



BÖLÜM 4

Kronik Psikiyatrik Hastalıklarda Reseptörler

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Giriş

Psikiyatrik hastalıkların, karmaşık patofizyolojilerinin altında yatan moleküler ve hücresel mekanizmalar henüz tam olarak aydınlatılamamıştır. Son yıllarda, nöral devreler ve sinaptik iletimin çeşitli mekanizmalarının, reseptör ve reseptör sonrası sinyalleme moleküler mekanizmalarının ve genlerin daha iyi anlaşılmasıyla özellikle duygudurum bozuklukları ve psikotik bozukluklar başta olmak üzere kronik psikiyatrik hastalıkların anlaşılmasında önemli ilerlemeler kaydedilmektedir (1).

ŞİZOFRENI

Dopaminerjik Reseptörler ve Şizofreni

Şizofreninin pozitif belirtilerinin limbik dopaminerjik iletimin hiperaktivitesinden kaynaklandığı hipotezi, tüm etkili antipsikotik ajanların dopamin D2 reseptörlerini bloke etmesi ve dopamin salınımını kolaylaştıran amfetaminin şizofreni benzeri psikotik semptomlara neden olmasından kaynaklanmaktadır (2). Dopamin teorisini destekleyen verilerin çoğu, antipsikotik ilaçlarla ilgili çalışmalardan elde edilmektedir.

D2 reseptörleri presinaptik alanda bulunmakta ve otoreseptör olarak görev yapmaktadır (3). D2 reseptörlerine dopamine bağlı olmadıklarında dopamin salgılanmasına izin verirken, dopamin artıp reseptörlere bağlandığında dopamin salınımını inhibe etmektedirler (3). Beyinde mezolimbik dopamin yolağı, mezokortikal dopamin yolağı, nigrostriatal dopamin yolağı, tuberoinfundibuler dopamin yolağı ve talamik yolaktır (4). Şizofrenide mezolimbik dopamin yolağının hiperaktif olduğu kabul edilmektedir. Sinaptik aralıkta dopamin artışına bağlı olarak pozitif belirtilerin (varsanılar ve sanrılar) oluştuğu düşünülmektedir (4). D2 reseptörlerini bloke eden antipsikotikler, aşırı etkinliği ve dopamini azaltarak pozitif belirtileri tedavi etmektedir (5). Şizofrenide dorsolateral prefrontal kortekse (DLPFK) ve ventromedial prefrontal kortekse (VMPFK) giden mezokortikal dopamin yolağının hipoaktif olduğu ve bu durumun bilişsel semptomlar, negatif belirtiler ve afektif belirtilerle ilişkili olduğu düşünülmektedir (4). D2 antagonistlerinin uygulanması mezokortikal yolağın aktivitesini daha da baskılayarak bu belirtileri kötüleştirir. Şizofreni de nigrostriatal ve tuberoinfundibuler dopamin yolları doğrudan etkilenmese de D2 reseptörlerinin blokajı

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