Bölüm 19

Perinatal Psikonöroimmünoloji: Prenatal Stres ve Bunun Fetal ve Postnatal Beyin Gelişimi Üzerine Olan Etkilerinin Araştırılma Protokolleri

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Özet

Prenatal stres (PS) erken davranışsal, nöroimmün ve bilişsel gelişmeyi etkiler. Gebe sıçan modelleri bu tür fetal programlamadaki mekanizmaları incelemede çok değerli bulunmuştur. Maternal stresin yeni gebe koyun modeli kronik in utero izleme ve manipülasyona izin vermek gibi özgün avantajlar vaad etmektedir. Bu bölüm tek ve çoklu-kaynaklı strese maruz kalma ve bunların yavrular üzerine olan pleiotropik etkileri için model olarak kullanılacak yöntemleri sunmaktadır.

Anahtar sözcükler DOHaD, Stres, Gebelik, Hayvan modelleri, Çoklu-darbe, Kuşaklar, Sıçan, Koyun

1 Giriş

Maternal ve paternal prenatal stres , fetal ve postnatal beyin gelişmesini programladığı bilinen, en yaygın olarak gözlemlenen ve geniş ölçüde akut ve kronik etki yapan durumlar bazılarını temsil eder [1]. Belli belirsizden derin tablolara kadar giden sonuçları içeren geniş bir yelpaze içinde davranış, özellikle duygusal denetleme ve özellikle yaşamın daha sonraki döneminde karşılaşılan saldırılara açık kalmayı ve nörogenezi etkileyen glial işlevin programlanması yoluyla nöroimmün işlev bulunmaktadır [2–6]. Prenatal stresin etkileri, travmanın zamanlaması, etkilenen gelişen fizyolojik sistemler, bireysel geno ve fenotip ve çevresel etkileşimler açısından oldukça pleiotropriktir. Sonuç olarak, insan sağlığını ilgilendiren altta yatan mekanizmaların anlaşılması çok sayıda hayvan modelinde çalışmayı gerektirmekte olup bunların her birinin kendine özgün üstünlükleri vardır. Biz burada yavrunun fenotipi üzerine, tek, çoklu- ve kuşaklar boyu mazuriyet ve gebe sıçan ve koyunda modellenmiş kalıtımsal mekanizmalar yoluyla karşılaşılan strese maternal katkıya odaklanmaktayız. Bu hayvan modellerinin seçilme nedeni bunların alanda kayıtlarının izlenmesidir. Gebe sıçan modelleri tek- ve çok-kuşak

8. Stresin beden ağırlığı ve yiyecek alımındaki değişikliklere fizyolojik korelasyonunun ölçülmesi.
9. Strese yanıt eksenlerinin immünohistokimyası.
   (a) Strese yanıtı değerlendirmek için GR, MR, CRH ve oksitosin reseptör yoğunluğu ve hücre içi yerleşimi nicelendirmek.
   (b) Prefrontal korteks, hippokampus, bazolateral amigdal ve paraventriküler hipotalamus gibi stres yanıtı ve duygusal bozukluklara katılan merkezi yapıların genel morfolojilerini (kortikal kalınlık, hacim, nöron dansitesi) değerlendirmek.

4 Sentez ve Sonuç

Perikonsepsüel [100] ve embriyonik gelişme dönemi yerine fetal gelişme sırasında stresin etkilerini taklit eden gebe sıçan ve koyundaki hayvan modellerini gözden geçirdik. Keza fetal programlanmanın kuşaklar boyu giden etkilerini de ele aldık. Burada önemli olarak, günümüzde sanki kesinleşmişe benzeyen bir olay, genetik ve henüz tam olarak tanımlanmamış epigenetik mekanizmalar yığının fetal gelişme sırasında karşılaşın akut veya kronik saldırıları sadece tek değil aynı zamanta çok- ve kuşaklar boyu bellekte saklayabildiğidir. Bu uyumcul veya kötü uyumlu fizyolojik fenomene sağlık ve hastalığın gelişimsel kaynakları (DoHAD) kavramı da denilmektedir. Psikonöroimmünoloji çatısı çekici bir çatı sağlamakta olup burada prenatal stresin anne ve yavru üzerine olan pleiotropik etkileri ele alınmaktadır.

Bu derlemede sunulan gebe sıçan ve koyun modellerine ait protokoller birbirlerini tamamlayıcı olup intrauterin ve postnatal ortamları olasılıkla manipüle edebilen ve fetal, yenidoğan ve maternal fizyolojik yanıtları direkt olarak ölçen prenatal stresin fetal ve postnatal etkilerinin yoğun şekilde teste tabi tutulmasına bir temel sağlamaktadır. Bunun ise, prenatal stresin öngörücü ve tanısal biyobelirteçlerinin idantifikasyonu ve keza anne ve evlatlarda "stresli beyin" fenotipini söndürecek terapötik yaklaşımların geliştirilmesi yönünden translasyonal bir karşılığı bulunmaktadır. Bu tür çalışmaların, anneler ve evlatları için sağlıklı bir gelişmeyi ve başarılı bir yaşlanmayı teşvik etmek üzere kuşaklar boyu süren strese maruz kalmaya ait kısır döngüyü kıracak klinik stratejiler geliştirilmesine yardımcı olacağını ummaktayız.

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