

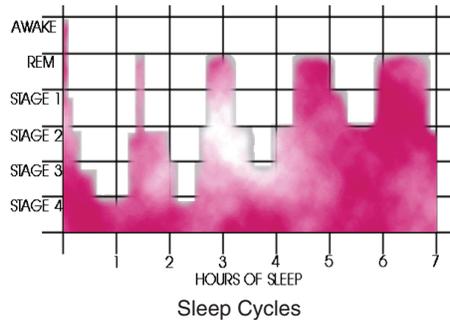


## The Sequential Hypothesis

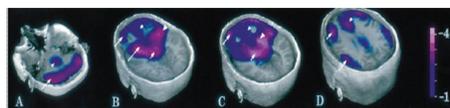
REM sleep, stage II sleep, and slow wave sleep are all important in the consolidation of memory. The idea that only REM sleep and no other stages of sleep were important in memory consolidation was a result of some of the early studies during the 1970s and 1980s that demonstrated that REM sleep would increase after learning but the same increase would not be seen for slow wave sleep.<sup>1,2,3</sup> More recently other studies have attributed a role for part of the memory consolidation process to slow wave sleep and the sleep spindles of stage II sleep.

Although many early researchers believed that either REM or slow wave sleep, but not both, were important for the consolidation of memory, the idea that both of these states are important and very importantly work together *in sequence* was first documented in 1977 by Antonio Giuditta M.D.<sup>4</sup> He realized that things in nature happen for a reason and when there are two sides to an argument, the truth typically resides somewhere in the middle. He was a visionary when few if any others could yet see the light. It was clear to him that during sleep cycles, slow wave sleep must precede REM sleep for a reason. He believed that newly acquired memory traces first underwent a processing step during slow wave sleep that allowed their further processing during REM sleep.

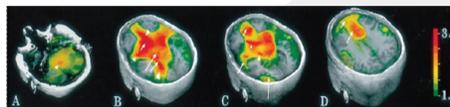
Dr. Giuditta believed that by discarding some memories while retaining others, an animal could adapt to changing circumstances. His initial theory in 1977 was that slow wave sleep was necessary for clearing unnecessary memories and experiences, and that REM sleep must be more important in keeping the memories that matter. It seemed to make sense to erase less important memories first, before implementing the step that keeps



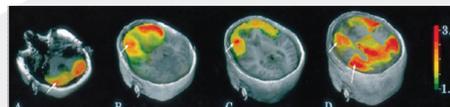
the good ones. The sequence of slow wave sleep invariably preceding REM sleep present throughout the cycles of the sleep of all mammals certainly seemed to support this logic. Additionally, human fetal sleep is largely REM sleep.<sup>5</sup> This decreases as we age.<sup>6</sup> The logic here is that REM sleep must be high initially as the animal is learning from scratch and that there is little need for slow wave sleep initially if there is nothing yet to forget.<sup>7</sup> A human fetus in its mother's uterus may spend fifty to eighty percent of its time in REM sleep. The question that comes to mind is what could that fetus possibly be learning? Mozart?



Wake to Slow Wave Sleep<sup>10</sup>



Slow Wave Sleep to REM Sleep<sup>10</sup>



REM Sleep to Wake<sup>10</sup>

Scientific theories are based on all of the information available at the time they are concocted, and are apt to change slightly as new information becomes available. Since the publishing of his initial theory in 1977, Giuditta has refined his theory to some degree<sup>8</sup> to account for the replay of firing of memory sequences during slow wave sleep, but he certainly deserves the credit for being the first to realize that the different stages of sleep are all important for different reasons, and that it is the sequence of the stages that is paramount.

Throughout mammals, slow wave sleep comes before REM sleep in each sleep cycle. This sequence happens for a reason and it is this sequence that is important in the consolidation of memory. This was first realized by Antonio Giuditta M.D. in 1977.<sup>9</sup>

- 1 Comptes Rendus de l'Academie des Sciences de Paris, 1971, 273, 2595-2598.
- 2 Comptes Rendus de l'Academie des Sciences de Paris, 1971, 273, 86-88.
- 3 Physiology and Behavior, 1981, 26, 587-594.
- 4 Giuditta, A. (1977). The biochemistry of sleep. In Biochemical correlates of brain structure and function (ed. A. N. Davidson), pp. 293-337. Academic Press, New York.
- 5 Science, 1966, 152, 604-619.
- 6 Anders, T., Sadeh, A., and Appareddy, V. (1995). Normal sleep in neonates and children. In Principles and practice of sleep medicine in the child (eds R. Ferber and M. H. Kryger), pp. 7-18. Saunders, Philadelphia.
- 7 Giuditta, A., et al. (1984). The neurochemical study of sleep: In Handbook of neurochemistry (ed. A. Lajtha), Vol. 8, 2nd edn, pp. 443-476. Plenum Press, New York.
- 8 Giuditta, A., et al. (2003). The role of sleep in memory processing: the sequential hypothesis. In Sleep and Brain Plasticity. (eds P. Maquet, C. Smith and R. Stickgold), pp. 157-178, Oxford University Press, New York.
- 9 Walter, T (2007) Chapter 16, The Sequential Hypothesis. In REM Illumination Memory Consolidation (pp. 173-176), Grove City, OH: Lotus Magnus.
- 10 Braun, A. R., et al. (1997). Regional cerebral blood flow throughout the sleep-wake cycle. Brain, 120, 1173-1197.