full of people interacting with each other (e.g., discussions, fights, pursuit, and sexuality). Finally, the dream report often contains strong emotions.

5 Similarities between dreaming and waking

Dreams are highly visual, in full color, rich in shapes, full of movement, and incorporate typical wakefulness categories such as people, faces, places, objects, and animals. Dreams also contain sounds (including speech and conversation) and, more rarely, tactile percepts, smells, and tastes, as well as pleasure and pain [11, 19].

These phenomenological similarities are reflected in neurophysiological similarities between waking

and dreaming. At least superficially, electroencephalography (EEG) looks remarkably similar in active waking and REM sleep. Positron emission tomography (PET) studies have shown that global brain metabolism is comparable between wakefulness and REM sleep [5, 20]. Such studies have also revealed a strong activation of high-order occipitotemporal visual cortex in REM sleep, consistent with the vivid visual imagery during dreams [21, 22].

Moreover, a remarkable consistency was observed between a subject’s cognitive and neural organization in dreaming and waking [8, 23]. For instance, children studies demonstrated that dream features show a gradual development that parallels their cognitive development when awake [24].

Dreams also reflect our interests and personality, just like mental activity during wakefulness. Formal content analysis has revealed that mood, imaginativeness, individuals of interest, and predominant concerns are correlated between our waking and dreaming selves [8, 11, 16].

6 Dissimilarities between dreaming and waking

Still many phenomenological dissimilarities exist between dreaming and waking [25]. During dreaming, dreamers have reduced voluntary control and volition. For example, they usually do not have conscious will that they would dream it; meanwhile, they cannot pursue goals and have no control over the dream’s content.

In dreams, dreamers have reduced self-awareness and altered reflective thought. They are not contextually aware of where they are (in bed) or of what they are doing (sleeping and dreaming).

Some dreams are characterized by a high degree of emotional involvement, including joy, surprise, anger, fear, and anxiety [26]. Dreamers

also have altered mnemonic processes. Memory would be drastically altered for the dream and within the dream. Unless the dreamer wakes up, most dreams are forever lost. Upon awakening, memory for the dream often vanishes rapidly unless written down or recorded, even for intense emotional dreams.

7 Relationship between dreaming and REM sleep

It was reported that 74%–80% of awakenings during REM sleep resulted in vivid dream recall, compared to only 7%–9% of the awakenings during NREM sleep [27]. It was only natural to conclude that, compared to NREM sleep, the distinct physiologies of REM sleep, and especially its fast, low-voltage EEG characteristics resembling those of wakefulness, were why individuals are conscious and dream during REM sleep and not during NREM sleep [28].

Early in the night, when stage N3 is prevalent, and predominantly, large slow waves are observed on EEG, awakenings yield few dream reports [29]. Moreover, these reports are often qualitatively different from typical REM sleep reports, usually being short, thought-like, less vivid, less visual and more conceptual, less animated in terms of motion, under greater volitional control, more plausible, more related to current issues, less emotional, and less pleasant [30]. Moreover, although the average length of REM sleep reports increases with the duration of the REM sleep episode, this is not true for NREM sleep reports [22]. Indeed, 10%–30% of all NREM sleep reports are indistinguishable from REM sleep reports, irrespective of the criteria used [31, 32].

Neuropsychological evidence indicates that dreaming and REM sleep can be dissociated: forebrain lesions may abolish dreaming and spare REM sleep, whereas brainstem lesions may nearly eliminate overt features of REM sleep without

abolishing dreams [33].

It has become clear over time that there is considerable mental activity that occurs during NREM sleep. Typically, it is more thought-like, fragmentary, and related to daily concerns compared with the vivid, hallucinatory, and predominantly visual narratives that are most commonly reported from REM sleep. Awakening during the REM period most often results in dream recall; recall rate drops rapidly if the awakening is delayed until after the REM period has ended. Other physiological features of REM sleep have been considered in terms of their relevance to dreaming; one is the muscle paralysis that accompanies that state, which is viewed as protection against acting out dreams.

8 Neurotransmitters and other chemicals changes during dreaming

What determines the characteristics of dreaming? It is now widely accepted that REM sleep is cholinergically potentiated and aminergicly suppressed [12]. More recently, using molecular techniques and selective manipulation of REM sleep, it has been confirmed that the cholinergic pedunculopontine tegmental neurons are REM-on cells and serotonergic dorsal raphe nucleus and noradrenergic locus coeruleus neurons are REM-off cells [34]. It has also become clear that GABA (γ -aminobutyric acid) and glutamate participate in this process [5].

Llewellyn thought that during dreaming, increasing mesolimbic DA is associated with increasing cholinergic neuromodulation. Thus, dynamic reciprocity characterizes not only aminergic/cholinergic systems but also mesocortical/mesolimbic dopaminergic systems and mesolimbic dopaminergic/cholinergic systems [35].

9 Potential limitations of different theories

Although the Freudian notion that dreams

have a “hidden meaning” disguised in symbolic language has become entrenched in popular folk psychology, there is scant empirical evidence to support this view. So far, Solms has tried to integrate his findings closely into Freud’s model of dreaming through several lesion studies. However, Solms believes that of the major elements of that model, clear neurobiological evidence for censorship is lacking [36].

As Solms argued [36], the level of dream recall can be modulated by dopamine agonists [37, 38] without concomitant modification of the duration and frequency of REM sleep. Dream recall can be suppressed by focal brain lesions (in the temporo-parieto-occipital junction and ventromedial prefrontal cortex) [26, 39]. These lesions do not have any appreciable effects on REM frequency, duration, or density [40].

Developments in the cognitive neuroscience of memory have recently led to a new brain-based framework for understanding dreaming, in which dream experience is considered a form 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.

The theory about dreaming proposed by Wamsley and Stickgold integrates “the threat simulation theory”, “memory consolidation”, and “default-network mode” hypotheses. However, their studies show that, during early-night NREM sleep (when memory reactivation in animals is at its strongest), dream content is more likely to reflect recent learning experiences than during REM sleep [41].

10 Phenomenon of memory reconsolidation

Since more than 100 years, in the memory research

field, consolidation has been defined as a time-dependent stabilization process that eventually leads to the permanent storage of newly acquired memory [42, 43].

However, empirical data indicate that the retrieval of a memory trace can induce an additional labile phase that requires an active process to stabilize the memory after retrieval [44]. Recently, this process has been called reconsolidation, and is hypothesized to be an important component of long-term memory processing [45, 46].

Reconsolidation is frequently studied using Pavlovian fear conditioning paradigms, and the procedure is described as follows. Training is conducted in the absence of any mnemonic manipulations and involves pairing a neutral stimulus (conditioned stimulus (CS)), such as a tone, with a reinforcing stimulus (unconditioned stimulus (US)), such as a footshock. Retrieval is induced in a reactivation session, which occurs at least 24 hours after training and consists of a presentation of the CS (typically in the absence of the US). The manipulation (such as protein synthesis inhibition) is applied either prior to, or immediately after, the reactivation session. Finally, at least 24 hours after the reactivation session, the memory is tested by re-presenting the cues and measuring the conditioned response (in this case, fear elicited by the CS) compared with animals in the non-manipulated control group. Many studies have reported that the manipulation groups lack responses in the testing session, indicating that the memory enters the labile state after the retrieval session [47, 48].

There are some conflicting findings on the presence of reconsolidation after retrieval, which have led to a discussion regarding the limiting factors. In some physiological, environmental, or psychological situations, memory normally does not reconsolidate. Such a phenomenon called boundary conditions has been described. For

example, in some circumstances, extinction rather than reconsolidation occurs after a reactivation trial [49, 50, 51].

The age of the memory, i.e., time from training [52, 53], memory strength (or amount of training) [54], length of the reactivation trial [55, 56], contextual choices [57], and predictability of the reactivation stimulus are important determinants of whether reconsolidation or extinction occurs after a reactivation trial.

Actually, more than a decade ago, the relationship between sleep and memory was extensively investigated. Stickgold et al. studied and proposed “sleep-dependent memory consolidation” and reported data to reveal the role of sleep in memory processing, as well as the different roles of NREM and REM sleep [58, 59]. Furthermore, they proposed that dreams might be associated with off-line memory reprocessing [60].

11 Dreaming and reconsolidation

To our knowledge, the importance of NREM and REM sleep in memory processing has been previously reported [61, 62, 63], and sleep, indeed, benefits memory consolidation. However, if we determine an aspect in which dreaming has more contribution, its key role in memory reconsolidation might be observed to be more reasonable than that of consolidation.

Owing to the reconsolidation process, two aspects must be explained to illustrate that dreaming correlates with reconsolidation. First, dreaming is associated with the reactivation of waking life. Second, dreaming could induce memory reconsolidation. Indeed, many studies have shown possible findings supporting our proposal. For example, except for certain factors (nightmares or bad dreams), dreaming could be seen as a reactivation of waking experience [64]. Furthermore, as also reported by Osan et al. [65], nonreinforced re-exposure has three possible

outcomes, namely (a) simple retrieval (i.e., absence of reconsolidation or extinction), (b) reconsolidation, and (c) extinction (a type of new memory consolidation), which potentiated the probable function of dreaming reactivation (reconsolidation). In the following section, we will discuss both aspects in detail.

Dreaming refers to the processing of reactivation/retrieval of all types of learning content before itself. Because REM sleep dreaming is characterized by high visuality, vividness, and clarity, we have to consider dreams as the first-choice of memory reactivation material, reiterating Leonardo da Vinci’s famous comment “seeing more clearly in dreams”.

First, from the perspective of phenomenology, dream content analyses have shown that the most sources of dreams come from the dreamers’ waking activity before. According to the data from Hobsons and colleagues, 65% of dream elements are associated with waking-life experiences [66]. In dreams, dreamers may encounter their relatives and friends, fulfill their latest schemes, complete their daily housework, and so on. Perhaps the most striking feature of conscious experiences during dreams is how altogether the inner world of dreams is similar to the real world of wakefulness. Many aspects of subjects’ daily life have been found to influence the dream content, including news events [67], musical practice [68], religious beliefs [69], chronic pain [70], mood [71], or a violent living environment [72]. This feature of dreams makes us consider that dreams are the reactivation of daily life, or more precisely, are associated with what dreamers have learned in the awake state.

Many reports of dreams often appeared to contain some unusual features [73], for example, the dreams of “a city in a suitcase” and “strawberries becoming enormous within minutes” described in the review by Desseilles and colleagues [74]; the “flying dream” that was

discussed in the dialogue between Hobson and Schredl [75]; and the example that Nir mentioned, in which a character had the name, clothes, and hairstyle of a male friend but the face of the individual's mother [18]. Meanwhile, during most dreams, events and characters are perceived to be real, although reflective thought processes such as thoughtful puzzlement about impossible events may be conserved in some dreams. This circumstance is similar to what subjects involved in behavioral experiments and trials of reconsolidation experience. As suggested by Tronson and Nader, "predictability of the reactivation stimulus" is a component of the boundary condition for memory reconsolidation [76, 77]. This assumption is consistent with the findings of Pedreira et al. [78], which were put forth based on the escape response elicited by the presentation of a visual danger stimulus in the crab *Chasmagnathus*. In this study, reconsolidation only took place when a predictive context concluded with an unexpected outcome.

The feasibility of the reconsolidated memory formation would be challenged, since the dream-resulted memories might not be useful directly because of their absurdity. Llewellyn thought except the value per se, the main function of these memories was to produce cues or "chains of association that regenerate memories" [35]. The more bizarre, dramatic, and absurd is the cue, the more resilient is the memory with which the cue has been associated [73]. This explanation could also be applicable to the dreaming-related memory reconsolidation.

Context is quite important in many reconsolidation studies, and contextual similarity/dissimilarity is considered as one of the boundary conditions by reconsolidation researchers [48]. Osan et al. [65] believed that only similar contextual re-exposure, rather than identical contextual re-exposure or radically different contextual re-exposure, could induce reconsolidation in non-

reinforced trials. If we review context referring to the feature of REM sleep dreaming, we will find that dreaming is an ideal context for memory reconsolidation. On one hand, the scene is so vivid and lifelike during dreaming that dreamers perceive it as real; on the other hand, most dreams are somewhat bizarre, which will not make the dreamers wake up. Similar to the right degree of contextual dissimilarity in reconsolidation, in this way dreaming could be appropriate for memory reconsolidation.

Second, the time window of memory reconsolidation and dreaming should be considered. Both the threat simulation theory proposed by Antti Revonsuo [2] and the Memory Consolidation proposed by Stickgold [59] definitely indicated that dreaming is helpful for the dreamers' future. This supports the theory of memory reconsolidation, which emphasized that retrieving, and hence reconsolidating, memories may provide the advantage of strengthening adaptive memories, without requiring re-exposure to the original learning situation [74], as well as memory updating [75] and erasing memory/memory deconsolidation [76]. If we try to find out more direct evidences to confirm their relationship, it would not be difficult. In 2011, Bladgrove et al. [78] studied the relationship between day-residue and dream by using a dream diary. In their study, they observed that after the frequent incorporation of memory elements from the previous day into dreams, they found a lower incorporation of memory elements from 2 to 4 days before the dream, but observed an increased incorporation of memory elements from 5 to 7 days. As they could not preclude the weekly periodic confound, there are two irrefutable findings. First, the first day effect is quite important in dreaming; second, the effective time window for incorporation of day-residue into dreams is one week. Actually, most of the researches referring memory reconsolidation were designed to evaluate the

reactivation and subsequent results 1 day after the conditioning. Furthermore, Clem and Hugarir's study revealed that memory reconsolidation would be impossible one week after the conditioning [79]. Another indirect evidence is that a 6-hour period is one of the boundary conditions of memory reconsolidation; moreover, no dream lasts longer than that.

Third, memory reconsolidation is considered related to memory updating, and was called as "cue-dependent amnesia" for many years [37]. Memory updating might be accompanied with unrelated memory elimination inevitably. For dreamers, memory is drastically altered for the dream. Upon awakening, memory for the dream often vanishes rapidly unless written down or recorded, even for intense emotional dreams. Unless the dreamer wakes up, most dreams are forgotten. It is possible that the loss of memory after dreaming is a by-product of reconsolidation. This explanation has also been supported by the hypotheses of neuroscientists and molecular biologists such as, Francis Crick (the "father" of DNA) and Graeme Mitchison in which they state that dreams eliminate "spurious memories" created in the brain by overlapping with the process of storing memories [80].

Fourth, dreaming is the result of cholinergic and aminergic transmitters, and both of these systems participate together in consolidation and reconsolidation. This could explain the relationship between dreaming and memory reconsolidation. For example, by using nicotine contextual fear memory reconsolidation in rats, Tian et al. [81] observed positive effects of the cholinergic system. Indeed, evidence showing that cholinergic neurons induce REM sleep dreaming is stronger [12]. In sleep research in rats, Stickgold et al. [82] demonstrated that the expression of an immediate early gene, *zif-268*, increases in the hippocampus during REM sleep. Furthermore, contextual fear conditioning in rats

conducted by Lee revealed that hippocampal *zif-268* protein expression is required during reconsolidation [81]. Similarly, Ribeiro et al. [61] found that exposure to learning conditions during waking leads to increased extrahippocampal *zif-268* expression during the ensuing REM sleep. Considering the positive correlation between the noradrenaline system and increase in *zif-268* expression, this phenomenon appears slightly paradoxical, as the activity of the cholinergic system is higher than that of the noradrenergic system during REM sleep. Ribeiro and his colleagues cited the findings of Greenberg et al. [83] and Shiromani et al. [84], and explained that robust cholinergic transmission in REM sleep could in principle compensate for the lack of noradrenaline, setting in motion molecular cascades that would result in the upregulation of *zif-268*.

Fifth, during REM sleep, limbic and paralimbic structures, including amygdaloid complexes, hippocampal, and anterior cingulate cortex (ACC) were found hyperactive [64], all these regions are considered to be associated with dreaming. Interestingly, both the amygdala and hippocampus were found to participate in reactivation and reconsolidation of emotional episodic memory [85].

In summary, a unified understanding of dreaming is still lacking, because of its features. However, a comparison of the dreams of individuals who frequently experience dreams with those of rats in reconsolidation studies reveals a similarity. They have higher visual ability in daily life and are usually more emotional. They encounter some familiar scenes (meeting a person somewhere) that are not exactly similar as those before. They take what they feel as real, even to vital. They are oblivious to the events that will occur and these are controlled by their own will. We believe that the most sophisticated mechanism is thalamic gating, which prevents

the dreamers from acting the dream, similar to an apparatus that helps researchers get rid of rats' biting. This is possibly the relationship between dreaming and reconsolidation.

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