The Phenotype of C9orf72 - associated Primary Progressive Aphasia: a case study

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Introduction

C9orf72-associated frontotemporal dementia usually presents with the behavioral variant but cases of primary progressive aphasia (PPA) have also been described. However, the phenotype of this is poorly understood.

Materials and Methods

We undertook a longitudinal single case study of a patient with a C9orf72 expansion who presented with progressive speech and language problems consistent with a diagnosis of PPA. We performed a range of cognitive and neurolinguistic assessments at two time-points. Neuroimaging with volumetric T1-weighted imaging on a 3T Siemens Trio MR scanner was also acquired.

Results

A 54-year-old gentleman presented with a two year history of progressive speech problems and a one year history of behavioural change. His first symptom was increasing effortfulness of speech production. He had also developed a decrease in motivation, emotional lability and increased appetite. In the family history it was noted that his mother had had dementia in her 60's. Genetic testing revealed an abnormal expansion in the C9orf72 gene.

Detailed neuropsychological and linguistic assessments showed an apraxia of speech, impaired repetition and an orofacial apraxia but with intact naming, single word and sentence comprehension, and normal performance in other cognitive domains apart from impaired executive function, social cognition and processing speed.

At his follow-up visit his speech production had deteriorated and he now had impaired performance on tasks of single word and sentence comprehension but with intact naming.

MRI showed relatively generalised symmetrical cortical atrophy with a frontal predominance and involvement of the caudate and hippocampus bilaterally. Atrophy had spread more posteriorly at the follow-up visit.

Conclusion

C9orf72-associated PPA in this gentleman was associated with an initial AOS with early behavioural changes, executive dysfunction and impaired social cognition. C9orf72 is a rare cause of PPA but should be tested for in those particularly with ALS and early behavioural change.

General Neuropsychology Assessment			Baseline Raw Score	Baseline Percentile	1yr follow-up Raw Score	1yr follow-up Percentile
General Intelligence						
WASI	**Vocabulary**		64	Verbal IQ: 107	44	Verbal IQ: 78
	Similarities		34		19	
	Block Design		8	Performance IQ: 90	8	Performance IQ: 83
	Matrix Reasoning		22		15	
Memory						
Recognition Memory Test	**Faces**		33	<5th	35	<5th
	Words		50	≥95th	42	≤50-75th
Camden Paired Associates Learning			18	≤50th-75th	15	≤25-50th
Attention and Executive Function						
Trails A	**Time (sec)**		41	≥5th-25th	136	<5th
Trails B	**Time (sec)**		214	<5th	300	<5th
WAIS-R Digit Symbol			29	<5th	20	<5th
Verbal Fluency	**F**		4	<5th	2	<5th
Category Fluency	**Animals**		13	≤5th-25th	12	≥5th
Stroop Ink-color naming	**Time (sec)**		153	<5th	108	<5th
WAIS-R Digit Span	**Forwards**	**/12**	9	≤50th-75th	8	≤50th-75th
	Backwards	**/12**	6	≥25th-50th	4	≥5th-25th
Visuosperceptual/Visuospatial Skills						
VOSP Object Decision			15	≥5th-25th	18	≤50th-75th
Arithmetic						
Graded Difficulty Arithmetic Test	**Total**		5	≤5th-25th	1	<5th
Social Cognition						
Mini-Social Cognition and Emotion Assessment		**/30**	20		19	
Detailed Linguistic Assessment						
Naming						
Graded Naming Test		**/30**	22	≥25th-50th	21	≥25th-50th
Verb Naming Test		**/20**	20		18	
Repetition						
Single Word Repetition		**/45**	29		27	
Nonword Repetition		**/20**	17		13	
Sentence Repetition		**/10**	4		7	
Single Word Comprehension						
Synonyms Test	**Concrete**	**/25**	22	≤50th-75th	18	≥5th
	Abstract	**/25**	21	≤50th-75th	18	≤5th -25th
Sentence Comprehension and Grammar						
PALPA 55 (Revised) Sentence Comprehension		**/24**	24		24	
Written Sentence Construction		**/50**	29		22	
Test of the Reception of Grammar (TROG)		**/20**	17	≤25th-50th	15	5th -25th
Reading						
Graded Nonword Reading Test		**/25**	22		11	
Spelling						
Graded Difficulty Spelling Test		**/30**	21		22	

Table 1. Summary of neuropsychometric scores: assessments performed at initial visit and 12 months afterwards.

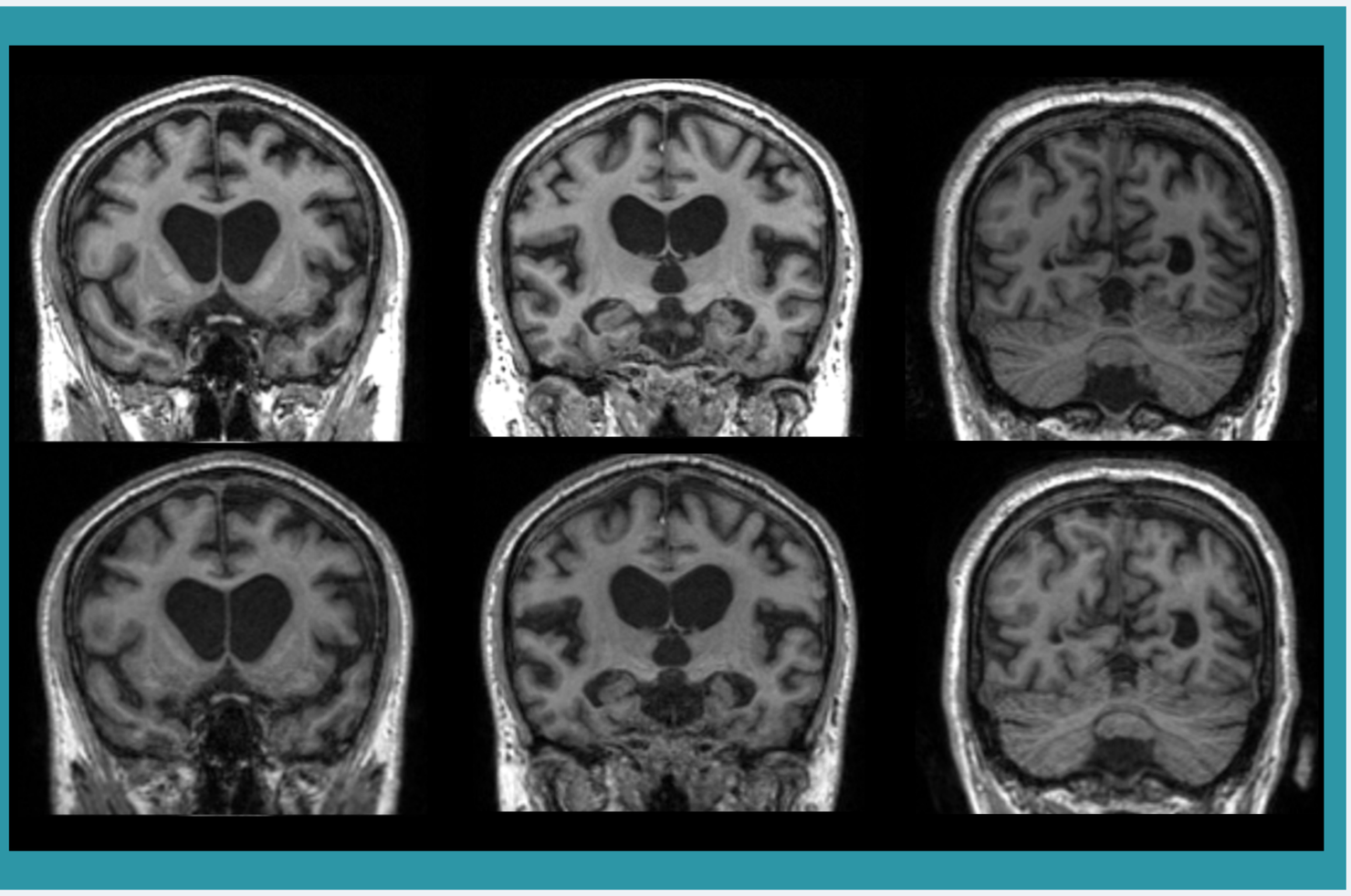

Figure 1. Coronal T1 volumetric imaging performed at initial visit (top) and 12 months afterwards (bottom).

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