Update on ALS and Related Neurodegenerative Disorders

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Case-Based Questions (please see page 3 for answers)

1.	Which of the following proteins are found to be aggregated most commonly in both sporadic ALS and FTLD-MND?	
	a.	Alpha-synuclein
	b.	Beta-amyloid
	c.	Phosphorylated-tau
	d.	TDP-43

2.	What is the most common gene associated with genetic alteration found in familial ALS and FTLD-MND?	
	a.	*APOE*
	b.	*C9orf72*
	c.	*Presenilin*
	d.	*SOD1*
	e.	*TDP43*

3.	Which of the following is the only way to a diagnosis of FTLD or ALS?	
	a.	Autopsy and neuropathological evaluation
	b.	Biofluid evaluation of CSF or blood
	c.	Muscle biopsy
	d.	Surgical biopsy of the spinal cord or frontal lobe
	e.	<INSERT ANSWER CHOICE>

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Question 1: Correct answer and rationale: <D: Atypical TDP43 aggregates are found in glia and neurons in the motor cortex and spinal cord for both ALS and FTLD.>

Question 2: Correct answer and rationale: <B: Increased numbers of hexanucleotide repeats in the *C9orf72* gene is the most common familial genetic alteration in ALS and FTLD-MND.>

Question 3: Correct answer and rationale: <A: Autopsy with appropriate sampling of brain, spinal cord, and muscle with H&E, special stain histopathology and immunohistochemical evaluation for TDP43 and possibly other markers of disease is the only current way to pathologically diagnose ALS and/or FTLD-MND.