Utility of next generation sequencing in paediatric neurological disorders: experience from South Africa

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INTRODUCTION

Next generation sequencing (NGS)-based tests have become routine first-line investigative modalities in paediatric neurology clinics in many high-income countries. These tests are both cost-effective and reliable in diagnosing many complex childhood neurological diseases. However, NGS-based testing in low-and middle-income countries is limited due to affordability constraints. The primary objective of this study was to evaluate the diagnostic yield and impact of targeted gene panel sequencing in a selected paediatric cohort attending a tertiary paediatric neurology clinic in the Western Cape Province of South Africa.

OBJECTIVES

The objective of this study was to evaluate the diagnostic yield of targeted gene panel sequencing in a paediatric cohort attending a tertiary neurology clinic in the Western Cape Province of South Africa.

METHODS

Retrospective study of 124 consecutive paediatric patients with neurological disease.

Patient's age: 6 weeks to 17years

Test: NGS-based multi-gene panels

Questionnaire: given to caregivers where pathological variant found

Duration: 41-month period

Results: Pathological variants phenotypical matching

RESULTS

Did the result help explain the reason for your child illness?	Results
Yes	25 (86%)
No	3 (10%)
Unknown	1 (3%)
Did the result help you to take better care for your child?	
Yes	14 (48%)
No	13 (44%)
Some/little	2 (7%)
Should prenatal testing become available, would you make use of it?	
Yes	28 (97%)
Not applicable	1 (3%)
Did knowing the result bring you and your family any closure?	
Yes	28 (97%)
Some/little	1 (3%)

DISORDER GROUPS	Pathogenic gene	Patho-genic	phenotype correlation
Neuromuscular Disorders	RYR1	3	3
	SMN1	1	1
	TTN	1	0
	CAPN3	1	0
	GBE1	1	1
	STAC3	2	2
	DMD	4	4
	SCN9A	2	2
	SMN1, SMNcopies2	1	1
	COL6A1	1	1
TOTAL		17(68%)	15(52%)

DISORDER GROUPS	Pathogenic gene	Patho-genic	phenotype correlation
Epilepsies	SCN1A	7	7
	COG5	1	0
	DYRK1A	1	1
	GABRB3	1	1
	UBE3A	1	0
	STXBP1	1	1
	KCNMA1	1	1
	KANSL1	1	1
	SCN2A	1	1
	TPP1	1	1
	CDKL5	4	4
	KCNQ2	3	3
	GNAO1	1	1
	SLC6A5	1	1
	NPRL3	1	1
	PCDH19	1	1
	CDKL5	1	1
	SMC1A	1	1
TOTAL		28 (44%)	26(41%)
Heredodegenerative disorders	ARSA	2	2
	ACAD5	1	0
	UGT1A1	2	0
	ABCD1	1	1
	PLP1	1	1
TOTAL		7(77%)	4(44%)
CP spectrum disorders	SCN2A	1	1
	ADAR	2	1
	SLC16A2	1	1
	BTD	2	0
	KCNA2	1	1
	QDPR	1	1
	ATM	1	0
	NPHP1	1	0
TOTAL		10(63%)	5 (31%)

RESULTS

The overall study diagnostic yield (DY) was 45%. Neuromuscular disorders 52% (13/25), cerebral palsy spectrum disorders 31% (5/16) and early-onset epilepsies 41% (26/63). With variants of uncertain significance in 38% (47/124).

The majority of caregivers (97%) viewed NGS-based testing as a positive experience .

CONCLUSION

The study enforces that NGS testing is achievable in resource-constrained settings. The high diagnostic yield in this study suggests that it is feasible to recommend NGS as a first-tier testing approach for children with neurological disorders.

REFERENCES

van Niekerk et al, 2025 In Press at the European Journal of Human Genetics. (accepted awaiting publication)

ACKNOWLEGDEMENTS

We thank all the families involved in this study and the clinicians who care for them.

This study was undertaken as part of an MPhil thesis (MvN) supervised by RS, RvT and SM.