Hipotez / Hypothesis

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KALP BİR POMPADAN ÖTE BİR ŞEY OLAMAZ MI?

COULDN'T HEART BE MORE THAN A PUMP?

Ahmet NACAR

Mustafa Kemal University Medical Faculty Department of Histology and Embryology, ANTAKYA

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ÖZET

Kalp nakillerinden sonra meydana gelen kişilik değişiklikleri, kalp ve beyin arasındaki karşılıklı iletişim, REM (rapid eye movement) uykusu sırasında kardiyovasküler düzenlemede amigdalanın rolü, yine REM uykusunun gelişmekte olan beyinde nöron gelişimi ve hafıza konsolidasyonu üzerindeki etkileri, atriyal ve beyin natriüretik peptitlerin çeşitli etkileri ve kardiyak nöral krista hücrelerinin kalp gelişimindeki rollerine dayanarak bu çalışmada kalbin ve özellikle SA (sinoatriyal) düğümün emosyonel hafıza işleme ve saklamada etkin olabileceği hipotezini öne sürdüm. Bunun da ötesinde SA düğümüne yapılacak çeşitli müdahelelerin, altında istenmeyen anıların ve yaşam deneyimlerinin yattığı düşünülen bazı psikiyatrik hastalıklarda tedavi amaçlı olarak kullanılabileceği önerisi de tartışıldı.

ABSTRACT

Based on the 1) personality changes observed following heart transplantations; 2) the two-way, dynamic, ongoing dialog between the brain and the heart and its reflection as alterations in heart rate variability; 3) the prominent role of amygdala in cardiovascular regulation during rapid eye movement sleep and 4) the importance of rapid eye movement sleep in the developing brain to establish proper neuronal circuits and its memory consolidation effect; 5) the role of cardiac neural crest cells in heart development and 6) the effects of Atrial and Brain Natriuretic Peptides; I hypothesize that the heart, particularly the SA node, could function in emotional memory processing and storage in collaboration with related brain regions. Moreover, intervention to SA node in certain psychiatric diseases with underlying unwanted memories and life experiences could be a novel choice of therapy.

BACKGROUND

Personality changes observed following heart transplantations have attracted researhers' attentions to different sources of emotions other than brain. Although some explanations have been made based on pre- and posttransplant medication and stress to explain those personality changes including tastes, behavioral patterns, and histories; alternative approaches which arised from living systems theory have provided evidences suggesting an active role for heart in emotion processing. Thus, a new discipline called neurocardiology in which the communicative relationship between the brain and heart via the nervous system was explored. Dr. Andrew Armour, one of the early pioneers in neurocardiology, introduced the concept of a functional "heart brain". He showed that the heart has its own intrinsic nervous system and called it "little brain in the heart" (1). Furthermore it was proposed that it is this nervous system that allows a heart transplant to work.

The two-way, dynamic, ongoing dialog has two ends; the brain and the heart. In the brain, the amygdala is probably the most implicated structure in emotional processing. Damage to amygdala in humans may lead to an increase in threshold of emotional perception and

expression(2); amygdala lesions cause impairments in emotional learning(3), deficits in the perception of emotions in facial expressions(4), and impaired memory for emotional events(5).

Neurocardiac interaction is assessed by heart rate variability (HRV) and reflects heart-brain interactions. HRV is a measure of the naturally occurring beat-to-beat changes in heart rate. Recent research conducted at the Institute of HeartMath has demonstrated that HRV dynamics are particularly sensitive to changes in emotional state reflected by changes in heart rhythm patterns with positive and negative emotions(6). Moreover, it was reported that amygdala seems to take prominent role in cardiovascular regulation during rapid eye movement sleep (REMs) (7). Amygdala is also reported to be one of the most active brain regions during REMs (8).

There are three theories concerning the functions of REMs. According to the Ontogenetic Hypothesis of REM sleep, this sleep phase (also known as Active Sleep in neonates) is particularly important to developing brain to establish proper neuronal circuits. That's why babies spend as much as 50 percent of their sleep in REMs. If we think the importance of emotions in early life learnings, one could suggest that emotional processing in REMs plays crucial roles in neural development. Moreover studies investigating the effects of Active Sleep deprivation have shown that deprivation early in life can result in behavioral problems, permanent sleep disruption, decreased brain mass (9).

The other theory about REMs suggests that REM sleep is important for consolidation of procedural and spatial memories. Furthermore, numerous studies have provided evidence for the efficacy of eye movement desensitization and reprocessing therapy (EMDR) in the treatment of posttraumatic stress disorder (10).

THE HYPOTHESIS

Taken together, I hypothesize that the heart, particularly the SA node, could function in emotional memory processing and storage in collaboration with related brain regions. Heart's contribution to brain's emotion processing circuitry could develop as follows: In early years of life, babies spend most of their time sleeping with a predominance of REM sleep. During this long periods of REM sleeps, emotions that are processed in certain brain regions are transferred and stored in the heart, particularly SA node. Since the basics of personality, intellectual capacity and learning are structured with the strong support of emotions in early years of life, and even in prenatal life; SA node is continuously encoded by brain regions such as amygdala in long REM periods of long babyhood and childhood sleeps. And in adulthood, SA node mostly gains its autonomy in emotional responses via its repertory of emotional memory stored mostly till adulthood. After adulthood, encoding and storage goes on but in a slower rate.

Furthermore heart could be the final decision center of behavioral responses to the data obtained from emotional processing. The emotional data stored in the heart, particularly SA node, could be the principal guide shaping our behavioral responses. In this heart-based emotional processing period, the related regions in the brain should be acting as a receptor and co-player. Emotional processing takes place in the brain, but brain should be asking to the heart before any action. Perhaps the emotional data stored in the heart, SA node, is the thing what we call *conscience*.

Here, it is worth to remind the role of cardiac crest cells in heart development (11). Myocardial expression of various neural markers were found to be expressed in regions containing the conduction system (12, 13). In addition, those cells' novel role in heart development has also been documented by Waldo et al (14). Therefore it makes sense to propose a strong neural function for particularly the conduction system.

Another evidence supporting the current hypothesis could come from the surprising set of diversified functional properties of natriuretic peptides. Shortly after the discovery of atrial natriuretic factor by Bold and collegues(15), its detailed chemical structure and fundamental effects were described and then called as Atrial Natriuretic Peptide (ANP). Another peptide called Brain Natriuretic Peptide (BNP) was initially purified from the brain. But it is present at the highest concentration in the heart(16). The behavioral effects of ANP and BNP were studied extensively by Bidzseranova et al(17-24) and found that this cardiac peptides play active roles in emotion-memory-behavior circle. Furthermore ANP was found to inhibit hypotalamic pituitary adrenocortical system(25) and has been demonstrated to exhibit anxiolytic activity(26). In other words, heart could be more than a pump.

In conclusion, potential evidences could be; 1) the functional and anatomical links between brain regions functioning in emotional processing such as amygdala and other related structures and the heart(1, 7, 27); 2) the concept of cellular memory; 3) reflection of the

relation between emotional states and the heart as alterations in HRV(28-31), since heart rate is initiated and mainly regulated by SA node; 4) the role of neural crest cells in heart development; 5) the effects of ANP and BNP; and 6) personality changes following heart transplants(32, 33).

To test the hypotheses; it makes sense to perform an intervention to SA node in certain psychiatric diseases with underlying unwanted memories and life experiences. Forexample, a behavioral study could be performed with rats grown up in stressful conditions from prenatal period to adulthood. Then their behaviors could be observed in an unstressful environment with a group of normally grown up rats. Following this, rats with previous stresses that show stress-related behavioral patterns could undergo some interventions in order to normalize their agitated responses. The intervention could be a local electric shock or interruption of certain neural circuits in the heart. Furthermore, SA node transplants could be performed. If it works, it means that the stressful emotional data in SA node is erased or could be replaced.

Moreover, to test the autonomy of SA node; certain stresses and the object's responses to those stresses before adulthood could be recorded. After adulthood, emotion-related brain regions like limbic lobe could be removed and its responses to same stresses could be observed in order to investigate the heart's, particularly SA node's predominance in responses to certain emotional stimuli.

CONCLUSION

Active and integrated role of the heart with the brain in emotional responses via functional and anatomical links, and ongoing explorations about the heart's role in emotional functions should be assessed as encouraging factors to find novel therapeutic approaches for certain psychiatric diseases. Since human's behavioral patterns are very complex, it is very hard to explain results of animal experiments, and to apply to human. But if we consider the increasing incidence of psychiatric disorders all over the world and the insufficiency of current therapies; every effort and idea should be evaluated deeply to find new treatment options.

REFERENCES

1. Armour A AJ: Neurocardiology. New York, Oxford University Press, 1994.
2. Aggleton J: The functional effects of amygdala lesions in humans: a comparison with findings from monkeys. New-York, Wiley-Liss, 1992.
3. Bechara A, Tranel D, Damasio H, Adolphs R, Rockland C, Damasio AR: Double dissociation of conditioning and declarative knowledge relative to the amygdala and hippocampus in humans. Science 1995; 269: 1115-1118.
4. Adolphs R, Tranel D, Damasio H, Damasio A: Impaired recognition of emotion in facial expressions following bilateral damage to the human amygdala. Nature 1994; 372: 669-672.
5. Cahill L: Modulation of long-term memory storage in humans by emotional arousal:adrenergic activation and the amygdala. New-York, Oxford University Press, 2000.
6. Ashby FG, Isen AM, Turken AU: A neuropsychological theory of positive affect and its influence on cognition. Psychol Rev 1999; 106: 529-550.
7. Desseilles M, Vu TD, Laureys S, Peigneux P, Degueldre C, Phillips C, Maquet P: A prominent role for amygdaloid complexes in the Variability in Heart Rate (VHR) during Rapid Eye Movement (REM) sleep relative to wakefulness. Neuroimage 2006; 32: 1008-1015.
8. Maquet P, Peters J, Aerts J, Delfiore G, Degueldre C, Luxen A, Franck G: Functional neuroanatomy of human rapid-eye-movement sleep and dreaming. Nature 1996; 383: 163-166.
9. Mirmiran M, Uylings HB, Corner MA: Pharmacological suppression of REM sleep prior to weaning counteracts the effectiveness of subsequent environmental enrichment on cortical growth in rats. Brain Res 1983; 283: 102-105.
10. Stickgold R: EMDR: a putative neurobiological mechanism of action. J Clin Psychol 2002; 58: 61-75.
11. Gorza L, Schiaffino S, Vitadello M: Heart conduction system: a neural crest derivative? Brain Res 1988; 457: 360-366.
12. El Sharaby AA, Egerbacher M, Hammoda AK, Bock P: Immunohistochemical demonstration of Leu-7 (HNK-1), Neurone-specific Enolase (NSE) and Protein-Gene Peptide (PGP) 9.5 in the developing camel (Camelus dromedarius) heart. Anat Histol Embryol 2001; 30: 321-325.
13. Verberne ME, Gittenberger-De Groot AC, Poelmann RE: Distribution of antigen epitopes shared by nerves and the myocardium of the embryonic chick heart using different neuronal markers. Anat Rec 2000; 260: 335-350.
14. Waldo K, Zdanowicz M, Burch J, Kumiski DH, Stadt HA, Godt RE, Creazzo TL, Kirby ML: A novel role for cardiac neural crest in heart development. J Clin Invest 1999; 103: 1499-1507.
15. de Bold AJ: Atrial natriuretic factor: a hormone produced by the heart. Science 1985; 230: 767-770.
16. Yasue H, Yoshimura M, Sumida H, Kikuta K, Kugiyama K, Jougasaki M, Ogawa H, Okumura K, Mukoyama M, Nakao K: Localization and mechanism of secretion of B-type natriuretic peptide in comparison with those of A-type natriuretic peptide in normal subjects and patients with heart failure. Circulation 1994; 90: 195-203.

17. Bidzseranova A, Gueron J, Balaspiri L, Telegdy G: Intracerebroventricularly administered atrial natriuretric peptide (ANP) antiserum attenuates fear-motivated learning behavior in rats. Peptides 1992; 13: 957-960.
18. Bidzseranova A, Gueron J, Penke B, Telegdy G: The effects of atrial natriuretic peptide on active avoidance behavior in rats. The role of transmitters. Pharmacol Biochem Behav 1991; 40: 61-64.
19. Bidzseranova A, Gueron J, Toth G, Penke B, Telegdy G: Effect of atrial natriuretic peptide on apomorphine-induced stereotyped cage-climbing behavior in mice. Eur J Pharmacol 1992; 211: 411-414.
20. Bidzseranova A, Gueron J, Toth G, Penke B, Telegdy G: Effect of atrial natriuretic peptide on dopa potentiation in mice. Brain Res Bull 1992; 28: 767-768.
21. Bidzseranova A, Gueron J, Toth G, Penke B, Varga J, Telegdy G: Behavioral effects of atrial and brain natriuretic peptides in rats. Neuroreport 1992; 3: 283-285.
22. Bidzseranova A, Gueron J, Toth G, Varga J, Telegdy G: Structure-activity studies on the effects of atrial natriuretic peptide, brain natriuretic peptide and their analogs on fear-motivated learning behavior in rats. Neuropeptides 1992; 23: 61-65.
23. Bidzseranova A, Toth G, Telegdy G: The effects of atrial natriuretic peptide on the open-field activity of rats. The role of neurotransmitters. Neuropeptides 1991; 20: 163-167.
24. Telegdy G, Bidzseranova A, Kovacs A, Gabos L: Antiamnesic properties of some neuropeptides and the involvement of neurotransmitters in the rats. Patol Fiziol Eksp Ter 1992:75-77.
25. Kellner M, Wiedemann K, Holsboer F: Atrial natriuretic factor inhibits the CRH-stimulated secretion of ACTH and cortisol in man. Life Sci 1992; 50: 1835-1842.
26. Strohle A, Kellner M, Holsboer F, Wiedemann K: Anxiolytic activity of atrial natriuretic peptide in patients with panic disorder. Am J Psychiatry 2001; 158: 1514-1516.
27. Cardinal RN, Parkinson JA, Hall J, Everitt BJ: Emotion and motivation: the role of the amygdala, ventral striatum, and prefrontal cortex. Neurosci Biobehav Rev 2002; 26: 321-352.
28. McCraty R, Atkinson M, Tiller WA, Rein G, Watkins AD: The effects of emotions on short-term power spectrum analysis of heart rate variability. Am J Cardiol 1995; 76: 1089-1093.
29. Yeragani VK, Pohl R, Berger R, Balon R, Ramesh C, Glitz D, Srinivasan K, Weinberg P: Decreased heart rate variability in panic disorder patients: a study of power-spectral analysis of heart rate. Psychiatry Res 1993; 46: 89-103.
30. Yeragani VK, Pohl R, Balon R, Ramesh C, Glitz D, Jung I, Sherwood P: Heart rate variability in patients with major depression. Psychiatry Res 1991; 37: 35-46.
31. Yeragani VK, Pohl R, Balon R, Jung I, Kareus R: Heart rate in panic disorder. Acta Psychiatr Scand 1991; 83: 79.
32. Pearsall P, Schwartz GE, Russek LG: Changes in heart transplant recipients that parallel the personalities of their donors. Integr Med 2000; 2: 65-72.
33. Pearsall PK: Are heart transplant recipients receiving cellular memories from their donated organ? A heuristic study. Hawaii Med J 2001; 60: 282, 300.

İLETİŞİM

Ahmet Nacar, MD
Associate Professor of Histology and Embryology
Mustafa Kemal University Medical Faculty
Department of Histology and Embryology
31100 Hatay, Turkey
e-mail: nacarphd@yahoo.com
Tel: +905065439256
Fax: +903262144977