

## Psikonöroimmünoloji Araştırmalarında Aşılama Modeli: Yayın Tarama

Çeviri: Dr. Yusuf TAMAM

### Özet

Bu bölüm psikososyal faktörlerin bağışıklık üzerine olan etkisini incelemek için aşı modelini kullanmanın arkasında yatan mantığı araştırmaktadır. Dolayısı ile önce kısaca aşı yanıtının mekanikleri ve, stres ve aşı yanıtı arasındaki birliktelik gibi ilişkileri inceleyen çalışmalar için literatürden örnekler sunmadan evvel psikonöroimmünoloji aşı araştırmalarında kullanılan protokoller tartışılacaktır. Gene bu bölümde, psikonöroimmünolojinin aşağıdaki türde kilit sorularını yanıtlamak için aşı modelinin kullanılma yolları araştırılacak olup bu kilit sorular: “Stresli yaşam olayları aşının ne zaman yapıldığına göre görülmekte midir?” “Antijenle daha önce karşılaşmış olmanın etkileri nedir?” “Stresin yanı sıra diğer psikososyal etmenler aşı yanıtını etkilemekte midir?”. Son olarak, psikososyal etmenler ve aşı yanıtı birlikteliğinin altında yatan mekanizmalar kısaca ele alınacak ve bunları daha iyi anlamak amacıyla gelecekte yapılması gereken araştırmalar ve gerçekten, risk altındaki popülasyonlarda aşı yanıtlarını iyileştirmek ve pekiştirmek için mevcut ve gelecekteki bilgilerin kullanılması tartışılacaktır.

**Anahtar sözcükler** Sağlığın korunması, İnfluenza, Müdalaleler, Sosyal destek, Stres, Aşı

## 1 Giriş: PNI Araştırma Bağlamında Aşı Neden İncelenir?

### 1.1 Alternatif Yaklaşımlar: Ölçümlerin Sayılması

Bağışıklık üzerine psikososyal etmenlerin etkisini araştırmak için birçok yöntem bulunmaktadır. İlk çalışmalar psikososyal stresin bağışıklığın sıralı ölçümleri üzerine olan etkisine yoğunlaşmıştır. Örneğin kronik strese maruz kalan kişiler ugun kontrollara göre, B-lenfositler [1, 2], yardımcı T-lenfositler [1, 3, 4], sitotoksik T-lenfositler [1, 5], doğal katil (NK) hücrelerin sayısı gibi [1, 5] bazı immün hücrelerin sayısında azalma ve tükürükteki salgıci immünoglobülin A konsantrasyonunda düşme gösterir [6–10]. Bununla beraber bu tür sıralı değişikliklerin klinik önemini belirlemek bunların sağlıklı kişilere ait normal sınırlar içinde kalması [11] ve daha iyi bir işlev veya artmış üretim yerine sadece hücre göçünü ve dolaşıma katılmayı yansıttıyor

talığı için risk altında olan gruplar için özellikle önemlidir. Bu evrede, hangi yaş grubunda hangi tip girişimin uygun olduğunu ve neyin psikolojik ve dolayısı ile immünolojik sağlık için en yararlı olduğunu kesinleştirecek daha fazla çalışmaya gerek vardır. Aşının yapıldığı gün gibi davranışsal girişimler de bu bağlamda önemli olabilir.

## 7 Sonuç

Sonuç olarak aşılamanın, herkesin aşıya karşı tatmin edici ve koruyucu bir antikor yanıtı vermemesine karşın halk sağlığı üzerine büyük bir etkisi olmuştur. Bunun yaştan ilerlemesi ile arttığı giderek artan şekilde ortaya çıkmıştır. Aşıya karşı antikor yanıtının çalışılması psikososyal maruziyetin bağışıklık ve sonuç olarak hastalıklara gösterilen direnci nasıl etkileyebildiği hakkındaki bilgilerimize katkıda bulunmaktadır. Günümüzde karşılaşılan zorluklar bu çalışmalardan geliştirilen metodolojilerin alttaki mekanizmaları açığa çıkartmaması ve aşıya verilen yanıtı pekiştirecek ve dolayı ile enfeksiyon hastalıklara karşı olan direncimizi optimize edecek uygulanabilir davranışsal müdahalelerin geliştirilmesi ve uygulanmasıdır.

## Kaynaklar

1. McKinnon W, Weisse CS, Reynolds CP et al (1989) Chronic stress, leukocyte subpopulations, and humoral response to latent viruses. *Health Psychol* 8:389-402
2. Schaeffer MA, Baum A, Reynolds CF et al (1985) Immune status as a function of chronic stress at Three Mile Island. *Psychosom Med* 47:85
3. Futterman AD, Wellisch DK, Zigelboim J et al (1996) Psychological and immunological reactions of family members to patients undergoing bone marrow transplantation. *Psychosom Med* 58:472-480
4. Kiecolt-Glaser JK, Glaser R, Shuttlesworth EC et al (1987) Chronic stress and immunity in family caregivers of Alzheimer's disease victims. *Psychosom Med* 49:523-535
5. De Gucht V, Fischler B, Demanet C (1999) Immune dysfunction associated with chronic professional stress in nurses. *Psychiatry Res* 85:105-111
6. Deinzer R, Kleineidam C, Stiller-Winkler R et al (2000) Prolonged reduction of salivary immunoglobulin A (sIgA) after a major academic exam. *Int J Psychophysiol* 37:219-232
7. Jemmott JB 3rd, Borysenko JZ, Borysenko M et al (1983) Academic stress, power motivation, and decrease in secretion rate of salivary secretory immunoglobulin A. *Lancet* 1:1400-1402
8. Jemmott JB 3rd, Magloire K (1988) Academic stress, social support, and secretory immunoglobulin A. *J Pers Soc Psychol* 55:803-810
9. McClelland DC, Alexander C, Marks E (1982) The need for power, stress, immune function, and illness among male prisoners. *J Abnorm Psychol* 91:61-70
10. Gallagher S, Phillips AC, Evans P et al (2008) Caregiving is associated with low secretion rates of immunoglobulin A in saliva. *Brain Behav Immun* 22:565-572. <https://doi.org/10.1016/j.bbi.2007.11.007>
11. Vedhara K, Fox JD, Wang ECY (1999) The measurement of stress-related immune dysfunction in psychoneuroimmunology. *Neurosci Biobehav Rev* 23:699-715
12. Bartrop RW, Luckhurst E, Lazarus L et al (1977) Depressed lymphocyte function after bereavement. *Lancet* 1:834-836
13. Esterling BA, Kiecolt-Glaser JK, Glaser R (1996) Psychosocial modulation of cytokine-induced natural killer cell activity in older adults. *Psychosom Med* 58:264-272
14. Irwin M, Patterson T, Smith TL et al (1990) Reduction of immune function in life stress and depression. *Biol Psychiatry* 27:22-30

15. Schleifer SJ, Keller SE, Camerino M et al (1983) Suppression of lymphocyte stimulation following bereavement. *JAMA* 250:374–377
16. Arnetz BB, Wasserman J, Petrini B et al (1987) Immune function in unemployed women. *Psychosom Med* 49:3–12
17. Khanfer R, Lord JM, Phillips AC (2011) Neutrophil function and cortisol:DHEAS ratio in bereaved older adults. *Brain Behav Immun* 25 (6):1182–1186. <https://doi.org/10.1016/j.bbi.2011.03.008>
18. Burns VE, Carroll D, Ring C et al (2003) Antibody response to vaccination and psychosocial stress in humans: relationship and mechanisms. *Vaccine* 21:2523–2534
19. Allsup S, Haycox A, Regan M et al (2004) Is influenza vaccination cost effective for healthy people between ages 65 and 74 years? A randomised controlled trial. *Vaccine* 23:639–645
20. Patriarca PA (1994) Editorial: A randomized controlled trial of influenza vaccine in the elderly: Scientific scrutiny and ethical responsibility. *JAMA* 272:1700–1701
21. Goodwin K, Viboud C, Simonsen L (2006) Antibody response to influenza vaccination in the elderly: a quantitative review. *Vaccine* 24:1159–1169. <https://doi.org/10.1016/j.vaccine.2005.08.105>
22. Nichol KL, Margolis KL, Wuorenma J et al (1994) The efficacy and cost effectiveness of vaccination against influenza among elderly persons living in the community. *N Engl J Med* 331:778–784
23. Simonsen L, Reichert TA, Viboud C et al (2005) Impact of influenza vaccination on seasonal mortality in the US elderly population. *Arch Intern Med* 165:265–272
24. Brown GW, Harris TO (1989) Social origins of depression: a study of psychiatric disorder in women. Routledge, London
25. Cohen S, Tyrell DAJ, Smith AP (1991) Psychological stress and susceptibility to the common cold. *N Engl J Med* 325:606–612
26. Rosengren A, Orth-Gomer K, Wedel H et al (1993) Stressful life events, social support, and mortality in men born in 1933. *BMJ* 307:1102–1105
27. Cohen S, Kamarck T, Mermelstein R (1983) A global measure of perceived stress. *J Health Soc Behav* 24:385–396. <https://doi.org/10.2307/2136404>
28. Macleod J, Davey Smith G, Heslop P et al (2002) Psychological stress and cardiovascular disease: empirical demonstration of bias in a prospective observational study of Scottish men. *BMJ* 324:1247–1251
29. Schulz R, Beach SR (1999) Caregiving as a risk factor for mortality: the Caregiver Health Effects Study. *JAMA* 282:2215–2219
30. Moynihan JA, Larson MR, Treanor J et al (2004) Psychosocial factors and the response to influenza vaccination in older adults. *Psychosom Med* 66:950–953
31. Burns VE, Carroll D, Ring C et al (2002) Stress, coping and hepatitis B antibody status. *Psychosom Med* 64:287–293
32. Burns VE, Drayson M, Ring C et al (2002) Perceived stress and psychological well-being are associated with antibody status following meningitis C conjugate vaccination. *Psychosom Med* 64:963–970
33. Pedersen AF, Zachariae R, Bovbjerg DH (2009) Psychological stress and antibody response to influenza vaccination: a meta-analysis. *Brain Behav Immun* 23:427–433. <https://doi.org/10.1016/j.bbi.2009.01.004>
34. Gulati U, Keitel WA, Air GM (2007) Increased antibodies against unfolded viral antigens in the elderly after influenza vaccination. *Influenza Other Respi Viruses* 1:147–156. <https://doi.org/10.1111/j.1750-2659.2007.00017.x>
35. Burns VE, Carroll D, Drayson M et al (2003) Life events, perceived stress and antibody response to influenza vaccination in young healthy adults. *J Psychosom Res* 55:569–572
36. Phillips AC, Burns VE, Carroll D et al (2005) The association between life events, social support and antibody status following thymusdependent and thymus-independent vaccinations in healthy young adults. *Brain Behav Immun* 19:325–333
37. Miller GE, Cohen S, Pressman S et al (2004) Psychological stress and antibody response to influenza vaccination: when is the critical period for stress, and how does it get inside the body? *Psychosom Med* 66:215–223
38. Phillips AC, Carroll D, Burns VE et al (2006) Bereavement and marriage are associated with antibody response to influenza vaccination in the elderly. *Brain Behav Immun* 20:279–289. <https://doi.org/10.1016/j.bbi.2005.08.003>
39. Talbot HK, Coleman LA, Zhu Y et al (2015) Factors associated with maintenance of antibody responses to influenza vaccine in older, community-dwelling adults. *BMC Infect Dis* 15:195. <https://doi.org/10.1186/s12879-015-0926-8>

40. Glaser R, Kiecolt-Glaser JK, Bonneau RH et al (1992) Stress-induced modulation of the immune response to recombinant hepatitis B vaccine. *Psychosom Med* 54:22–29
41. Glaser R, Sheridan JE, Malarkey Wet al (2000) Chronic stress modulates the immune response to a pneumococcal pneumonia vaccine. *Psychosom Med* 62:804–807
42. Vedhara K, Cox NK, Wilcock GK et al (1999) Chronic stress in elderly carers of dementia patients and antibody response to influenza vaccination. *Lancet* 353:627–631
43. Segerstrom SC, Schipper LJ, Greenberg RN (2008) Caregiving, repetitive thought, and immune response to vaccination in older adults. *Brain Behav Immun* 22:744–752. <https://doi.org/10.1016/j.bbi.2007.11.004>
44. Wong SY, Wong CK, Chan FW et al (2013) Chronic psychosocial stress: does it modulate immunity to the influenza vaccine in Hong Kong Chinese elderly caregivers? *Age (Dordr)* 35:1479–1493. <https://doi.org/10.1007/s11357-012-9449-z>
45. Vedhara K, McDermott MP, Evans TG et al (2002) Chronic stress in non-elderly caregivers: psychological, endocrine and immune implications. *J Psychosom Res* 53:1153–1161
46. Graham JE, Christian LM, Kiecolt-Glaser JK (2006) Stress, age, and immune function: toward a lifespan approach. *J Behav Med* 29:389–400
47. Keegan BM, Noseworthy JH (2002) Multiple sclerosis. *Annu Rev Med* 53:285–302. <https://doi.org/10.1146/annurev.med.53.082901.10390953/1/285>
48. Poser CM, Paty DW, Scheinberg L et al (1983) New diagnostic criteria for multiple sclerosis: guidelines for research protocols. *Ann Neurol* 13:227–231. <https://doi.org/10.1002/ana.410130302>
49. Gregory CA, Hodges JR (1996) Clinical features of frontal lobe dementia in comparison to Alzheimer's disease. *J Neural Transm Suppl* 47:103–123
50. Neary D, Snowden JS, Gustafson L et al (1998) Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. *Neurology* 51:1546–1554
51. Pinquart M, Sorensen S (2003) Associations of stressors and uplifts of caregiving with caregiver burden and depressive mood: a meta-analysis. *J Gerontol B Psychol Sci Soc Sci* 58:P112–P128
52. Pinquart M, Sorensen S (2003) Differences between caregivers and noncaregivers in psychological health and physical health: a metaanalysis. *Psychol Aging* 18:250–267. <https://doi.org/10.1037/0882-7974.18.2.250>
53. Floyd FJ, Gallagher EM (1997) Parental stress, care demands, and use of support services for school-age children with disabilities and behavior problems. *Fam Relat* 46:359–371
54. Hastings RP, Daley D, Burns C et al (2006) Maternal distress and expressed emotion: cross-sectional and longitudinal relationships with behavior problems of children with intellectual disabilities. *Am J Mental Retard* 111:48–61
55. Higgins DJ, Bailey SR, Pearce JC (2005) Factors associated with functioning style and coping strategies of families with a child with an autism spectrum disorder. *Autism* 9:125–137
56. Maes B, Broekman TG, Dosen A et al (2003) Caregiving burden of families looking after persons with intellectual disability and behavioural or psychiatric problems. *J Intellect Disabil Res* 47:447–455
57. Gallagher S, Phillips AC, Drayson MT et al (2009) Parental caregivers of children with developmental disabilities mount a poor antibody response to pneumococcal vaccination. *Brain Behav Immun* 23:338–346. <https://doi.org/10.1016/j.bbi.2008.05.006>
58. Gallagher S, Phillips AC, Drayson MT et al (2009) Caregiving for children with developmental disabilities is associated with a poor antibody response to influenza vaccination. *Psychosom Med* 71:341–344. <https://doi.org/10.1097/PSY.0b013e31819d1910>
59. Jabaaij L, Grosheide PM, Heijtkink RA et al (1993) Influence of perceived psychological stress and distress on antibody response to low dose rDNA hepatitis B vaccine. *J Psychosom Res* 37:361–369
60. Jabaaij L, Van Hattum J, Vingerhoets AJJM et al (1996) Modulation of immune response to rDNA hepatitis B vaccination by psychological stress. *J Psychosom Res* 41:129–137
61. Marsland AL, Cohen S, Rabin BS et al (2001) Associations between stress, trait negative affect, acute immune reactivity, and antibody response to hepatitis B injection in healthy young adults. *Health Psychol* 20:4–11
62. Petry J, Weems LB, Livingstone JN (1991) Relationship of stress, distress, and the im-

- munologic response to a recombinant hepatitis B vaccine. *J Fam Pract* 32:481–486
63. Dhabhar FS, McEwen BS (1996) Stress-induced enhancement of antigen-specific cell-mediated immunity. *J Immunol* 156:2608–2615
  64. Petrie KJ, Booth RJ, Pennebaker JW et al (1995) Disclosure of trauma and immune response to a hepatitis B vaccination program. *J Consult Clin Psychol* 63:787–792
  65. Gallagher S, Phillips AC, Ferraro AJ et al (2008) Psychosocial factors are associated with the antibody response to both thymus-dependent and thymus-independent vaccines. *Brain Behav Immun* 22:456–460
  66. Snyder BK, Roghmann KJ, Sigal LH (1990) Effect of stress and other biopsychosocial factors on primary antibody response. *J Adolesc Health Care* 11:472–479
  67. Cohen S, Miller GE, Rabin BS (2001) Psychological stress and antibody response to immunization: a critical review of the human literature. *Psychosom Med* 63:7–18
  68. Boyce WT, Adams S, Tschann JM et al (1995) Adrenocortical and behavioral predictors of immune response to starting school. *Pediatr Res* 38:1009–1017
  69. Gallagher S, Phillips AC, Ferraro AJ et al (2008) Social support is positively associated with the immunoglobulin M response to vaccination with pneumococcal polysaccharides. *Biol Psychol* 78:211–215. <https://doi.org/10.1016/j.biopsycho.2008.01.001>
  70. Edwards KM, Burns VE, Reynolds T et al (2006) Acute stress exposure prior to influenza vaccination enhances antibody response in women. *Brain Behav Immun* 20:159–168
  71. Edwards KM, Burns VE, Adkins AE et al (2008) Meningococcal A vaccination response is enhanced by acute stress in men. *Psychosom Med* 70:147–151
  72. Edwards KM, Burns VE, Allen LM et al (2007) Eccentric exercise as an adjuvant to influenza vaccination in humans. *Brain Behav Immun* 21:209–217
  73. Edwards KM, Campbell JP, Ring C et al (2010) Exercise intensity does not influence the efficacy of eccentric exercise as a behavioural adjuvant to vaccination. *Brain Behav Immun* 24:623–630. <https://doi.org/10.1016/j.bbi.2010.01.009>
  74. Phillips AC, Gallagher S, Carroll D et al (2008) Morning vaccine administration is associated with an enhanced response to vaccination in men. *Psychophysiology* 45:663–666
  75. Long JE, Drayson MT, Taylor AE et al (2016) Morning vaccination enhances antibody response over afternoon vaccination: a cluster-randomised trial. *Vaccine* 34:2679–2685. <https://doi.org/10.1016/j.vaccine.2016.04.032>
  76. Long JE, Drayson MT, Taylor AE et al (2016) Corrigendum to ‘Morning vaccination enhances antibody response over afternoon vaccination: a cluster-randomised trial’ [*Vaccine* 34 (2016) 2679–2685]. *Vaccine* 34:4842. <https://doi.org/10.1016/j.vaccine.2016.08.031>
  77. Pressman SD, Cohen S, Miller GE et al (2005) Loneliness, social network size, and immune response to influenza vaccination in college freshmen. *Health Psychol* 24:297–306
  78. O'Connor TG, Wang H, Moynihan JA et al (2015) Observed parent-child relationship quality predicts antibody response to vaccination in children. *Brain Behav Immun* 48:265–273. <https://doi.org/10.1016/j.bbi.2015.04.002>
  79. Smith TW, Glaser K, Ruiz JM et al (2004) Hostility, anger, aggressiveness, and coronary heart disease: an interpersonal perspective on personality, emotion, and health. *J Pers* 72:1217–1270
  80. Morag M, Morag A, Reichenberg MA et al (1999) Psychological variables as predictors of rubella antibody titers and fatigue - a prospective double blind study. *J Psychiatr Res* 33:389–395
  81. Phillips AC, Carroll D, Burns VE et al (2005) Neuroticism, cortisol reactivity, and antibody response to vaccination. *Psychophysiology* 42:232–238
  82. Marsland AL, Cohen S, Rabin BS et al (2006) Trait positive affect and antibody response to hepatitis B vaccination. *Brain Behav Immun* 20:261–269. <https://doi.org/10.1016/j.bbi.2005.08.009>
  83. Kohut ML, Cooper MM, Nickolaus MS et al (2002) Exercise and psychosocial factors modulate immunity to influenza vaccine in elderly individuals. *J Gerontol* 57:557–562
  84. Vedhara K, Bennett PD, Clark S et al (2003) Enhancement of antibody responses to influenza vaccination in the elderly following a cognitive-behavioural stress management intervention. *Psychother Psychosom* 72:245–252