

GELİŞİMSEL PSİKONÖROİMMUNOLOJİ

6. BÖLÜM

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GİRİŞ

Psikonöroimmunoloji, immun sistem ile davranış ve Santral Sinir Sistemi (SSS) arasındaki iki yönlü ilişkiyi araştıran bir bilim dalıdır. Sosyal, psikolojik ve davranışsal faktörlerin immun sistem aktivitesi üzerindeki ve immun sistemin biliş, duygu ve davranışlar üzerindeki etkileri ile bu çift yönlü etkileşimin fiziksel ve ruhsal hastalıklarla ilişkisi psikonöroimmunolojik bağlamda değerlendirilmektedir (1). Son yıllarda kullanılan “immunopsikiyatri” terimi de aynı tanıımı karşılamaktadır (2).

TARİHÇE

Ruh sağlığı ve sinirbilim alanındaki gelişmelerle birlikte psikonöroimmunoloji araştırmaları hız kazanmış olsa da çok eski dönemlerden beri konuyla ilgili gözlemsel ve deneysel çalışmaların olduğu görülmektedir. Eski Yunan uygarlığında ruhsal bozuklukların vücut sıvı dengesindeki bozukluklardan ileri geldiği düşünülmüş, Platon zihin, beden ve ruh dengesizliklerinin duygusal strese yol açtığını savunmuştur. Sonrasında 18. ve 19. yy’de özellikle çocukluk dönemindeki zorlu yaşam olaylarının psişe üzerine olumsuz etkileri olduğu, bunun erişkinlikte de devam ettiği, kişinin sosyal ve duygusal yaşamını etkilediği gösterilmiştir. Psikonöroimmunoloji terimi ilk kez 1975 yılında Ader ve Cohen tarafından kullanılmıştır (3).

Psikonöroimmunolojinin temelini oluşturan önemli bir gözlem immunolojik koşullanma ile ilgilidir. Oral sakarin çözeltisinin (koşullu uyaran)

immunosupresif ilaç siklofosfamid (koşulsuz uyaran) ile birlikte uygulanmasının farelerde koşullu bir tepkiye yol açtığı gösterilmiştir. Koşullanan farelere tekrar sakarin çözeltisi verildiğinde immun cevabın azaldığı gözlenmiştir. Bu sonuçlar, davranışsal koşullanmanın immun sistemin basılanmasına yol açan etkilerinin kesin kanıtlarını sağlamıştır (4). Sonrasında Ader ve arkadaşları davranışın immun sistem üzerine etkisinin iki yönde de olabileceğini göstermişlerdir (5).

Modern psikopatoloji alanı, araştırmacıların dikkatini ruhsal bozuklukların altında yatan biyolojik mekanizmalara odaklamak konusunda önemli ilerleme kaydetmiştir, ancak yine de, sosyal, psikolojik, nörolojik, immunolojik, genetik ve genomik süreçler dâhil olmak üzere çok çeşitli yollarla dikkate alınmaktadır (1).

İMMUN SİSTEME GENEL BAKIŞ

İmmun sistemin işlevi vücudu yabancı patojenlerden koruyarak biyolojik güvenliği sağlamaktır. Fiziksel hasar veya enfeksiyonlara karşı savunma işlevinde rol alan molekül, hücre ve dokuların hepsi birden immun sistemi oluşturmaktadır. Sistem, doğal (doğuştan gelen) ve edinsel (adaptif/kazanılmış) immunité olarak ikiye ayrılmaktadır.

Doğal İmmunité

Vücudun doku hasarına ve mikrobiyal enfeksiyonlara karşı ilk savunma sistemidir. Doğal immunité cevabı hızlıdır (dakikalar/saatler içinde), spesifik değildir, uzun süreli koruma sağlamaz. Bu sistem bağışıklık hücrelerinin (makrofaj, nötrofil,

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Tik Bozuklukları/PANDAS/OKB

Tourette Sendromu (TS) ve OKB tanılı çocuklar ve ergenlerde IL-12 ve TNF- α düzeyi yüksektir. TS'de ayrıca adhezyon molekülleri de yüksek düzeyde saptanmaktadır. OKB ile TNF- α gen polimorfizmi, Tourette sendromu ile IL1RN polimorfizmi ilişkilendirilmektedir (33).

Toxoplasma IGG pozitifliğinin çocuklar ve ergenlerde OKB ve yaygın anksiyete bozukluğu riskini 4-5 kat artırdığı belirtilmektedir (93). Sosyal fobi ise geç başlangıçlı kızamık, kabakulak ve su çiçeği enfeksiyonları ile ilişkilendirilmektedir (94).

Çocukluk çağı "Streptokok Enfeksiyonları" ile "İlişkili Otoimmün Nöropsikiyatrik Bozukluklar" (PANDAS), grup A hemolitik streptokok enfeksiyonu geçirdikten sonra tikler, istemsiz hareketler ve obsesif kompulsif semptomların görüldüğü, çocuklarda tanımlanan bir sendromdur. Antistreptokok antikorları ve bazal beyin ganglionlarının proteinleri (otoantijenleri) arasında çapraz bir reaksiyonun varlığı bilinmektedir. Bu antijenler, streptokok proteinlerine benzer bir yapıya sahip olan nörotransmisyon, nöronal metabolizma ve hücrel sinyalleşme ile ilgili bazı enzimleri (aldolazlar ve enolazlar) içermektedir. OKB belirtileri olanlarda bazal gangliyonlara karşı gelişen antikorlar pozitif saptanmakta ve BOS'ta yüksek düzeyde saptanan glisin, glutamaterjik tonus artışını göstermektedir. İmmün tedaviler ile OKB semptomlarında görülen düzelme, bu antikorların OKB patogeneğinde veya semptomları PANDAS ile ilişkilendiren grupta önemli role sahip olduğunu desteklemektedir (95).

Psikoz, Şizofreni

Şizofrenide Toxoplasma gondii enfeksiyonlarının sıklığının arttığı belirtilmiştir (90). Çocukluk dönemi psikozunda serum TNF- α , IL-1 β , IL-6, IL-5, IL-10, IFN- γ düzeyleri yüksek saptanmıştır (96). İlk psikotik atak sırasında pro-inflamatuvar (TNF- α) yanıtın artmış olarak saptanması çocukluk dönemi stresi ile de ilişkilendirilmiştir (97). Çocuklukta artmış IL-6'nın genç erişkinlikte psikoz riskini artırdığı bildirilmiştir (98). Çocuklar ve ergenlerde yapılan bir sistematik derlemede şizofrenide TNF- α düzeylerinin normal, IL-10'un ise düşük olduğu belirtilmiştir (33).

Yeme Bozuklukları

Obezite inflamasyonla ilişkilendirilse de anoreksiya nervozada da pro-inflamatuvar bir durum görüldüğü bilinmektedir. IL-6 ve IL- β 'nın hipotalamik nöropeptidlerin salınımını düzenleyerek kilo kontrolü üzerinde rol aldığı düşünülmektedir (99). Yeme bozukluklarında ayrıca bağırsak mikrobiyomlarının ve stres reaktivitesinin serotonerjik sistemi ve nöroinflamasyonu aktive ettiği belirtilmektedir (100).

SONUÇ

İmmunolojik hipotezler, çocukluk çağı davranışsal ve nörogelişimsel bozuklukların etiolojisine yönelik önemli açıklamalar sağlamaktadır. Biyopsikososyal tıbbi model ve psikonöroimmunoloji çocuk ruh sağlığını anlama ve iyileştirme süreçlerinde açık ve anlaşılır bilgiler sunmaktadır. Ayrıca çocukluk dönemi psikiyatrik bozukluklarında immün sistem işlevlerini araştırmak tedavi sürecinde de fayda sağlamaktadır.

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