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Objective: The Texas Functional Living Scale (TFLS) is a measure of adaptive functioning commonly utilized across the geriatric population. Current research suggests that those with Alzheimer's disease and other dementias perform poorly on the TFLS, compared to those with mild cognitive impairment (MCI) and normal cognition (Cullum et al., 2001). Additional research is needed to examine the influence anxiety and depressive symptoms have on activities of daily living (ADLS) in individuals being evaluated for memory disorders. This study will examine the effects of anxiety and depression on adaptive functioning across all patients, and within samples of those with dementia and MCI. It is hypothesized that higher reported anxiety and depressive symptoms will predict lower scores of ADLS.
Participants and Methods: Patients at a memory disorder clinic (N = 756; 58.2% female) were screened for cognitive impairment using the Montreal Cognitive Assessment (MoCA). A brief neuropsychological evaluation (BNE) was then conducted in which the TFLS, Geriatric Depression Scale (GDS), and Geriatric Anxiety Inventory (GAI) were administered, among other measures.
Results: A stepwise hierarchical regression was conducted on the entire sample to examine the effects of anxiety and depressive symptoms on TFLS performance, controlling for cognitive impairment using the MoCA. Lower MoCA scores explained a significant amount of variance in TFLS performance (R^2 = 0.456, F(1, 754) = 632.78, p < .001). MoCA scores (b = 1.27, p < .001), the GAI (b = 0.14, p = .019), and the GDS (b = 0.10, p = 0.039) were significant predictors of poor TFLS performance across the entire sample. Although the MoCA, GDS, and GAI were each significant predictors of the TFLS, the increased variance explained by the GDS and GAI individually was incremental (ΔR^2 = 0.003, F(1, 752) = 3.90, p = .049). Stepwise hierarchical regressions were also conducted on subsamples diagnosed with MCI (N = 171) and dementia (N = 394). For those with MCI, MoCA scores explained a significant amount of variance in TFLS performance (R^2 = 0.044, F(1, 169) = 7.80, p = .006). Neither the GAI nor GDS explained significant additional variance. Only MoCA scores (b = .30, p =.006) predicted TFLS performance. For those with dementia, MoCA scores explained significant variance in TFLS scores (R^2 = 0.338, F(1, 392) = 200.47, p < .001). The GAI explained additional significant variance when added (ΔR^2 = 0.009, F(1, 391) = 5.26, p = .022). The GDS did not explain any additional variance. Both the MoCA (b = 1.29, p < .001) and the GAI (b = -0.15, p = .002) significantly predicted TFLS performance.
Conclusions: While results suggest that anxiety and depressive symptoms alone do not explain a significant degree of variance within scores of adaptive functioning across the entire sample, elevated ratings of anxiety and depressive symptoms were significant predictors of lower scores of ADLS, suggesting some support for our hypothesis. Additionally, anxiety symptoms significantly explained increased variance in TFLS scores for those diagnosed with dementia, suggesting a potential relationship between anxiety levels and poor adaptive functioning for dementia patients.

Categories: Neurodegenerative Disorders
Keyword 1: memory disorders
Keyword 2: adaptive functioning
Keyword 3: depression
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60 Impact of Reducing the Nuclear Mutant ATXN1 on Spinocerebellar Ataxia-Like Phenotype

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Objective: Spinocerebellar ataxia type one (SCA1) is an autosomal dominant neurodegenerative disease caused by an expanded CAG repeat that encodes glutamine (polyQ) in the affected ATXN1 gene. SCA1 pathology is commonly characterized by the degeneration of the cerebellar Purkinje cells (PC) and brainstem. Symptoms include motor dysfunction, cognitive impairments, bulbar dysfunction, and premature death. *Atxn1*$^{175Q/2Q}$ knock-in mice were previously developed to

https://doi.org/10.1017/S1355617723007312 Published online by Cambridge University Press

model SCA1 by inserting 175 expanded CAG repeats into one allele of the Atxn1 gene, producing mice expressing ATXN1 throughout the brain and displaying SCA1 symptoms. Previous research has indicated the role of localization of the ATXN1 protein to the nucleus in pathology. Therefore, the *Atxn1*$^{175QK772T/2Q}$ mouse model was created by disrupting the NLS in the expanded *Atxn1*$^{175Q/2Q}$ mice by replacing lysine with threonine at position 772 in the nuclear localization sequence (NLS). Since this amino acid change previously blocked PC disease in another mouse model, the *Atxn1*$^{175QK772T/2Q}$ mice were created to examine how the NLS mutation affects neuronal cells. RNA sequencing analysis was previously performed and found differentially expressed genes (DEG) with *Atxn1*$^{175Q/2Q}$ downregulated compared to *Atxn1*$^{175QK772T/2Q}$ and *Atxn1*$^{2Q/2Q}$ in the cerebellum, medulla, cortex, hippocampus, and striatum. The aim was to analyze these brain regions to validate the RNAseq differential gene expression at a protein level.
Participants and Methods: Therefore, western blots were performed on the following mouse models (n=12): wild type mice (*Atxn1*$^{2Q/2Q}$), mice with the nuclear localization sequence mutation (*Atxn1*$^{2QK772T/2Q}$), and mice with 175 expanded CAG repeats (*Atxn1*$^{175/2Q}$). Based off the RNAseq data, the cerebellum was tested with ion channel genes (Cav3.1, Kcnma1, and Trpc3) and the striatum was tested with a gene found in medium-spiny neurons (DARPP-32).
Results: In the cerebellum, *Atxn1*$^{175/2Q}$ was significantly downregulated compared to *Atxn1*$^{175QK772T/2Q}$ in Cav3.1, Trpc3, and Kcnma1. Atxn1$^{175Q/2Q}$ was significantly downregulated compared to *Atxn1*$^{2Q/2Q}$ in Trpc3 and Kcnma1. *Atxn1*$^{175QK772T/2Q}$ was significantly downregulated compared to *Atxn1*$^{2Q/2Q}$ in Trpc3. In the striatum, there was significantly reduced DARPP-32 expression found between *Atxn1*$^{2Q/2Q}$ and *Atxn1*$^{175QK772T/2Q}$, *Atxn1*$^{2Q/2Q}$ and *Atxn1*$^{175Q/2Q}$, and *Atxn1*$^{175Q/2Q}$ and *Atxn1*$^{175QK772T/2Q}$.
Conclusions: Therefore, the significantly reduced gene expression at the protein level in the cerebellum and striatum validate RNAseq differentially expressed genes. Additionally, the downregulation of both the *Atxn1*$^{175Q/2Q}$ and *Atxn1*$^{175QK772TQ/2Q}$ compared to *Atxn1*$^{2Q/2Q}$ in the striatum supports the lack of learning of those mouse models on the rotarod, suggesting that the nuclear localization mutation does not rescue learning. Interestingly, the downregulation of *Atxn1*$^{175Q/2Q}$ compared to *Atxn1*$^{175QK772TQ/2Q}$ likely supports the age-related motor decline rescue in the rotarod seen in *Atxn1*$^{175QK772T/2Q}$ and not *Atxn1*$^{175Q/2Q}$.

Categories: Neurodegenerative Disorders
Keyword 1: ataxia
Keyword 2: movement disorders
Keyword 3: genetic neuropsychology
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61 Factors Affecting Executive Functioning in Patients with Parkinson's Disease

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Objective: Parkinson's disease (PD) is one of the most prevalent neurodegenerative conditions that leads to progressive degeneration in areas of the brain that control movement. As the disease progresses, cognition is also frequently affected, primarily executive functioning. Multiple factors may be involved in the relationship between PD and cognitive dysfunction. This study seeks to determine the association between disease duration (i.e., years since PD diagnosis), vascular comorbidities, and cognitive reserve (CR) and their relationship with executive functioning, in a clinic-referred PD population.
Participants and Methods: Participants included English-speaking subjects with a diagnosis of PD made by the patient's treating neurologist (i.e., movement disorders specialist) who received their neurological care and had undergone a comprehensive neuropsychological evaluation at Thomas Jefferson University Hospital in Philadelphia, PA over the past five years. The sample consists of 67 patients. Comprehensive medical and psychiatric histories were obtained, and individuals with severe psychopathology (e.g., bipolar disorder or schizophrenia), medical or other neurological disorders (e.g., seizure disorder, stroke, documented head injury that was more severe than a mild TBI or intracranial bleeding) that could account entirely for cognitive impairment were excluded. An overall domain score of executive functioning was calculated by averaging each participant's T-scores for the individual neuropsychological tests. Regression

https://doi.org/10.1017/S1355617723007312 Published online by Cambridge University Press