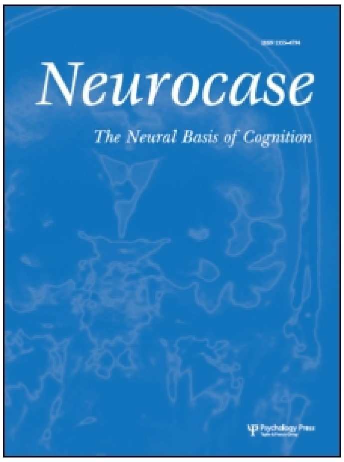

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Creative Innovation: Possible Brain Mechanisms

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Abstract

This article reviews and develops some theories about the neurobiological basis of creative innovation (CI). CI is defined as the ability to understand and express novel orderly relationships. A high level of general intelligence, domain-specific knowledge and special skills are necessary components of creativity. Specialized knowledge is stored in specific portions of the temporal and parietal lobes. Some anatomic studies suggest that talented people might have alterations of specific regions of the posterior neocortical architecture, but further systematic studies are needed. Intelligence, knowledge and special skills, however, are not sufficient for CI. Developing alternative solutions or divergent thinking has been posited to be a critical element of CI, and clinical as well as functional imaging studies suggest that the frontal lobes are important for these activities. The frontal lobes have strong connections with the polymodal and supramodal regions of the temporal and parietal lobes where concepts and knowledge are stored. These connections might selectively inhibit and activate portions of posterior neocortex and thus be important for developing alternative solutions. Although extensive knowledge and divergent thinking together are critical for creativity they alone are insufficient for allowing a person to find the thread that unites. Finding this thread might require the binding of different forms of knowledge, stored in separate cortical modules that have not been previously associated. Thus, CI might require the co-activation and communication between regions of the brain that ordinarily are not strongly connected. The observations that CI often occurs during levels of low arousal and that many people with depression are creative suggests that alterations of neurotransmitters such as norepinephrine might be important in CI. High levels of norepinephrine, produced by high rates of locus coeruleus firing, restrict the breadth of concept representations and increase the signal to noise ratio, but low levels of norepinephrine shift the brain toward intrinsic neuronal activation with an increase in the size of distributed concept representations and co-activation across modular networks. In addition to being important in divergent thinking, the frontal lobes are also the primary cortical region that controls the locus coeruleus-norepinephrine system. Thus creative people may be endowed with brains that are capable of storing extensive specialized knowledge in their temporoparietal cortex, be capable of frontal mediated divergent thinking and have a special ability to modulate the frontal lobe-locus coeruleus (norepinephrine) system, such that during creative innovation cerebral levels of norepinephrine diminish, leading to the discovery of novel orderly relationships.

Introduction

This article will discuss the possible brain mechanisms underlying creativity. Webster's II University Dictionary (Soukhanov, 1988) gives three definitions of creativity: having the power or ability to create, productive, marked by originality. Writing a list of non-words, randomly applying colors to a canvas, or generating a random list of variables may be novel or original but not creative. Thus, the Webster's dictionary definition is inadequate. According to Bronowski (1972), creativity is finding unity in what appears to be diversity. Great art works have a myriad of colors and forms and great musical works have a large variety of melodies and rhythms, but in both paintings and symphonies the artist is able to develop a thread that unites diverse elements and displays order. Creative scientists such as Copernicus were able to see order in what appeared to be a disorderly solar system and Einstein was able to see the thread that unites matter and energy. Thus, in this paper creativity is defined as the ability to understand, develop and express in a systematic fashion, novel orderly relationships.

Helmholtz (1826) and Wallas (1926) suggested that creativity has four stages, preparation, incubation, illumination and verification. Preparation is the acquisition of the skills and knowledge that allow a person to create. For example, Einstein developed superb skills in physics and math before he made his great discoveries and Picasso learned to draw forms and mix colors before he painted his masterpieces.

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Many important scientific discoveries are made when a scientist perceives significance in apparently accidental occurrences. The scientists, however, who made these discoveries must be prepared to understand the importance of these accidents. Kuhn (1996) noted that many important discoveries are initiated by the observation of an anomaly. Although these discoveries are based on an anomaly, it is the ‘‘prepared mind’’ that enables creators to perceive the importance of the phenomenon they observed. Thus, it is highly probable that creative people were incubating ideas about the phenomenon prior to the observation, but the observation altered the cognitive processes such that with the observation they have what has been termed an ‘‘Aha!’’ experience. It is this ‘‘Aha’’ experience or epiphany that Helmholtz (1826) and Wallas (1926) termed illumination. Subsequently, creative people such as scientists have to perform experiments that attempt to disprove or support their hypothesis. This is the process of verification.

In this paper, the terms preparation and verification, as suggested by Wallas (1926), will be used. The constructs of incubation and illumination, however, have received much criticism. For example, Metcalfe and Wiebe (1987) demonstrated that the subjective feeling of knowing (illumination) did not predict performance on insight problems. Weisberg (1986) suggested that creativity does not require great leaps (e.g., illumination) and the processes that lead to many great discoveries might not be subconscious incubation, but rather a series of conscious steps. Even according to Helmholtz and Wallas, illumination, rather than being an independent factor, appears to be the culmination of the incubation process. Since there is not consensus on the stages of creativity and the staging of creativity is not the focus of this paper, instead of discussing incubation and illumination as independent stages the term ‘‘creative innovation’’ will be used. Although this paper primarily discusses preparation and creative innovation, verification and production are critical components of the creative process. Much, however, is already known about these processes and thus, they will not be discussed here.

Preparation

General Intelligence: The creative person needs knowledge and skills. To many psychologists intelligence is a measure of a person's ability to acquire the knowledge and skills that will allow them to adapt to their environment (Sternberg, 1997). Sternberg and O'Hara (1999) suggest that there are several possible relationships between intelligence and creativity, from overlapping to unrelated.

Guilford (1973), who played an important role in generating interest in creativity, thought that creativity was a subset of intelligence. Guilford attempted to develop psychometric tests that could measure creativity. These tests are similar to those developed by Torrance (1974). Most of these tests assess subjects' ability to develop novel uses of common objects. For example, subjects would be asked to name in a fixed time interval the different ways in which they might be able to use a brick. Guilford found that students with low IQ consistently performed poorly on these tests, but for the students with high IQ, their performance on creativity tests did not highly correlate with their IQ. After reviewing the relationship between intelligence and creativity Torrance (1975) suggested that IQ and creativity are only moderately related. Finally, Barron and Harrington (1981) found a weak relationship between the creativity of architects and their IQ. They concluded that above an IQ of about 120, the IQ does not predict creativity as much as it does if the IQ is below 120. This theory suggests that there is an IQ threshold. A person needs to be above this threshold to be intelligent enough to learn and have sufficient knowledge about the domain of their creativity. Barron and Harrington also found that although the threshold was 120 for architects, different IQ thresholds might be found for other disciplines. Studies that assessed the IQ's of known creative people have provided converging evidence for the postulate that after a threshold is reached there is not a direct relationship between intelligence and creativity. For example, Simonton (1994) and Herr *et al.* (1965) using this method found that the correlation between IQ and creativity is weak. Thus, intelligence is a necessary but not sufficient component of creativity.

Specific Knowledge and Special Talents: Studies of patients with discrete brain lesions suggest that a person can have specific cognitive disabilities. Developmental disorders can also be associated with specific cognitive disabilities. There are multiple reports of children with specific disabilities in reading, math, drawing, music, and route finding who develop into creative geniuses. For example, there are many great artists, such as Picasso, who did not do well in school because of language disabilities and even mathematical geniuses such as Einstein had language learning disabilities. Thus, general intelligence or what Spearman (1905) called the ‘‘g’’ factor alone can not explain specific disabilities or specific talents and several theorists have placed more emphasis on special factors or what Spearman called the ‘‘s’’ factor. For example, Howard Gardner (1985) suggested that people have multiple intelligences and if creativity is related to intelligence it would appear to be related to a specific factor or a special form of intelligence.

Weisberg (1999) examined the relationship between knowledge and creativity. The basic conclusion he drew from this review is that domain-specific knowledge is a prerequisite for creativity. Domain-specific knowledge in humans appears to be stored in areas of the posterior neocortex. One of the most important evolutionary changes in the brain of humans is the development of the supramodal association areas of the inferior parietal lobe, including the supramarginal and the angular gyri (Brodmann's areas 40 and 39) as well as the posterior portion of the temporal lobe (Brodmann's area 37). Lesion and functional imaging studies have revealed that these areas are important in mediating many higher cognitive activities such as language, mathematics, and spatial computations.

One of Gall and Spurzheim's (1810) postulates is that the larger the area of brain devoted to a function the better that function is performed. Gall's postulate has already received support from the work of Geschwind and Levitsky (1968) who showed that the left temporal planum, which mediates language, is larger than that on the right and anatomic asymmetries have been demonstrated in other areas (Geschwind and Galaburda, 1985; Foundas *et al.*, 1999). Spitzka (1907) noted that several eminent mathematicians and physicists had large parietal lobes, but little research was performed to document this observation. One of the most creative physicists of the modern era, Albert Einstein, was aware that one of the best means to understand the brain mechanisms underlying creativity is to study the brains of creative individuals. Although Einstein wished to be cremated, he also wanted his brain to be used for research and therefore instructed that after death his brain be used for this purpose. Einstein died on 18 April, 1955. Thomas Harvey, the pathologist at the Princeton (New Jersey) Hospital, removed Einstein's brain. Rather than keeping the brain intact, as Paul Broca had done with Leborgne's brain, Harvey sectioned the brain into 240 blocks and sent it to a variety of people. Unfortunately, little was reported until 30 years later when Diamond and coworkers (1985) performed a histological analysis of both right and left Brodmann's area 9 (a portion of the superior frontal gyrus) and area 39 (the angular gyrus). They found that, when compared to the brains of control subjects, area 39 on the left side of Einstein's brain contained a higher glial cell to neuron ratio. These investigators attempted to explain this result by suggesting that this unusual ratio was, "... a response by glial cells to greater neuronal metabolic need ..." They also suggested that this increased metabolic need may be related to Einstein's unusual conceptual powers. The report of Diamond *et al.* (1985) was severely criticized because with aging there is a loss of cortical neurons and their control subjects were younger than Einstein (Hines, 1998). Diamond and coworkers provided no information about the control subjects' socio-economic status, their cause of death, or their premorbid health. Even if one assumes that methodological errors did not account for the results reported by Diamond *et al.* (1985), it is not apparent from this report how a relative reduction of neurons could account for Einstein's creativity. Einstein had developmental language disorders manifested by a delay in speaking. According to Hoffman and Dukas (1972), in a letter Einstein wrote in 1954 he said, "My parents were worried because I started to talk comparatively late, and they consulted a doctor because of it. I cannot tell how old I was at that time, but certainly not younger than three." Einstein also had developmental dyslexia (Kantha, 1992). Dejerine (1891) demonstrated that lesions of the left angular gyrus (Brodmann's area 39) induce acquired alexia and it is possible that people with developmental dyslexia may also have abnormalities in this region. Kantha (1992) suggested that the abnormalities reported by Diamond *et al.* (1985) may have been related to Einstein's dyslexia rather than his genius. Alternatively, as we will discuss in the next section, creativity according to James (1890) requires "transitions from one idea to another ... unheard of combination of elements, the subtlest associations of analogy ... where partnerships can be joined or loosened ..." and thus connectivity, including the myelinated subcortical connections, might be important for creativity and the high index of glial cell found in Einstein's brain might have indicated a high degree of connectivity.

Witelson *et al.* (1999) viewed the pictures of Einstein's brain, taken in 1955 before it was sectioned, and based on these photographs they attempted to learn if the brain had aberrant morphology. They found that at the end of the Sylvian fissure, rather than there being an ascending ramus that divided the supramarginal gyrus into rostral and caudal divisions, the Sylvian fissure in Einstein's brain ended at the postcentral sulcus. Based on these observations, not only did Witelson and her colleagues suspect that Einstein had an enlarged left inferior parietal lobe but also unlike most people, Einstein's parietal lobe was not divided. They suggested that this large and uninterrupted or more highly connected supramodal cortex allowed Einstein to have a functional advantage in performing mathematics and spatial computations. In a previous paper; however, Witelson and Kigar (1992) suggest that the posterior ascending ramus is the continuation of the main stem of the Sylvian fissure and unlike gyri that are formed by the infolding of cortex, the Sylvian fissure, including the ascending ramus, results from uneven growth of the outer cortex relative to inner structure. That Einstein did not have an ascending ramus, therefore, may suggest that the growth of his inferior parietal cortex was not as great as in those who do have such a fissure. In addition, whereas creative people such as Einstein are extremely rare, Foundas and her coworkers (1999) note that the posterior ascending gyrus is not present in 15 to 20% of people's brains. Thus, an uninterrupted supramarginal gyrus cannot solely account for Einstein's exceptional creativity.

Geschwind and Galaburda (1985) suggested that the delay in development of the left hemisphere may allow the right hemisphere, that mediates spatial computations, to become highly specialized. Although a person's insight into the mechanisms underlying their creative process is limited (Metcalfe and Wiebe, 1987), according to Einstein his creativity was heavily dependent on spatial reasoning, and the abnormal development of his left hemisphere may have allowed his right hemisphere to become highly specialized for spatial computations. Recently Miller and coworkers (2000) described a series of patients with frontal temporal dementia who acquired new musical or visual-artistic abilities. Many of these patients had evidence of left temporal dysfunction and the authors posited that the degeneration of the left anterior temporal lobe may lead to facilitation of artistic or musical skills.

Studies of patients with focal lesions and experiments using functional magnetic imaging (fMRI) or positron emission tomography (PET) have revealed that specific portions of the brain are critical for storing different forms of knowledge. Not all people who have high levels of specialized knowledge or talent are creative, but we also know that to be creative one often needs to have specialized knowledge. Unfortunately, there have not been many systematic studies of talented and creative people to learn if they have either gross structural or histological features that are different from matched control subjects. One of the few studies that examined this possibility was performed on musicians with perfect pitch. Bever and Chiarello (1974) using a dichotic listening task demonstrated that whereas non-musicians are right hemisphere dominant for identifying melodies, skilled musicians are left hemisphere dominant. Using in vivo magnetic resonance (MRI) morphometry of the brains of musicians and non-musicians, Schlaug *et al.* (1995) demonstrated that the size of the left planum temporale relative to the right, was greater in musicians than non-musicians. The planum temporale is an area of the cortex that contains the auditory association cortex.

Whereas composers are likely to have more creative skills than musicians, most composers are musicians and great musicians do not just play the written notes, they interpret, and this interpretation is often creative. In the future, anatomic studies of people who have creative skills and special talents in other domains also need to be investigated. Although the presence of specific anatomic differences in creative people could account for a high degree of specialized knowledge, specialized knowledge might also depend on a region's cellular organization and the neuro-chemicals (transmitters and modulators) found in this region.

According to Hebb (1976), learning and memory are based on modifications of synaptic strength among neurons that are simultaneously active (i.e. neurons that fire together, wire together). A corollary of Hebb's hypothesis might be that the more neurons with which a person is endowed, the greater their ability to learn and store knowledge. Thus, a person with high levels of knowledge might have more neurons in the brain region that stores these representations and this could be reflected in the size of this region. Partial support for this hypothesis came from the works of Rosenzweig (1972) as well as Rosenzweig and Bennett (1996) who found that rodents who were put in an enriched environment and who could learn better, had a thicker cerebral cortex with an increase in the number of dendritic spines that are critical for neuronal connectivity and the storage of knowledge. The degree of neuronal connectivity might be influenced by nerve growth factors. For example, in a study of the effects of environmental enrichment on levels of brain nerve growth factor, its receptors, and their relationships to cognitive function, Pham and coworkers (1999) found that animals placed in the enriched condition had significantly higher levels of nerve growth factor when compared to the control animals housed in unenriched environments.

If, according to Hebb's rule, learning and memory are based on modifications of synaptic strength between neurons that are simultaneously active, an increase in the sensitivity of synaptic coincidence detection would also lead to better learning and memory. The N-methyl-D-aspartate (NMDA) gated ion channel is a neural depolarization coincidence detector and the influx of calcium through this channel enables an increase in synaptic strength. Thus, enhanced NMDA gated ion channel activity could enhance learning and memory.

While these observations suggest that cognitive attributes such as specialized knowledge may be related to the size of neuron networks, their degree of connectivity and the ability to alter the strength of connections, specialized knowledge, like general intelligence, is necessary but not sufficient for creative innovation. Thus, in the next section the possible neurobiological basis of creative-innovation will be discussed.

Creative-innovation

Divergent thinking

Creativity requires the novel understanding and expression of orderly relationships. Novelty requires that the creative person take a different direction from the prevailing modes of thought or expression, which is called divergent thinking. The concept of divergent thinking was put forth by William James (1890) who stated, "Instead of thoughts of concrete things patiently following one another in a beaten track of habitual suggestion, we have the most abrupt cross-cuts and transitions from one idea to another . . . unheard of combination of elements . . . we seem suddenly introduced into a seething caldron of ideas . . . where treadmill routine is unknown and the unexpected is the only law" (Albert and Runco, 1999).

Oliver Zangwell (1966) suggested that frontal lobe dysfunction would disrupt divergent thinking. There might be two components to divergent thinking, disengagement and developing alternative solutions. In order to find a creative solution to a problem that has remained unsolved a person must alter the means by which they have previously attempted to solve this problem. Berg (1948) developed the Wisconsin Card Sorting test in which subjects are required to sort a deck of cards according to the various dimensions illustrated on these cards (e.g. shape, color, number). The subjects are not informed of the sorting principles (e.g. shape) but must deduce this from the response of the examiner after each sort. Throughout this test the sorting principles change (e.g. from shape to color) and the subjects must switch her or his strategy based on the examiner's responses. Milner (1984) demonstrated that patients who had frontal lobectomies for the surgical treatment of intractable epilepsy were impaired at this test, suggesting that the frontal lobes might be critical for the ability to disengage and shift to new solutions. Cognitive perseveration, the inability to switch set or change the form of an activity, is often observed in brain-impaired individuals who have frontal lobe injuries. Denny-Brown and Chambers (1958) proposed that whereas the frontal lobes mediate avoidance behaviors, the temporal-parietal lobes mediate approach behaviors and thus with frontal injury there is inappropriate approach. Luria (1969) demonstrated in a series of studies that patients with frontal lobe dysfunction are stimulus (environmentally) dependent and even on simple motor tasks ("When I put up one finger you put up two and when I put up two you put up one.") they have a propensity to produce behavior that is entrained by the stimulus (a disengagement failure).

James (1890) suggested that the ability to change strategies was important in divergent thinking. Converging evidence for the postulate that the frontal lobes are important for the ability to disengage and shift to new strategies (divergent thinking) comes from studies of regional blood flow in normal subjects who are performing the Wisconsin Card Sorting Test or performing a divergent thinking tests similar to those described by Guilford (1967) and Torrance (1988). When normal subjects were performing the Wisconsin Card Sorting Test (Weinberger *et al.*, 1986) they activated their frontal lobes. When creative subjects were providing alternative uses of bricks, their frontal lobes showed more activation than those who were less creative (Carlsson *et al.*, 2000).

Studies of patients with lesions (Damasio and Anderson, 1993; Stuss and Knight, 2002) and functional imaging studies suggest that the frontal lobes are important for disengagement and developing alternative strategies (divergent thinking). The means by which the frontal lobes accomplish this, however, remains unknown. The frontal lobes have strong connections to the polymodal and supramodal regions of the temporal and parietal lobes (Pandya and Kuypers, 1969). Perhaps these connections are important for inhibiting the activated networks that store semantically similar information while exciting or activating the semantic conceptual networks that have been only weakly activated or not activated at all. Activation of these remote networks might be important in developing the alternative solutions so important in divergent thinking. Support for the postulate that the frontal lobe might be important in either activating or inhibiting semantic networks comes from a recent study, using positron emission tomography (PET), that suggested different roles for medial and lateral rostral prefrontal cortex (Brodmann's area 10), with the former involved in suppressing internally-generated thought and the latter in maintaining them (Burgess *et al.*, 2003).

Novelty seeking

In addition to being able to perform divergent thinking, creative people are often looking for what is new and different and thus are novelty seekers. Creative people, especially writers, composer-musicians and fine artists, have a very high rate of substance abuse such as alcoholism (Post, 1994, 1996). Studies of large cohorts of college students also found that the students who use marijuana tend to be novelty seeking and more creative (Eisenmen *et al.*, 1980). The reason for the relationship between substance abuse and creativity has not been determined. One hypothesis is that drugs enhance creative performance, but studies of creativity under normal versus intoxicated states do not reveal that drugs enhance creativity (Lang *et al.*, 1984; Lapp *et al.*, 1994). Another possibility is that creative people are prone to addiction. In order to be creative one has to produce works that are original or novel. Cloninger and coworkers (1993) presented a psychobiological model of personality that includes 3 temperaments or character dimensions. One of these dimensions is novelty seeking and creative people would have to be considered novelty seekers. Several investigators have found that novelty seekers are at increased risk for drug abuse. There is some evidence that exposure to novelty activates the mesolimbic dopamine (DA) system of the brain (Bardo *et al.*, 1996). This is the same neural substrates that mediate the rewarding effects of drugs of abuse, such as alcohol. The mesolimbic dopaminergic system projects to the nucleus accumbens and this portion of the ventral striatum along with its connections to the limbic system (e.g. amygdala) have been posited to be important in alcohol addiction. Tupala and coworkers (2001) evaluated the densities of dopamine receptors and transporters in the nucleus accumbens and amygdala of the brain of people who have a history of alcohol abuse. When compared with controls, the mean number of dopamine receptor sites in the brain of the alcoholic subjects was lower in both the nucleus accumbens and the amygdala than that of the control subjects. These results indicate that dopaminergic functions in these limbic areas may be impaired among people who abuse alcohol. These results also suggest that people with alcohol addiction might use alcohol and novelty as a means of stimulating DA function because they find this stimulation is highly rewarding.

There is another possible relationship between the use of drugs and creative innovation. While drugs have been shown to intervere with creative production, some drugs lower arousal and as we will discuss in a subsequent section, creative innovation is enhanced by low arousal states. In contrast, drugs such as amphetamines might impede creative innovation because they heighten arousal.

Connectivity

Creativity was defined in the beginning of this paper as the ability to understand, develop and express in a systematic fashion novel orderly relationships. Since the work of Paul Broca (1863) it has repeatedly been demonstrated using the lesion method, laterality studies (dichotic listening and visual half field), electrophysiological studies and functional imaging that the brain is organized in modular fashion. Thus, the understanding, development and expression of orderly relationships might require communication between these modules. Perhaps the strongest evidence for brain modularity is hemispheric specialization, the left hemisphere being dominant for language, even in the majority of left-handed people (McGlone, 1984), motor control of skilled movement (Liepmann, 1920) and categorical processing (Kosslyn, 1998). In contrast, the right hemisphere appears to be important in spatial cognition (Benton *et al.*, 1975), including spatial imagery (Butters *et al.*, 1970), face recognition (Benton, 1990) and coordinate coding (Kosslyn, 1998). The right hemisphere also appear to be important in emotional communication and might also be dominant for mediating many primary emotions (Heilman *et al.*, 2000). Whereas the right hemisphere appears to have a global attentional perspective, (Robertson *et al.*, 1988; Barrett *et al.*, 1998) the left hemisphere has a more focused attentional perspective. Many other right-left hemisphere dichotomies have been described that cannot be fully addressed in this paper. Works of scientific or artistic creativity often require that one use the skills and knowledge mediated by both hemispheres. For example, the novelist who is writing about an emotional response of a character must use the knowledge of facial emotional expressions stored in the right hemisphere together with the verbal lexicon stored in the left hemisphere. The sculptor must imagine the rotation of spatial images mediated by the right hemisphere while he uses the motor skills mediated by the left hemisphere. The astronomer must combine the spatial computations mediated by the right hemisphere with arithmetic skills mediated by the left hemisphere. Thus, interhemispheric communication might be important for combining the knowledge and skills that are important for creative innovation. James (1890) suggested that creativity requires an "...unheard of combination of elements and the subtlest associations...." Spearman (1931) suggested that creative ideas result from the combination of two or more ideas that have been previously isolated. Because the right and left hemispheres store different forms of knowledge and mediate different forms of cognitive activity, different neuronal architectures probably exist within the association cortices of each of the hemispheres. A possible method of resolving a previously unsolved problem is to see this problem "in a new light" and a means of seeing a problem in a new light is to use a different form of knowledge and a different cognitive strategy that might be mediated by the hemisphere that is opposite to the one previously used.

The largest structure connecting independent modular systems is the corpus callosum. Lewis (1979) administered the Rorschach test to eight patients who had undergone a cerebral commissurotomy and noted that disconnection of the two cerebral hemispheres tended to destroy creativity as measured by this test. Bogen and Bogen (1988) noted that although the corpus callosum transfers high level information, normally this interhemispheric communication is incomplete. Bogen and Bogen posited that incomplete interhemispheric communication permits hemispheric independence and lateralized cognition, important in the incubation of ideas. These authors mention Frederic Bremer, who suggested that the corpus callosum subserves the highest and most elaborate activities of the brain, in a word, creativity. They also suggest that it is the momentary suspension of this partial independence that accounts for illumination. They did not say, however, what could account for this momentary suspension of partial independence.

The corpus callosum is primarily comprised of myelinated axons whose cells bodies are in the pyramidal layers of the cerebral cortex. The cerebral connectivity important for creativity might not only be inter-hemispheric, but also intrahemispheric. In addition to the myelinated axons that carry information between the hemispheres, from the thalamus and basal ganglia to the cortex, and from the cortex to the basal ganglia, thalamus, brain stem and spinal cord, these myelinated axons also carry information between cortical regions in the same hemisphere. These intrahemispheric connections facilitate intrahemispheric communication, which might also be important for creative innovation because widespread connectivity allows creative people to combine the representations of ideas that have been previously isolated.

In a prior discussion of Einstein's brain we mentioned that it appeared that Einstein's parietal lobe had extremely well developed subcortical white matter. This finding might suggest that Einstein's creativity was related to his enhanced intra- and interhemispheric connectivity.

According to Eysenck (1995), "...genius is found only in males..." There are, however, many cultural factors that might inhibit women's creativity. It there are sex differences in creativity that are not related to cultural factors, these differences might be related to structural differences in the brain. Whereas men's brains are larger than those of women, the cerebral cortex of women's brains is as thick as men's suggesting that the size differences between men and women might be related to men having more white matter than women. If Eysenck's observation is correct, and sex differences are not entirely related to cultural factors, they might be related to differences in connectivity. Support for this connectivity hypothesis comes in part from studies of aging. With aging there is a decrease of creativity, especially in the sciences (Abra, 1989). Using neurostereology, quantitative anatomical studies of the aging brain in nondemented people revealed that the difference in total number of neurons in subjects that ranged from 20 to 90 years was less than 10%, but the total myelinated fiber length showed a large reduction as a function of age (Pakkenberg *et al.*, 2003).

Connectionist or parallel distributed processing (PDP) models suggest that there are processing units or nodes that are similar to the neurons found in the brain and PDP models strongly emulate the fundamental properties of neural networks. Information in PDP networks is stored in the strengths of connections between units (as in the brain) and concepts are represented as patterns of activity involving many units (i.e. as distributed representations) (Rumelhart *et al.*, 1986; Martindale, 1995). The connections between concepts are related to each other to the degree that their elaboration derives from the same information (the same connection strengths), and their corresponding patterns of unit activity overlap. A large number of units linked by a set of connections defines a domain of knowledge from which any one of a large number of concepts can be generated. Psychological studies of priming effects on lexical decision latency provide a particularly clear demonstration of the capacity of this type of model to account for empirical results. In a lexical decision task, words are flashed one at a time on a screen and the subject has to indicate, as rapidly as possible, if the word displayed is, or is not, a real word. In a priming paradigm, before the target word or non-word appears on the screen, a prime word appears. If the prime is strongly related to the target (e.g. the prime is doctor and the target is nurse), the response time is less than when the prime and target are unrelated (e.g. doctor-zebra). This is because, when a related prime appears, it generates a distributed concept representation that involves activation of many of the units that define the distributed representation of the target. As much of the target-distributed representation is already activated when the target appears, response latency to the target is reduced.

Mednick (1962) suggested that in generating associative responses to a stimulus, creative individuals are characterized by a flatter associative hierarchy than are less creative individuals. Hence, creative people might have the ability to activate more highly distributed networks. There are two means by which connectionist architectures might account for creativity. Entities in the environment lead to activation of selected units, thereby leading to the generation of the patterns of activation that instantiate concepts of those entities. There may, however, be the capacity for the discretionary-intentional activation of selected units in a network, thereby producing novel patterns of activation corresponding to novel concepts. In this way, the network represents an internal model of some domain of knowledge, and the discretional ability to activate selected units corresponds to the ability to ask ''what if'' questions. This capability provides the basis for a modest creative element. For example, using one's internal model of house interiors, one can readily imagine the elements that might be put in a bedroom large enough to accommodate a sofa and a fireplace.

A greater measure of creativity might be achieved by using networks representing knowledge in one domain to help organize a quite different domain that might nevertheless share some attributes, a sort of creativity by metaphor. Many different network architectures probably exist within the association cortices of the brain. This raises the possibility that this creativity by metaphor might involve the recruitment of networks of substantially different architecture in order to escape the constraints of existing (learned) internal models represented in the networks usually used for thinking in a particular domain. The manipulation of concepts in a network of a completely different architecture would allow the asking of particularly novel ''what if'' questions. An example may help to illustrate this elusive concept. Richard Feynman, the Nobel prize winning physicist, often began with abstract visual representations of his ideas, which he subsequently translated into mathematical terms. Apparently the architecture of the networks supporting his visual representations permitted him the manipulative freedom to escape conventional formulations, thereby providing the basis for creative innovation.

Support for Mednick's (1962) proposed theory that creative individuals are characterized by a flatter associative hierarchy than are less creative individuals and partial support for the postulate that creative innovation is related to the recruitment of different networks come from electroencephalographic (EEG) studies of normal subjects who, during creative thought, demonstrated an increase of anatomically distributed coherence of EEG oscillations (Petsche, 1996; Jausovec and Jausovec, 2000). The mechanism by which the size of brain networks is modulated and co-activated is unknown, but in the next section several possible mechanisms will be discussed.

The brain networks discussed above are comprised of neurons and their excitatory or inhibitory connections to other neurons. Excitatory neurons give off the neurotransmitter glutamate and the inhibitory neurons give off gamma amino butyric acid or GABA. The neurons in these networks, however, can also be modulated by other neurotransmitters such as the catecholamines and changes in the brain levels of these catecholamines might play an important role in creativity.

Arousal and catecholamines

One of the best means of developing a neuropsychological or neuropharmacological hypothesis about a specific behavior is to study groups of people who can or cannot produce this behavior, find out the conditions that are most likely to be associated with this behavior and learn what common factor or factors distinguish these groups (finding the ''thread'' that unites). Several scientists have reported that they were able to solve a difficult scientific problem during sleep or when they were either falling asleep or awakening from sleep. One of the most famous examples of this phenomenon is August Kekule, who in 1865, while attempting to learn the structure of benzene, went to sleep and dreamed of a snake chasing its tail. This dream provided Kekule with the idea that benzene is in a ring-like structure. Recently, Kekule's recounting of this episode has undergone careful scrutiny with strong arguments that he never had such a dream (Strunz, 1993). Dehaene (1997), however, in his book *The Number Sense* states, ''They [mathematical geniuses] say that in their most creative moments, which some describe as 'illuminations', they do not reason voluntarily, nor think in words, nor perform long formal calculations. Mathematical truth descends on them, sometimes even during sleep, as in Ramanujan's case.'' Before and after sleep, however, people are often in a state of relaxed wakefulness. Creative people who are actively working on a problem describe moments of insight when they were able to solve previously insoluble problems. Often these moments of insight come at a time when the person is relaxed and at rest. In 1897, Ramón y Cajal (1999) wrote a book entitled *Advice for a Young Investigator*, where he suggested, ''If a solution fails to appear after all of this, and yet we feel success is just around the corner, try resting for a while. Several weeks of relaxation and quiet in the countryside bring calmness and clarity of the mind. Like the early morning frost, this intellectual refreshment withers the parasitic and nasty vegetation that smothers the good seed. Bursting forth at last is the flower of truth, whose calyx usually opens after a long and profound sleep at dawn, in those placid hours of the morning that Goethe and so many others consider especially favorable for discovery.'' Easterbrook (1959) and Eysenck (1995) suggested that high cortical arousal induced by stress is often associated with conscious attempts at problem solving, but this high arousal might suppress the emergence of remote associations, and a lower degree of cortical arousal might allow unusual associations to become manifest. Stress is associated with high levels of norepinephrine and relaxation with low levels.

Many mental diseases have been associated with alterations of neurotransmitters and especially the catecholamines. Many investigators have noted a relationship between psychopathology and creativity; however, many of these reports are anecdotal and while these reports might provide us with hypotheses about creativity one must be cautious about drawing conclusions. Kraepelin in 1921 was perhaps the first to note that manic-depressive psychosis was often associated with enhanced creativity (Weisberg, 1994). Several investigators have reported that many of our most creative writers, composers, painters and scientists have suffered with depression, either bipolar or monopolar (Poldinger, 1986; Andreasen and Glick, 1988; Richards *et al.*, 1988; Slaby, 1992; Post, 1996). One thread that unites dreaming, resting or relaxing and depression is changes in neurotransmitter systems. In all these states there appears to be a reduction of catecholamines including norepinephrine (McCarley, 1982).

Support for the postulate that catecholamines modulate the size of neuronal networks comes from several studies. Kischka and coworkers (1996) used a lexical priming task similar to the one described earlier. When they administered L-dopa to normal subjects and tested priming they found that direct semantic priming (e.g. doctor-nurse) was only marginally influenced. The administration of L-dopa, however, significantly reduced the effects of indirect priming (doctor-thermometer). Based on these results, Kischka *et al.* (1996) suggested that dopamine increases the signal to noise ratio in semantic networks by reducing the spread of semantic activation. Although Kischka *et al.* (1996) attributed this effect to the dopaminergic system, L-dopa is a precursor to both dopamine and norepinephrine and the administration of L-dopa to these subjects may have also increased the level of norepinephrine. In the Remote Associates Test, subjects are presented with a series of trials in which they are given three words and are requested to find a word that is associated with all three words. Like the priming task discussed earlier, this test might assess the size of lexical-semantic networks. Many people who are creative have high trait anxiety (Carlsson *et al.*, 2000), but during stress (state anxiety), performance on this test deteriorates (Martindale and Greenough, 1973). One of the reasons why stress may reduce performance on this task is that stress increases activity of the noradrenergic system. Further support for this noradrenergic postulate comes from the results of a study in which students with test anxiety dramatically improved their scores on the Scholastic Aptitude Test (SAT) when they took the beta adrenergic blocker propranolol (Faigel, 1991). Propranolol is a centrally acting beta blocker that reduces the influence of noradrenaline on neurons. The SAT assesses both crystallized knowledge and fluid reasoning. Perhaps beta blockade improves performance on this test because it reduces the influence of norepinephrine on the neuronal networks, allowing increased cognitive flexibility.

To directly test the hypothesis that norepinephrine modulates cognitive flexibility, Beversdorf and coworkers (1999) tested normal subjects' ability to solve problems when treated with ephedrine, or propranolol. They found the anagram test that relies heavily on cognitive flexibility was performed better after subjects took popranolol than after they took ephedrine. Propranolol is both a central and peripheral acting beta-adrenergic antagonist. To learn if the increase in cognitive flexibility induced by propranolol was produced by central or peripheral nervous system blockade, Broome *et al.* (2000) tested another group of normal subjects with an anagram task and compared the effects of propranolol, which enters the central nervous system, and nadolol, a purely peripheral beta-blocker. Subjects' solution times on the anagram test were more rapid with propranolol than with nadolol, suggesting that only central beta-adrenergic blockade increases cognitive flexibility.

Norepinephrine, which is increased during stress, changes the signal-to-noise ratio by suppressing intrinsic excitatory synaptic potentials relative to the potentials elicited by direct afferent input (Hasselmo *et al.*, 1997). The bias toward external input that occurs with high norepinephrine states might be important for "flight or fight" activities, but may prevent asking "What if" questions of the networks that store cognitive representations. In addition, connectionist modeling has suggested that a moderate amount of noise allows networks to settle into optimal solutions. Suppressing intrinsic excitatory potentials may prevent many association neurons that do not receive direct afferent input from achieving firing threshold. The reduced activity of association neurons may lead to the activation of relatively sparse and constricted associative networks, but as discussed above creativity depends on the activation of highly distributed representations that allow one to perform inference and generalization. Further support for this norepinephrine postulate comes from a study of the role of the locus coeruleus in the regulation of cognitive functions. Investigators have concluded that high levels of tonic locus coeruleus activity, which increases the levels of norepinephrine in the cortex, favors "bottom-up" processing, important for monitoring and attending to external stimuli and increasing behavioral responsiveness to unexpected or novel stimuli (Aston-Jones *et al.*, 1991). In contrast, low levels of locus coerulus activity might be important in "top down" processing, that is critical for the innovation stage of creativity.

Further support for the catecholamine-creative-innovation hypothesis comes from EEG studies. Martindale and Hasenfus (1978) performed a series of experiments to investigate the relationship between arousal and creativity. To measure arousal these investigators used the electroencephalogram. Since the work of Berger (Jasper and Carmichael, 1935) it has been known that with high levels of arousal there is desynchronization of the EEG, but with relaxed wakefulness there is well developed alpha activity. These investigators found that during an analogue of creative innovation there was better developed alpha than during an analogue of elaboration. Based on their ability to write creative stories the authors placed subjects into either the creative or uncreative groups. In the resting state there were no differences in the EEGs of these two groups but during the time they were developing their stories ("innovation stage") the creative subjects demonstrated better developed alpha activity than did the uncreative subjects, suggesting that the creative subjects were operating at a lower level of arousal. Foote and coworkers (1991) reviewed the evidence that increased activation of the locus coeruleus, by way of its massively divergent efferent noradrenergic projections to the cerebral cortex, participates in arousal and can convert the EEG from non-alert to alert or aroused states.

Studies of physiological arousal in depression, as determined by EEG power analysis, have revealed that depressed patients have reduced arousal that is altered with treatment (Nieber and Schlegel, 1992; Knott *et al.*, 2000). If lower levels of physiological arousal allow one to increase the extent of concept representations, promote divergent thinking and increase cognitive flexibility, then it would follow that people with depression might have a propensity to be creative.

Although the neurons that provide the cerebral cortex with catecholamines such as dopamine and norepinephrine are located in the midbrain (e.g. ventral tegmental area) and pons (locus coeruleus) the activity of the catecholaminergic systems are modulated by the frontal lobes. The frontal lobe is the only cortical area to project to the locus coeruleus (Arnsten and Goldman-Rakic, 1984) which contains the noradrenergic neurons that project to the cerebral cortex, and the frontal lobes appear to be able to exert an inhibitory influence on the locus coerulus (Sara and Herve-Minvielle, 1995). Increased locus coerulus activity is associated with increased levels of cortical norepinephrine and this induces EEG desynchronization. Neurophysiological studies have revealed that stimulation of only certain parts of the cerebral cortex induce desynchronization of the EEG (physiological arousal) and these include the frontal cortex and the anterior cingulate gyrus (Segundo *et al.*, 1955) that are strongly interconnected. Functional imaging studies of patients with depression have shown reduced cerebral blood flow (i.e. reduced synaptic activity) in the dorsolateral prefrontal cortex (Liotti and Mayberg, 2001). The observed reductions in dorsolateral prefrontal blood flow might be related to the relative failure of depressed patients to be attentive and to develop thoughts or plans about future activities (pathological disengagement). Instead they are engaged in internally defined plans (e.g. introspection, rumination). The reduced activity in dorsolateral prefrontal cortex and anterior cingulate cortex that occurs in depressed patients left to their own devices might be important for creative innovation because the frontal lobes are the primary cortical area that controls the locus coeruleus. Reduced activity in these frontal and cingulate regions, by virtue of reduced input to locus coeruleus, could provide the basis for reductions of cortical norepinephrine, associated reductions in signal-to-noise ratio and the recruitment of widely distributed representations.

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Creative innovation: Possible brain mechanisms

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Abstract

This article reviews and develops some theories about the neurobiological basis of creative innovation (CI). CI is defined as the ability to understand and express novel orderly relationships. A high level of general intelligence, domain-specific knowledge and special skills are necessary components of creativity. Specialized knowledge is stored in specific portions of the temporal and parietal lobes. Some anatomic studies suggest that talented people might have alterations of specific regions of the posterior neocortical architecture, but further systematic studies are needed. Intelligence, knowledge and special skills, however, are not sufficient for CI. Developing alternative solutions or divergent thinking has been posited to be a critical element of CI, and clinical as well as functional imaging studies suggest that the frontal lobes are important for these activities. The frontal lobes have strong connections with the polymodal and supramodal regions of the temporal and parietal lobes where concepts and knowledge are stored. These connections might selectively inhibit and activate portions of posterior neocortex and thus be important for developing alternative solutions. Although extensive knowledge and divergent thinking together are critical for creativity they alone are insufficient for allowing a person to find the thread that unites. Finding this thread might require the binding of different forms of knowledge, stored in separate cortical modules that have not been previously associated. Thus, CI might require the co-activation and communication between regions of the brain that ordinarily are not strongly connected. The observations that CI often occurs during levels of low arousal and that many people with depression are creative suggests that alterations of neurotransmitters such as norepinephrine might be important in CI. High levels of norepinephrine, produced by high rates of locus coeruleus firing, restrict the breadth of concept representations and increase the signal to noise ratio, but low levels of norepinephrine shift the brain toward intrinsic neuronal activation with an increase in the size of distributed concept representations and co-activation across modular networks. In addition to being important in divergent thinking, the frontal lobes are also the primary cortical region that controls the locus coeruleus-norepinephrine system. Thus creative people may be endowed with brains that are capable of storing extensive specialized knowledge in their temporoparietal cortex, be capable of frontal-mediated divergent thinking and have a special ability to modulate the frontal lobe-locus coeruleus (norepinephrine) system, such that during creative innovation cerebral levels of norepinephrine diminish, leading to the discovery of novel orderly relationships.

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