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Cognitive, Anxiety, and Mood Disorders in the Fragile X-associated Tremor/Ataxia Syndrome (FXTAS)

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Abstract

Objective—The authors evaluated patients with Fragile X-associated Tremor/Ataxia Syndrome (FXTAS), a neurodegenerative disorder associated with a CGG repeat expansion in the premutation range in the fragile X mental retardation 1 gene (*FMRI*).

Method—Neurological, psychiatric, and neuropsychological evaluations were completed on 15 males with FXTAS.

Results—Seven cases were diagnosed with dementia; seven were diagnosed with mood and/or anxiety disorders. Twelve subjects demonstrated deficits on neuropsychological testing.

Conclusions—Physicians assessing dementia patients are urged to consider this newly-described syndrome, especially in patients with dementia associated with a movement disorder and in patients with family history of mental retardation. If FXTAS is a possible diagnosis, the physician may obtain *FMRI* DNA testing; patients who are positive on DNA testing should have an MRI, be referred to neurology, and receive genetic counseling

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Keywords

FXTAS; fragile X premutation; dementia; anxiety disorder; mood disorder

Introduction

The Fragile X-associated Tremor/Ataxia Syndrome (FXTAS) is a newly described neurodegenerative disorder in a subgroup of carriers with the *FMRI* premutation {55–200 CGG repeats, 1, 2}. Neurological features include progressive intention tremor, ataxia, Parkinsonism, neuropathy, and autonomic dysfunction. Psychiatric features include anxiety, irritability, depression, agitation, psychosis, and fronto-subcortical dementia {including memory and executive function deficits, 3, 4, 5}. Onset is generally after age 50, and individual patients may initially present with primarily neurological symptoms, psychiatric symptoms, or both. Because of the appearance of tremor, ataxia, bradykinesias, and masked facies, co-morbid with anxiety, mood, psychotic, and cognitive disorders, there is some clinical similarity of this syndrome to Parkinson's disease (PD). There are some important differences in the motor symptoms, however. The tremor in FXTAS is typically kinetic in nature. Gait ataxia (characteristic of FXTAS) is not typical in PD. As such, FXTAS may be more similar in appearance to Parkinson's plus syndromes or essential tremor {ET, 6}. FXTAS also occurs in female carriers, although dementia is less common than in males {7–10}.

The molecular mechanism of involvement in FXTAS is completely different than the molecular mechanism of fragile X syndrome (FXS) that is seen in individuals with the full mutation (> 200 CGG repeats). In FXS, there is transcriptional silencing of the *FMRI* gene secondary to methylation {11}. Therefore, little or no *FMRI*-mRNA is produced in subjects with the full mutation, leading to a lack of the *FMRI* protein (FMRP) and to features of FXS, including mental retardation or significant learning disabilities beginning in childhood. In contrast, individuals with the premutation have enhanced levels of *FMRI*-mRNA and normal or almost normal FMRP levels. Enhancement of transcription in the premutation leads to *FMRI*-mRNA levels that are 2 to 8 times above normal {12}. The elevated mRNA associates with a number of proteins that are critical for neuronal function including myelin basic protein, lamin A/C, α B-crystallin, and hnRNPA2 {13}. These proteins are subsequently sequestered into intranuclear inclusions in neurons and astrocytes {14, 15}. There is neuronal and astrocyte cell death presumably related to the dysregulation of the proteins found in the inclusions {13, 16}. The radiological features of FXTAS include atrophy of the cerebral hemispheres, brainstem and cerebellum {2, 17}. There is also white matter alteration that is best seen on T2 weighted MR images {2, 17}. The middle cerebellar peduncles (MCPs) demonstrate symmetrical hyperintensities in up to 60% of individuals affected with FXTAS and there can be increased T2 signal intensity in subependymal and deep white matter of the frontal and parietal lobes {2, 17, 18}.

Diagnostic criteria for definite FXTAS include the presence of the premutation, tremor and/or ataxia with the presence of the MCP sign {2, Table 1}. In a recently published study, male subjects with the *FMRI* premutation and clinical evidence of FXTAS were found to

have increased scores on the somatization, obsessive compulsive, interpersonal sensitivity, depression, phobic anxiety, and psychoticism scales on the Symptom Checklist-90-Revised (SCL-90-R) compared to controls {19}. Interestingly, in the same study, premutation males without clinical evidence of FXTAS were nonetheless shown to have elevated scores on the obsessive compulsive and psychoticism scales, suggesting that these symptoms may represent a prodromal phase.

Methods

We present a series of 15 cases seen at the University of California, Davis M.I.N.D. Institute for the evaluation of FXTAS. These cases were identified through the evaluation of fragile X families with a proband with FXS or through direct referrals of known premutation carriers with neurological symptoms. These cases were the first 15 cases seen in this study, which included a full neurology, psychiatry, and neuropsychology evaluation. All cases are grandfathers of children with FXS. All subjects signed an IRB approved consent form for our studies. Our evaluation included a medical history and examination, a neurology consultation, a psychiatry consultation (including past and current history of anxiety, mood, psychotic and cognitive disorders, past and current psychotropic medication use, and clinical assessment of cognitive function), a neuropsychological testing battery, and MRI. The neuropsychological assessment, in particular the Rey Auditory Verbal Learning Test {RAVLT, 20, assessing learning and memory}, Controlled Oral Word Association Test {COWAT, 21, assessing verbal fluency}, Behavioral Dyscontrol Scale -2 {BDS-2, assessing executive function, 22}, and Stroop Color and Word Test {23, assessing executive function} were used in conjunction with the clinical exam to further assess cognition found on clinical exam. We used normative data for the RAVLT generated from the Mayo Older American Normative Study {MOANS, 24} as it provides more accurate norms for this age group. The average range for most neuropsychological tests ends at about the 25th percentile and the range of unequivocal impairment starts at around the 9th percentile. In the final analysis, this criterion would be shifted up or down depending on the patient's overall ability. In addition, the Neuropsychiatric Inventory {NPI, 25} was used to assess psychiatric symptoms observed by family members in more detail.

Brain MR imaging was done at 1.5T. Sagittal and axial T1, and axial T2 weighted sequences were available from all subjects. Frontal, parietal, temporal and cerebellar cortical volumes were graded as being normal or as showing mild, moderate or severe volume loss as manifest by size of regional sulci. White matter of the frontal, parietal and occipital lobes, and white matter of the cerebellum and brain stem were graded in a similar manner for alterations in signal intensity on T2 weighted images. T2 signal intensity alterations in cerebellar and brain stem white matter were further characterized as to their anatomic location. Lateral and third ventricular size was characterized from axial images. Image analysis was completed by an experienced neuroradiologist (JABr).

Results

Among the FXTAS cases with cognitive disorder diagnoses based on clinical examination, (n = 8, cases 2, 4, 6, 9, 11, 12, 13, 14), the median age was 65 (mean 67), the median years

since onset of FXTAS was 7 years (mean 9), median CGG repeats was 97 (mean 111), and median FXTAS clinical stage was 4. Among the other patients, median age was 66 (mean 64), median years since FXTAS onset was 7 years (mean 5), median CGG repeats 94 (mean 84), and median clinical stage was 2. There was no significant difference in CGG repeat number or duration or stage of FXTAS between the cases with and without a cognitive disorder diagnoses.

Six cases (cases 1, 7, 9, 11, 12, 14) were diagnosed with mood disorders, while 4 cases (cases 4, 7, 9, 11) were diagnosed with anxiety disorders. Table 2 details demographic data, number of CGG repeats, years of FXTAS, age of FXTAS onset, FXTAS stage, psychiatric diagnoses, degree of MCP sign, and other MRI findings, as well as a description of FXTAS stages. Table 3 details the neuropsychological testing results. Table 4 details Spearman correlations calculations between FXTAS stage and IQ, which were not correlated in any of the 15 cases.

Discussion

FXTAS is a newly-described neurodegenerative disorder with neurologic and psychiatric symptoms. As with other neurodegenerative disorders, the psychiatric co-morbid conditions of mood, anxiety, and cognitive disorders appear to be common in this condition. Among the 15 subjects with FXTAS described in this report, seven present with a consistent dementia syndrome, while one was diagnosed with cognitive disorder NOS/minimal cognitive impairment based on clinical examination. Twelve patients demonstrated at least mild executive function deficits as reflected in the BDS-2 and the RAVLT scores respectively (Table 3).

Our patients with dementia generally showed a pattern of cognitive deficits consistent with frontal and subcortical impairment (including behavioral disinhibition and other signs of disturbed executive function combined with memory impairment) {26–38}. The median MMSE score of our dementia patients was 25, consistent with mild dementia, and several patients had more impaired executive function and poor social judgment. It is important to note that some of the patients, without significant memory impairment, nevertheless demonstrated executive function deficits (Cases 14 and 15).

Research indicates that individuals with FXTAS perform more poorly than healthy controls on a number of neuropsychological measures {4, 5}. These include the WAIS-III Performance (nonverbal) IQ, as well as measures of executive cognitive functioning, working memory, and information processing speed. It should be emphasized that the relative weaknesses observed in Performance IQ can be in part attributed to slowed motor performance as a result of intention tremor. In addition, some patients, without evidence of significant cognitive decline on formal neuropsychological tests, demonstrated impairment on the NPI (Cases 1, 5, 7, 8, and 14). Some of these individuals do have memory and executive function deficits. Indeed, 11 cases (1 did not complete the NPI) showed impairment on the NPI (a score greater than or equal to 4), primarily in the areas of apathy, disinhibition, and anxiety, consistent with the findings in the Bacalman et al. study {3}. While 7 cases could be diagnosed with a cognitive disorder on clinical interview alone, case

6 was diagnosed with dementia based on neuropsychological testing. In order to assess subtleties of cognitive impairment, there is a role for routine neuropsychological testing of cases with the premutation. For example, Case 7 (not diagnosed with dementia) reported significant anomia that was confirmed by testing of verbal fluency on the COWAT, and Case 5 (not diagnosed with dementia) demonstrated low average verbal learning despite superior verbal intelligence. These cases demonstrate that neuropsychological deficits are detected prior to onset of clinically-evident dementia, although we do not know if all will progress to dementia. Longitudinal studies are essential to address this important question. Previous studies have demonstrated that CGG repeat number correlates inversely with IQ and positively with brain atrophy on MRI {39}.

Among our 15 patients, seven were diagnosed with mood and/or anxiety disorders. The cases with depressive disorder NOS were typically cases subsyndromal for major depression but not meeting the chronicity required for a diagnosis of dysthymic disorder. The anxiety disorder patients had clinical features more resembling generalized anxiety disorder (tonic levels of anxiety) than panic disorder. Five of the mood or anxiety disorder patients were also diagnosed with FXTAS dementia or cognitive disorder NOS. While a speculative connection at this early stage of research into FXTAS, it is possible that some FXTAS patients with mood and/or anxiety disorders, who have not yet manifested cognitive impairment, may be experiencing mood and/or anxiety symptoms related to RNA toxicity in the premutation {19}. This is consistent with the recent paper by Hessel et al., where, in patients with the premutation allele, *FMRI*-mRNA was significantly associated with mood and anxiety symptoms in younger men without FXTAS, as well as in patients with FXTAS {19}. The mood and anxiety problems are not necessarily a precursor to dementia because they are common in females with the premutation and the females do not usually develop dementia with FXTAS {7, 19}.

Apathy was noted in seven of the cases. This is a common component of a dys-executive syndrome, and therefore could be symptomatic of executive cognitive problems whether the individual has or has not yet progressed to frank clinical dementia. Often the apathy is associated with depression and the two disorders are difficult to discriminate. Depression (which may include apathy among its presenting symptoms) has been reported as a prodromal phase of dementia (such as in Huntington's disease), and is associated with norepinephrine dysfunction in Alzheimer's disease {40–45}. Due to the common co-occurrence of mood and cognitive disorders in dementia, cognitive performance may depend on the mood state and therefore may improve with antidepressant treatment {46}. Due to functional interruption of fronto-subcortical neural pathways, patients with FXTAS subcortical dementia may present with executive function deficits, disinhibited or inappropriate social behavior, apathy and/or emotional lability {3, 37}. It should also be recognized that the decline in motor and cognitive functioning in FXTAS represents significant coping challenges for the patients, spouses, and families. Thus, mood and anxiety disorders may be caused by true physiological changes and psychological responses that are inherent in the adjustment process.

The natural history of FXTAS dementia awaits prospective clarification. Since FXTAS is understood as a degenerative process related to elevated *FMRI*-mRNA and the neurological

findings tend to progress, it is probable that cognitive and associated psychiatric symptoms may be expected to progress apace {2, 47, 48}. Unlike the dementia of the Alzheimer's type (DAT), where a loss of 2–4 MMSE points per year is typical in the untreated state, the rate of progression in FXTAS is presently undetermined {49, 50}. CGG repeat size has been correlated with the age of onset of FXTAS, degree of white matter disease, and cortical atrophy {39, 51}, and with the age of death in the post mortem studies {14}. Therefore, CGG repeat size could be an indicator of severity or risk, although further studies are needed.

Currently, there is no specific intervention for this disorder except treatment of neurological symptoms {2, 18}. It seems reasonable to offer empirical treatment for the specific psychiatric deficits in FXTAS. As with other dementia syndromes, off-label use of cognition-enhancing agents such as cholinesterase inhibitors (FDA approved for DAT), appear warranted to preserve memory function {52}. Due to the common occurrence of mood and anxiety symptoms, antidepressants are also appropriate; although tricyclic antidepressants should generally be avoided due to anticholinergic side effects {53–54}. Finally, atypical antipsychotics may be considered, as in other dementia syndromes for delusions, hallucinations, agitation, and night-time behavioral disturbances {55–58}.

Structural limitations of our study include recall challenges. We sought to obtain lifelong history of psychiatric illness and detailed description of current mental functioning from 15 patients, the majority of whom had validated cognitive impairment. A distant history of mildly impairing mood or anxiety disorder might not be readily recalled, especially with sufficient detail to retrospectively make an unequivocal diagnosis of, e.g., major depression or obsessive-compulsive disorder. Hence, due to this imprecision, several of our cases appeared better-described as depressive disorder NOS or anxiety disorder NOS. In addition, as a manifestation of disturbed executive function, patients have limited insight into their illness, which further adds to being poor informants about their medical and psychiatric histories.

There is also an issue of diagnostic attribution in psychiatric symptoms in dementia. It is common in practice to “embed” current mood, anxiety, or psychotic symptoms “into” a diagnosis of a cognitive disorder (e.g., “dementia with behavioral disturbances”) rather than rendering a discrete diagnosis of another psychiatric illness in addition to dementia. To the degree possible, we sought to delineate separate psychiatric diagnoses for mood and anxiety disorders. Presumably, a sufficiently rigorous prospective design and longitudinal follow-up of premutation subjects assessed well in advance of the development of clinical symptoms of FXTAS could better address the question of a pre-FXTAS psychiatric prodromal state with mood and/or anxiety symptoms antedating a later clear diagnosis of FXTAS dementia.

The apparent risk for dementia in the FXTAS premutation must take into account the possibility that patients in this age group are also at statistical risk for other forms of dementia, e.g., Alzheimer disease, and previous studies have been reported with FXTAS and Alzheimer disease {14, 59} or FXTAS and PD {14, 15}. In addition, cases 7, 12, and 15 had history of prior stroke (albeit with good functional recovery in each case), which makes co-occurrence of vascular disease (even in the absence of frank dementia) possible as an

additional cause of cognitive deficits. Cases #9, 11, 12, and 14 each had a diagnosis of depressive disorder in addition to a cognitive disorder, which raises the possibility of some of these patients' cognitive impairments being consequent to their mood disorders, although cases #9, 11, and 12 were all receiving antidepressant therapy at the time of their evaluations. As such, any assumption that dementia in a patient with FXTAS is solely due to FXTAS dementia must be tempered. As the genetics and pathophysiology of this illness are complex, the role of possible exacerbating and protective factors are yet to be elucidated. Conventional assessment for other dementia syndromes (e.g., Dementia of the Alzheimer's Type, Vascular dementia) should be included in clinical cases of dementia in FXTAS patients.

Physicians encountering patients with fronto-subcortical dementia in the context of a movement disorder should consider the diagnostic possibility of FXTAS dementia, especially when MRI findings include cerebral and cerebellar cortical atrophy, brain stem volume loss and/or increased T2 signal intensity in the MCPs and in cerebral white matter. Referral for neurological evaluation and management of the movement disorder is indicated. Concurrent mood and anxiety disorders may represent associated psychiatric symptoms or may be coincident disorders. Curiously, in the Hessler et al. paper, elevated *FMRI*-mRNA was associated with psychiatric symptoms but not IQ in the males with FXTAS, suggesting that mood and anxiety symptoms may not be directly connected to cognitive deficits per se {19}. IQ was not increased in premutation males relative to controls, nor was it associated with *FMRI*-mRNA. There was a significant negative correlation between CGG repeat size and IQ in the premutation males; this was possibly driven by cognitive loss in the FXTAS cases. It is also possible that the slight reduction in FMRP in the individuals with high CGG repeat sizes contributed to somewhat lower IQ; this effect could not be detected with FMRP-IQ correlations due to limitations in FMRP measurement techniques.

Although clinical recommendations for other cases may be premature based on this series of fifteen cases, some interventions may be contemplated. Similar to the psychopharmacological treatment of other dementia conditions, empirical symptom-targeted treatment with cholinesterase inhibitors, antidepressants, and antipsychotics may be considered on an individual case basis for cognitive, mood/anxiety, and psychotic symptoms, respectively (60, 61)

To confirm the fragile X premutation state, confirmatory fragile X DNA testing should be obtained, as well as genetic analysis of family members for fragile X involvement. This could lead to greater case finding of FXS-affected family members, with subsequent clinical services for these FXS patients. We are recommending routine testing of grandparents of children with FXS so that early diagnosis of neurological symptoms and early symptomatic treatment for the neurological and psychiatric manifestations of FXTAS can be started in those with the premutation (60, 61). Genetic testing of the patient and family members should routinely be accompanied by genetic counseling so that all members of the pedigree can understand their genetic risk for FXS, FXTAS, and related conditions. Future research will focus on the early application of promising neuroprotective pharmacology before the full development of the FXTAS syndrome in at-risk premutation carriers. Prognosis for this disorder awaits prospective elucidation.

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Table 1

Diagnostic Criteria for FXTAS* (Mandatory Criterion: *FMRI* Allele size of 55–200 CGG Repeats)

1	Definite:
	<ul style="list-style-type: none"> A. One clinical major criterion (clinical major criteria: intention tremor and gait ataxia; clinical minor criterion: parkinsonism) <i>and</i> B. One radiological major criterion (radiological major criterion: symmetric white-matter lesions involving the middle cerebellar peduncles; radiological minor criteria: white-matter lesions in cerebral white matter, moderate-to-severe generalized atrophy)
	or
	<ul style="list-style-type: none"> C. Presence of inclusions (the presence of intranuclear – neuronal and astrocytic – inclusions has been added as an additional criterion for FXTAS, on the basis of examination of post-mortem brain tissue).
2	Probable:
	<ul style="list-style-type: none"> A. Two clinical major criteria
	or
	<ul style="list-style-type: none"> B. One radiological major criterion <i>and</i> C. One clinical minor criterion
3	Possible:
	<ul style="list-style-type: none"> A. One clinical major criterion <i>and</i> B. One radiological minor criterion

* adapted from Hagerman and Hagerman 2004 {49} & Jacquemont et al. 2003 {2}

Table 2

Psychiatric co-morbidity in FXTAS: All Patients Caucasian Males (grid on next page)

Case	Age	Education	CGG	Years FXTAS	Age onset	FXTAS Stage*	Psychiatric diagnosis (psychotropic medication at time of evaluation)	MCP Sign**	Other MRI Findings**
1	59	15	94	9	50	4	Depressive d/o NOS (escitalpram 30mg qd)	severe	mild frontal atrophy and thin corpus callosum, moderate white matter T2 changes in hemispheres and pons
2	62	12	88	7	55	5	Dementia (donepezil 5 mg qhs)	mild	mild atrophy, mild white matter T2 changes.
3	70	16	90	12	58	2	None (none)	no	moderate atrophy, mild white matter T2 changes
4	69	21	112	3	66	3	Anxiety d/o NOS Dementia (none)	moderate	mild atrophy, moderate cerebral and pons white matter T2 changes
5	58	16	97	4	54	4	None (none)	mild	mild atrophy, mild pons white matter signal change.
6	64	12	72	10	54	4	Dementia (none)	No	mild general atrophy
7	66	18	116	5	61	4	Dysthymic d/o Anxiety d/o NOS (alprazolam 0.25 mg prn, venlafaxine 37.5 mg qd)	No	mild white matter T2 change in cerebral hemispheres and pons
8	50	11	112	0	NA	1	None (none)	moderate	moderate cortical atrophy and mild cerebral white matter T2 changes
9	78	12	130	20	58	4	Major Depressive d/o Anxiety d/o NOS Dementia (citalopram 20 mg qd)	mild	moderate brainstem white matter changes and moderate cortical atrophy
10	76	14	84	14	62	2	None (none)	unknown	moderate general atrophy (no T2 images)
11	65	18	94	7	58	4	Dementia Depressive d/o NOS Anxiety d/o NOS (alprazolam 0.5 mg bid, sertraline 150 mg qd)	moderate	mild cerebral and pons white matter signal changes, moderate diffuse atrophy.
12	72	9	75	3	69	2	Dementia Depressive d/o NOS (venlafaxine 75 mg qd)	No	mild atrophy
13	65	12	103	16	49	2	Early/Mild Dementia (none)	moderate	moderate cerebral and brainstem atrophy, moderate cerebral and pons white matter T2 changes
14	65	21	105	7	58	3	Cognitive d/o NOS Depressive disorder NOS (none)	mild	moderate cerebral atrophy
15 Median	70 65	16	78	1	69 58	2	Adjustment d/o (in remission) (none)	Yes	mild atrophy, old 2.5cm anterior frontal cortical infarct

d/o = disorder NOS = not otherwise specified

* Stage 0: Normal function

Stage 1: Subtle or questionable signs i.e. subtle tremor or mild balance problems, but no interference with activities of daily living (ADLs)

Stage 2: Minor, but clear, tremor and/or balance problems: minor interference with ADLs

Stage 3: Moderate balance and/or tremor problems interfering with ADLs and at least occasional falls

Stage 4: Severe tremor and/or balance problem. Requires assistance with ADLs and uses a cane or walker

Stage 5: Uses wheelchair on a daily basis

Stage 6: Bedridden and cannot perform ADLs

** MR findings, if abnormal, rated as mild, moderate or severe for atrophy and for white matter increased signal intensity on T2 weighted images.

Neuropsychological testing data on all subjects

Table 3

Case # (CGG repeats)	WAIS ^a FSIQ	VIQ	PIQ	MMSE ^b	Stroop ^c (T-score)	COWAT ^d (raw)	COWAT (SS)	COWAT (%)	BDS-2 ^e	RAVLT ^f (Trial VI)	MOANS ^g (SS)	MOANS ^g (%ile)	RAVLT (Trial VII)	MOANS (SS)	MOANS (%ile)	NPI ^h
1 (94)	115	117	110	28	46	65	16	98	24	12	12	72-81	12	12	72-81	14
2* (88)	83***	93***	73***			6	2	<1	3							29
3 (90)	128	127	124	30	55	69	17	99	18	10	12	72-81	10	13	82-89	3
4* (112)	90	94	85	27	36	33	10	41-59	15	3	5	3-5	4	7	11-18	15
5* (97)	112	122	99	29	47	38	10	41-59	22	9	9	29-40	7	8	19-28	32
6* (72)	89	96	81	26	52	31	9	29-40	16	4	5	3-5	2	5	3-5	1
7* (116)	102	110	91	29	46	11	2	<1	18	9	10	41-59	8	10	41-59	22
8* (112)	83	78	91	30	48	18	4	2	12	7	8	19-28	4	6	6-10	28
9* (130)	78	86	74	16		11	5	3-5	3	2	5	3-5	0	5	3-5	36
10* (84)	90	97	83	30	47	17	5	3-5	11**							
11* (94)	100	111	86	23	43	25	7	11-18	13	7	8	19-28	6	8	19-28	26
12* (75)	73	80	69	24		20	6	6-10	8	2	5	3-5	2	6	6-10	3
13* (103)	95	91	99	29	45	32	9	29-40	14	6	7	11-18	6	8	19-28	30
14 (105)	102	104	98	27		32	9	29-40	16	11	12	72-81	12	13	82-89	44
15* (78)	101	107	92	29	35	35	10	41-59	20	6	8	19-28	5	8	19-28	7

Note: Most of the cases have MOANS scores in the normal range, which would include 29-40, and 41-59.

* Scores reflect either the cognitively impaired range or scores that are discrepant from overall VIQ. A average range for the standard scores (SS) would be 8-12.

** old version BDS, not BDS-2

*** prior IQ, not testable on day of evaluation

^aWechsler Adult Intelligence Scale – Third Edition

^bMiniMental State Exam

^cStroop-Interference

^dControlled Oral Word Association Test

^eBehavioral Dyscontrol Scale - 2

^fRey Auditory Verbal Learning Test

^gMayo's Older Americans Normative Studies

^hNeuropsychiatric Inventory

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Table 4

Spearman Correlations of FXTAS Stage and IQ

	FSIQ	VIQ	PIQ
FXTAS stage	.075	.280	-.213
Sig. (2-tailed)	.792	.311	.446
N	15	15	15

FSIQ= Full Scale IQ, VIQ = Verbal IQ, PIQ = Performance IQ

FXTAS stage was not correlated with IQ in the 15 cases