



BÖLÜM 13

Genetik Varyantlar ve Dil ve Konuşma Bozukluklarının Değerlendirilmesi

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Varyant nedir?

2000’li yılların ortalarına kadar sıkça kullandığımız, toplumda %1’den daha sık görülen değişimlere “polimorfizm” ve toplum sıklığı %1’den daha az görülen değişimlere ise “mutasyon” terimleri artık yerini “varyant” terimine bırakmıştır. Günümüzde yeni nesil dizileme sistemlerinin, genetik hastalıkların tanısında aktif olarak kullanılması ile ortaya çıkan “yeni tanımlanmış-novel” genetik değişimlerin fazlalığı, genetik değişimlerin polimorfizm-mutasyon terimleri ile tanımlanmasının yetersiz kaldığını göstermiştir. 2015 yılında Amerika Medikal Genetik Derneği (ACMG)’nin yayınladığı kılavuza göre tüm genetik değişimler “varyant” adını almış, kliniğe etkisine göre de “patojenik”, “muhtemel patojenik”, “klinik anlamı bilinmeyen (VUS)”, “benin” ve “muhtemel benin” olmak üzere beş ana sınıfta kategorize edilmiştir (1). Bu kılavuzda varyantlar toplum sıklığı, ailedeki kalıtım durumu, varyantın proteine etkisi ve fonksiyonel analizlerin olup olmaması ışığında patojenik veya benin diye sınıflandırılmakta, herhangi bir sınıfa giremeyenler ise VUS olarak isimlendirilmektedir. Yani bir varyantın patojenitesi o varyantın tipine (yanlış anlamalı, delesyon, vs. gibi) göre değil; toplum içerisinde görülme sıklığı, protein yapısına etkisi ve ailede hasta olan ve olmayan bireylerdeki

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Tablo 1. Gen isimleri ve ilişkili dil ve konuşma bozukluğu kliniği (DEVAMI)

SETBP1	18q12.3	Çocukluk çağı konuşma apraksisi	(45)
		Gelişimsel dil bozukluğu	
SETD1A	16p11.2	Çocukluk çağı konuşma apraksisi	(45)
SETX	9q34.12	Disleksi	((41)
		Çocukluk çağı konuşma apraksisi	
SMCR8	11p11.2	Çocukluk çağı konuşma apraksisi	(35)
SRPX2	Xq22.1	Otizm spektrum bozukluğu	(97,98)
TDP-43	1p36.22	Afazi	(82)
TNRCB	22q13.1	Çocukluk çağı konuşma apraksisi	(45)
TTRAP	6p22.3	Disleksi	(76,99)
WDR5	9q34.2	Çocukluk çağı konuşma apraksisi	(45)
ZEHX4	8q21.13	Çocukluk çağı konuşma apraksisi	(45)
ZGRF1	15q25.1	Çocukluk çağı konuşma apraksisi	(35)
ZNF385D	3p24.3	Gelişimsel dil bozukluğu	(49)

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