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Inspiration from dreams in neuroscience research

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Abstract

Dreams have been cited as the source of creative ideas in many areas in both the arts and sciences. Two key examples from neuroscience research in the twentieth century were described by Otto Loewi (1873-1961) and John Eccles (1903-1997). Their dreams were pivotal in scientific discoveries which established chemical synaptic transmission. Recent work has led to some progress in understanding the biologic purpose of sleep and dreaming.

INTRODUCTION

Inspiration from dreams has been reported from diverse fields of human activity including music, literature, mathematics and science. In the area of neuroscience, two dreams stand out as examples in which scientific enquiry has been facilitated by creative ideas which came during sleep. The dreams of Otto Loewi (1873-1961) and John Eccles (1903-1997) demonstrate how their discoveries related to synaptic transmission were directed at a pivotal stage by such inspiration. These dreams highlight the intriguing question of how the brain continues to work whilst asleep.

OTTO LOEWI

Otto Loewi was awarded the Nobel Prize in physiology or medicine with Henry Dale in 1936 for their work which established chemical synaptic transmission [1]. Fig 1. He was born in Frankfurt, Germany in 1873 and graduated in medicine from the University of Strasbourg in 1896. Following studies in chemistry and experimental methods in Germany he was appointed first to the University of Marburg and from 1907 was Professor of Pharmacology at the University of Graz, Austria. He studied the effects of adrenaline and noradrenaline on diabetes and blood pressure and the response of the heart to vagal nerve stimulation.

Figure 1

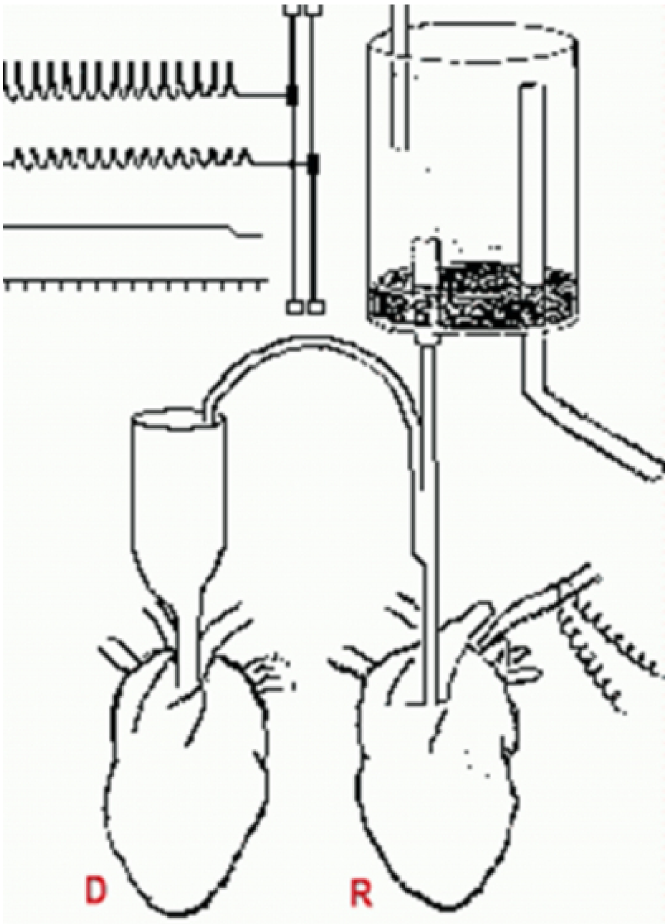
Figure 1: Otto Loewi

From around 1900 it was generally accepted that neurones were connected by synapses and initially most neurophysiologists believed that signal transmission between cells was electrical. Emil Dubois-Reymond made the earliest suggestion of a chemical synaptic process in 1877 though his theory was not supported by any experimental evidence [2].

Thomas Elliott working in Cambridge in 1904 was the first to propose that sympathetic nerve impulses may act by liberating adrenaline whilst Walter Dixon in 1907 working at Saint Thomas's Hospital London made a similar hypothesis for a muscarine-like substance in parasympathetic nerve impulses [3,4]. The notion of chemical transmission developed gradually and arose from the observation that acetylcholine and adrenaline affected organ function in a way similar to neural stimulation.

Figure 2

Figure 2: Otto Loewi's classic experiment stimulating two frogs hearts



By 1920 the definitive evidence for chemical mediation was still lacking. This was the main focus of Loewi's work at Graz. Following a period of unfruitful research, Loewi had a dream which was the inspiration for his crucial experiment. The details were recorded in his autobiography; 'the night before Easter Sunday of that year (1920) I woke, turned on the light and jotted down a few notes on a tiny slip of thin paper. Then I fell asleep again. It occurred to me at six o'clock in the morning that during the night I had written down something most important, but I was unable to decipher the scrawl.' [5] He tried unsuccessfully to recall the dream or interpret his note. On the Sunday night he went to bed and read for a time before turning out the light. He then awoke between two and three in the morning, which was unusual for him, and he knew what the nature of his dream had been that night and the previous night. He got out of bed and immediately went to the laboratory to put into action his new idea.

Loewi's experiment involved the stimulation of two hearts from frogs [6]. His simple but elegant work used beating frog's heart with vagus nerve intact in a saline bath Fig 2. The fluid from the bath was then irrigated into a heart preparation with the vagus nerve removed. Stimulation of the vagus caused the first heart to slow whilst the injected fluid slowed the second one. Loewi called the chemical substance 'vagusstoff' whilst the substance released in sympathetic nerve stimulation he referred to as 'acceleranstoff'. In 1926 vagusstoff was identified as acetylcholine whilst in 1936 acceleranstoff was found to be adrenaline.

JOHN ECCLES

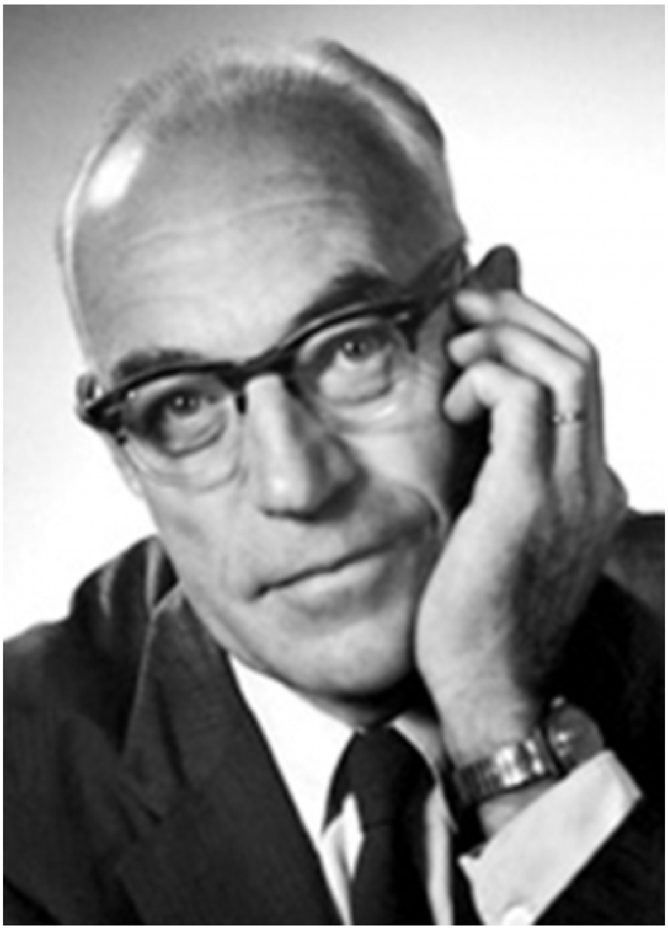
Despite the award of the Nobel Prize in 1936 to Loewi and Dale, the debate on chemical transmission was far from settled. Neurophysiologists led by John Eccles disputed the concept that chemical mediation occurred in the central nervous system principally because of the fast rate of signal transmission. For a number of years the chemical-electrical controversy continued and was fought vigorously but with mutual respect from the protagonists. A significant breakthrough occurred when Eccles team performed a series of experiments at the University of Otago, New Zealand in 1951which provided unequivocal evidence that central nervous system transmission was a chemical process [7].

John Carew (Jack) Eccles was one of the foremost neurophysiologists of the twentieth century [8]. Fig 3. He was born in Melbourne, Australia in 1903 and graduated with first class honours from the University of Melbourne in 1925. He travelled to Oxford as a Rhodes Scholar where he came under the tutelage of Sir Charles Sherrington. At Oxford he joined Sherrington's team studying spinal reflexes in the cat which culminated in the classical monograph published in 1932, 'Reflex Activity of the Spinal Cord' by Creed, Denny-Brown, Eccles, Liddell and Sherrington [9]. His long period of research at Oxford, Sydney, Dunedin, Canberra, Chicago and Buffalo spanned five decades and in 1963 he was awarded the Nobel Prize in Physiology or

Medicine with Huxley and Hodgkin for his work on the synapse.

Figure 3

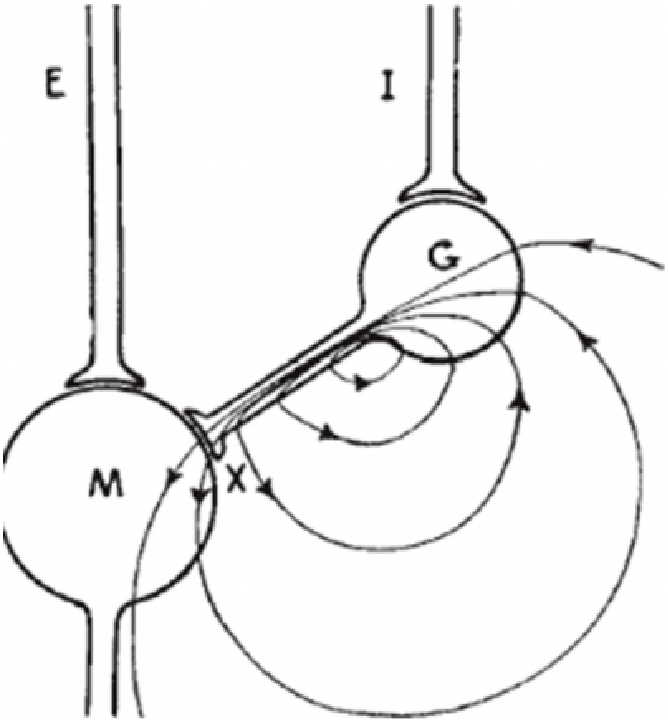
Figure 3: John Eccles



A key element of Eccles' work was also inspired by a dream. In 1944 Eccles met the philosopher Karl Popper who influenced him in the need to formulate clear hypotheses and test them by rigorous experiment. Whilst at the University of Otago as Professor of Physiology, his work was on the mode of electrical synaptic activity based on ephaptic studies. His Golgi-cell theory originated in a dream in 1947 [10]. He recalled in his memoirs; 'Then in 1947 I developed an electrical theory of synaptic inhibitory action which conformed with all the available experimental evidence. Incidentally this theory came to me in a dream. On awakening I remembered the near tragic loss of Loewi's dream so I kept myself awake for an hour or so going over every aspect of the dream, and found it fitted all experimental evidence.' The details were diagrammed and published in Nature in 1947 and became known as the Golgi-cell theory of inhibition [11] Fig 4. It was an ingenious model which used the current flow of an excited interneurone to generate an electronic foci on neurones upon which the synapses were placed.

Figure 4

Figure 4: Model of Golgi-cell inhibition. I : inhibitory neuron, E : excitatory neuron, M : motorneuron, G : golgi cell



The opportunity for rigorous testing came in 1951 in experiments, which utilised the new technique of intracellular glass electrodes. Microelectrodes were inserted into cat spinal anterior horn cells and recordings made following stimulation of quadriceps nerve which was known to have a direct inhibitory action in a monosynaptic reflex. The experiment clearly established a chemical process of transmission and disproved (or falsified in Popper's terminology) the Golgi-cell theory [7]. To his credit Eccles was quick to acknowledge his error and subsequent research firmly established chemical synaptic transmission in the central nervous system and ushered in a new era of brain science and neuropharmacology.

The dreams of Loewi were described in his autobiography and were also personally related to his colleague and friend Henry Dale and his nephew Renate Justin [12]. The versions varied slightly in relation to their timing and the number of dreams experienced. Eccles broad interest in the mind-brain problem extended to some speculations on the nature and purpose of dreams in the dialogues with Popper published in the text, 'The Self and its Brain.'[13] From his knowledge of

Loewi's experiences he was aware of the potential for creative inspiration from dreams which he utilized at a key point in his own research. Eccles first spoke publicly of his dream in an address at the Henry Dale centenary symposium in 1976 [10].

CURRENT PERSPECTIVES FROM DREAM RESEARCH

Attempts to understand the nature and purpose of dreams date back to antiquity and include frequent references in sacred texts especially the Old and New Testaments of the Bible. It is clear that dreaming is an almost universal experience and there has been some growth in understanding its biologic basis. Progress in dream studies began in the 19th century with the psychoanalytic approach of Freud in his monograph ‘Interpretation of Dreams' [14]. The landmark work of Dement and Kleitman in 1957 established the link between dreaming and rapid eye movement (REM) sleep whilst in the 1970's the activation-synthesis model of Hobson and McCarthy proposed that dreaming was initiated by random neural activity in the brainstem during REM sleep [15,16]. More recently, brain-imaging studies have confirmed that several brainstem nuclei, the hypothalamus, superior colliculus, thalamus and somatosensory cortices are specifically activated during REM sleep [17]. These same circuits are concerned with consciousness and from one perspective; consciousness arises in sleep because the centres of wakefulness are activated. When subjects are aroused during or soon after REM sleep they are almost always able to report a dream whereas non-REM sleep is much less frequently associated with dream recall. It has been suggested that rapid eye movements are due to eye scanning the dream images which mostly move horizontally.

The traditional model of dreams which originated with Freud is that they are restorative and allow the brain to rest and discard any unwanted data accrued during the day. This homeostatic process allows the brain to recover from deleterious or redundant memories. More recent studies have suggested a progressive model which proposes that dreaming reflects ‘off-line' processing of acquired information consolidating or integrating it into a more useful form [18]. A report by Wagner et al revealed a striking capacity for sleep to foster creative thinking [19]. They found that subjects taught a rote mathematical process were twice as likely to discover a creative shortcut if they were allowed a night of sleep between initial training and retesting, than if they were given the same interval time awake during the day. The sleeping brain appears to be able to search out new associations or novel approaches to problem solving rather than simply performing a resting process.

Generally the only dreams which are remembered are the ones which occur around the time of waking. This was clearly evident in the inspirational dreams recounted by Loewi and Eccles. Also the most effective way of recalling a dream is to record and analyse the details at that time. In both examples the dreams were recorded immediately afterwards and documented in written form. They occurred at a time that the researchers were actively engaged in the particular problem with their minds highly focused on the concepts involved. Despite their best efforts, they lacked the ability to solve the problem at hand. The breakthrough came through their dreams, perhaps through the brains capacity during sleep to process the information in a new and more creative way.

Despite some progress in the scientific study of dreams and dreaming, it remains a relatively immature area of science. This is not surprising as it is a subfield of the study of consciousness and shares many of the same problematic features related to consensus in definitions and physiologic and biologic correlates. Historically there are numerous other reports of dreams providing creative inspiration in both the arts and sciences. Examples include Mary Shelley's dream which was the basis for her gothic novel, Frankenstein [20]. The German chemist Frederich Kekulé had a series of dreams which led to his discovery of the tetravalent nature of carbon and the formation of the structure theory of organic chemistry [21]. The reports of Loewi and Eccles in their research on synaptic transmission highlight the power of dreams as an inspiration for creative new ideas that have become foundational to modern brain science.

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