

GELİŞİMSEL PSİKONÖROENDOKRİNOLOJİ

7. BÖLÜM

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GİRİŞ

Gelişimsel psikonöroendokrinoloji, endokrin sistem ve santral sinir sistemi (SSS) arasındaki yapısal ve işlevsel ilişki kapsamında gelişim basamaklarına özgü biyolojik ve davranışsal özellikleri inceler (1). Bu kapsamda iki sistem arasındaki hücrel, moleküler ya da fizyolojik düzeydeki etkileşimlerin gösterilmesi hem sağlıklı gelişim sürecinin tanımlanması hem endokrin sistem hastalıkları ile psikiyatrik bozuklukların anlaşılmasında önemlidir.

TARİHÇE

Sinirbilim alanında yapılan araştırmalarla birlikte psikiyatride önemli ve ilgi çekici bir konu hâline gelen psikonöroendokrinolojinin temelleri antik döneme dayanmaktadır. M.Ö. 4. yy'da Hipokrat tarafından tanımlanan dört vücut sıvısının (sarı safra, kara safra, kan, balgam) beyni etkileyerek ruhsal hastalıklara neden olduğu düşüncesi, diğer filozoflar tarafından da desteklenmiştir. Ayrıca bu dönemde, kara safranın melankoliye yol açtığı öne sürülerek tedavisinden de bahsedilmiştir. Romalı hekim Galen (M.S. 130-200) anatomi ve patoloji alanındaki gelişmelere önemli katkılar sağlayarak bu kuramları genişletmiştir. Rönesans döneminde pek çok endokrin bezin anatomisi tanımlanmış, 18. yy'de endokrin işlevler üzerine çalışmalar yapılmış, 19. yy ve sonrasında kimyasal nörotransmitterler, hipotalamik-hipofizer kontrol üzerine araştırmalar yoğunlaşmıştır. Endokrin hastalıklarda psikiyatrik semptomların değerlendirilmesi

bu dönemde başlamıştır. Şizofreninin adrenal bez üretimindeki bir bozukluktan ortaya çıktığı teorisine ile şizofreni tedavisinde adenalektomiye yer verilmiştir. Bleuler, endokrin bozuklukların davranışsal sonuçları üzerine gözlemlerini tartışmış, Kraepelin "Demantia Praecox" patogenezinde endokrin sistemin rol oynadığını öne sürmüştür, Freud hormonların psişe üzerine zarar verici etkisinin "nevroz"un temellerinden biri olabileceğinden bahsetmiştir. Özellikle 20. yy ikinci yarısından sonra, pek çok nörotransmitter, peptit ve hormonların tanımlanması ve moleküler düzeyde yapılan çalışmalarla birlikte psikonöroendokrinoloji alanındaki gelişmeler hız kazanmıştır. Son yıllarda psikiyatrik bozuklukların büyük çoğunluğunun patofizyolojisinde önemli rol oynayan hipotalamik-hipofizer yolak hormonları, nöropeptidler ve bunlar üzerinde düzenleyici kontrole sahip nörotransmitterler araştırılmaktadır (2). Bu bağlamda, beyin gelişiminde etkili bazı nöroendokrin yolaklar yapısal ve işlevsel olarak ele alınarak bunların psikiyatrik bozukluklarla ilişkisi incelenecektir.

HİPOTALAMİK-HİPOFİZER YOLAKLAR

Hipotalamik hormonlar (CRH, TRH, GnRH, Somatostatin, GHRH, Dopamin) hipotalamik-hipofizer portal sistem içinde ön hipofize (adenohipofiz) taşınarak buradaki hormonların (ACTH, TSH, FSH, LH, GH, Prolaktin) sentezini uyarır veya inhibe eder. Hipotalamusta sentezlenen diğer hormonlar (Oksitosin ve Arjinin-Vazopressin) ise nörosekretuar liflerle arka hipofize (nörohipofiz) taşınarak buradan dolaşıma geçer.

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kokortikoid ve androjen (testosteron, DHEA) artışının görüldüğü, yaş ilerledikçe steroid hormon konsantrasyonlarının azaldığı ifade edilmektedir. Erkeklerde bipolar bozukluk ergenlikte artış göstermektedir. Bu gençlerde testosteron düzeyinin daha yüksek olduğu, manik dönemlerde DHEA düzeyinin arttığı, östradiol yüksekliğinin ise duygudurum dalgalanmaları ile ilişkili olduğu belirtilmektedir (152).

Yeme Bozuklukları

Anoreksiya nervoza (AN) tanılı gençlerde yüksek kortizol düzeyleri görülmektedir (154). Kız ergenlerde saç kortizol düzeyinin sağlıklılara göre daha düşük olduğunu belirten çalışmalar da bulunmaktadır (155).

Bebeklik ve ergenlik dönemindeki AN'de GH-IGF-1 ekseninde bozulma sonucunda gelişim geriliği ve malnütrisyon görülmekte, kilo alımı ve besin desteğinin sağlanması ile eksen işlevlerinde düzelme olmaktadır (156, 157).

Yeme bozukluğunda hipogonadotropik hipogonadizm eşlik eden diğer endokrin bozukluktur (154). Erken gelişim döneminde testosteron maruziyeti ve normal erkek yönündeki gelişim yeme bozukluğu için koruyucudur. Ergenlik ve sonrasında cinsiyet hormonlarının (erkeklerde androjen, kızlarda östrojen) yüksek olması yeme bozukluğu riskini azaltmaktadır (158).

Ötiroid hasta sendromu (normal/düşük TSH ve T4, düşük T3) AN'ye en sık eşlik eden tiroid işlev bozukluğudur. Klinik olarak hipotiroidi belirtileri gözlenmektedir (154).

Travma Sonrası Stres Bozukluğu (TSSB)

Çocuk ve erişkin yaş grubunda TSSB ile ilgili yapılan araştırmalar, bu olguların kortizol düzeylerinin kontrollere göre anlamlı olarak daha düşük olduğunu göstermektedir (159). Ancak kortizol düzeyinin daha yüksek ya da kontrollerle benzer olduğunu öne süren çalışmalar da bulunmaktadır (160, 161). Travma maruziyetinden sonra azalan kortizol düzeylerinin zamanla artarak normal düzeye ulaştığı belirtilmektedir (161). Ergenlik döneminde kızlarda östrojen artışı ile birlikte TSSB görülme sıklığı artmaktadır (162). TSSB tanılı ergenler değerlendirildiğinde kızlarda, yaşça daha büyük olanlarda ve eşlik eden içe atım belirtileri varlığında daha yüksek kortizol düzeylerinin gö-

rüldüğü, özellikle kızlarda TSSB semptomlarına paralel olarak kortizol düzeylerinin de arttığı ifade edilmektedir (163). Kimi yayımlarda ise kortizol ile TSSB semptomları arasındaki bu pozitif yönlü ilişkinin yaşla birlikte tersine döndüğü bildirilmektedir (164).

SONUÇ

Gelişimsel psikonöroendokrinoloji alanında endokrin faktörlerin sinir sistemi gelişimi üzerindeki önemli etkileri, hormonal bozukluklarda görülen bilişsel ve/veya davranışsal anormallikler ve psikiyatrik bozukluklara eşlik eden nöroendokrin değişiklikler üzerine araştırmalar yapılmaktadır. Hem psikiyatrik bozuklukların etiyopatogenezi, tanı-tedavi süreçlerinde hem endokrin hastalıkların izleminde oldukça önemli bir yere sahiptir.

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