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## Neurocognitive Profile of a Woman with Susac's Syndrome: Further Evidence of Cognitive Variability

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*Objective:* Susac's syndrome is a rare autoimmune disease characterized by encephalopathy, retinal artery occlusions, hearing loss, and lesions to the corpus callosum. To date, only four papers (five cases) have described the neuropsychological effects of the syndrome. Extant case reports of Susac's syndrome have documented varying levels of cognitive impairment; some studies have identified diffuse cerebral dysfunction, while others describe more focal impairments in attention, memory, and executive functioning. *Method:* The goal of this case study was to provide comprehensive neurocognitive data obtained from another case of confirmed Susac's syndrome. As such, we present the case of a 42-year-old woman with a two-year history of Susac's syndrome. At the time of the neuropsychological evaluation, the patient described ongoing difficulties with memory, word-finding problems, problems with math, and poor problem-solving. Physical/sensory changes included hearing loss, tinnitus, and migraines. *Results:* Neuropsychological test results revealed the patient to be a woman of estimated average to high average premorbid intellect who exhibited a number of focal inefficiencies in the context of a generally intact profile. Particular cognitive weaknesses emerged on select tasks involving visuoconstruction, encoding of a wordlist, and bilateral speeded finger oscillations. She also committed three failures to maintain set on a task of cognitive flexibility. There was no evidence of memory deficits. *Conclusions:* Our findings provide further evidence of cognitive interindividual variability in a confirmed case of Susac's syndrome.

**Keywords:** Susac's syndrome; Neuropsychological outcomes; Differential diagnosis; Interindividual variability.

### INTRODUCTION

Susac's syndrome is a rare autoimmune disease, only 304 cases have been reported (Dörr et al., 2013), with an unknown pathologic process, that was first described in 1979 by John Susac and colleagues (Susac, Hardman, & Selhorst, 1979). The condition is characterized by a triad of symptoms including encephalopathy, retinal artery occlusions, and hearing loss following microvascular lesions that typically involve the corpus callosum (Susac et al., 1979). According to a recent review, the most

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common initial symptom is headache, followed by visual and auditory problems (Dörr et al., 2013). Eventually, cognitive impairments and associated psychiatric features emerge secondary to acute encephalopathy and microinfarctions (Coppeto, Monteiro, Currie, & Lessell, 1984; Monteiro et al., 1985).

Susac's syndrome was originally hypothesized to occur exclusively in females, likely due to the fact that the first 20 patients diagnosed with the syndrome were women ages 21–41 (Bogousslavsky et al., 1989; Susac, 2004). Subsequent cases in males disproved this hypothesis; yet the ratio of females to males is still estimated to be 3:1 (Ballard, Butzer, & Donders, 1996; Susac, 2004). Although most confirmed cases of Susac's syndrome develop during early adulthood, the condition has been diagnosed in individuals up to age 70 (Rennebohm, Egan, & Susac, 2008). There does appear to be a racial bias for the condition, given that the majority of cases have been reported in white individuals from North America and Europe (Dörr et al., 2013).

A diagnosis of Susac's syndrome is typically made following magnetic resonance imaging (MRI), retinal fluorescein angiography, and audiometry (Greco et al., 2014); additional laboratory tests to rule out other conditions may also be necessary. As one might expect, multiple sclerosis (MS) and Susac's syndrome may be confused with each other due to similarities in callosal involvement. One defining difference between the two is lesion location; that is, in Susac's syndrome, callosal lesions typically involve central rather than peripheral fibers, while the ventral border of the corpus callosum near the septum pellucidum is implicated in MS (Susac et al., 2004). Susac's syndrome may also be confused with other conditions affecting the central nervous system (CNS), such as acute disseminated encephalomyelitis (ADEM), encephalitis, meningitis, lupus, and CNS vasculitis (Susac, 2004).

More specifically, results from neuroimaging studies (e.g., MRI) in this population typically demonstrate small, multifocal patterns of supratentorial white matter (WM) lesions that involve the corpus callosum (Susac, 1994). Review of MRI results of cases with suspected Susac's syndrome (i.e., patients presented with initial clinical symptom triad, though diagnosis was not confirmed) has also revealed involvement of deep gray nuclei (i.e., basal ganglia and thalamus; 70%), parenchymal enhancement (70%), and leptomeningeal enhancement (33%) (Susac et al., 2003). Popular neuroimaging techniques (i.e., FLAIR, protein density-weighted, or T2-weighted images) can typically capture the small microinfarctions, while newer imaging methods that are not yet readily available in all clinical cases, such as diffusion tensor imaging, may be even more sensitive in identifying fiber damage and integrity in normal-appearing white matter (Kleffner et al., 2008).

To date, there are no controlled studies or clinical trials examining the treatment of Susac's syndrome, though a plethora of anecdotal, case-by-case information is available (e.g., O'Halloran, Pearson, Lee, Susac, & Berger, 1998; Susac, 1994; Susac et al., 1979). The most likely reason for this is due to the rarity of the condition. With this acknowledged, there are a number of treatment approaches described in available literature. The most common treatments involve immunosuppression, such as high-dose corticosteroid therapy and/or other intravenous agents, such as cyclophosphamide, immunoglobulin, mycophenolate mofetil, and more recently rituximab has been introduced as a viable treatment option (Monteiro et al., 1985; Rennebohm et al., 2008; Susac et al., 1979). Studies have also documented effective treatment of the syndrome using anticoagulant drugs in addition to steroids (Hahn, Lannin, & Sarwal, 2004; Tashima, Uyama, Hashimoto, Yonehara, & Uchino, 2001). Interestingly, some patients

may improve spontaneously, without specific immunosuppressive treatment (Gordon, Hayreh, & Adams, 1991). Given the potential for negative treatment side effects (e.g., cognitive impairment, hearing/vision loss), treatment methods should be swift and aggressive (Rennebohm et al., 2008). Overall, treatment outcomes have generally been inconclusive (Susac, 1994), which may be attributed to differences in vulnerability among individual patient immune systems (Rennebohm & Susac, 2007), as well as the low incidence rate of the condition.

### **Neurocognitive and psychiatric functioning in Susac syndrome**

Very little is known about the neuropsychological sequelae in Susac's syndrome. In fact, there are only four published studies reporting neuropsychological data from five individuals with this condition. A review of all 304 cases published worldwide estimate that about three-fourths of patients will present with encephalopathy, while 48 and 39% of patients present with cognitive impairment and confusion, respectively (Dörr et al., 2013). Despite high rates of cognitive changes, Susac's syndrome has not been associated with a particular cognitive pattern or cognitive trajectory. Rather, case studies have reported varying levels of dysfunction/deficits across cognitive domains with limited data identifying cognitive course from diagnosis through treatment. Of those cases published, information is limited due to the use of brief test batteries (e.g., often at bedside), a tendency to provide deficit-focused results, a failure to report tests administered, and/or no indication of length of time between initial and follow-up assessments. A brief review of existing cases involving cognitive testing is provided in Table 1.

As evident in Table 1, presentation, course, and recovery of cognitive and emotional functioning is characterized by interindividual variability. One aspect of consistency is that at least some level of cognitive decline is reported in all five case studies (Assuras & Lacy, 2011; Ballard et al., 1996; Heiskala et al., 1988; Saw et al., 2000). Specifically, in three of the five cases, deficits were described as diffuse, with both cerebral and subcortical disruption (Ballard et al., 1996; Heiskala et al., 1988). Additionally, two of these cases, impairments were consistent with a dementia level of functioning during the acute stage of the syndrome (Heiskala et al., 1988). Finally, one patient who was evaluated once years after diagnosis and treatment, continued to evidence deficits, though how those deficits compared to cognitive at the time of syndrome onset is unknown (Assuras & Lacy, 2011).

Regarding specific neurocognitive domains, evidence of reduced and fluctuating attention/concentration has been described in two studies (Ballard et al., 1996; Saw et al., 2000). Simple verbal skills were described as "intact" in one case (Assuras & Lacy, 2011), while severe dysarthria was noted in another, even at 9-month follow-up exam (Ballard et al., 1996). Higher level language abilities were impaired in two other individuals at the time of testing (Heiskala et al., 1988; Saw et al., 2000). Regarding memory, there is evidence for both reduced episodic memory (Assuras & Lacy, 2011; Heiskala et al., 1988) and recognition (Ballard et al., 1996). Deficits have also been reported on visuospatial tasks, such as visual reasoning (Heiskala et al., 1988). In terms of higher order executive functions, one patient with Susac's syndrome presented with concrete and perseverative thinking, impulsiveness, and impaired novel problem-solving abilities (Heiskala et al., 1988). Finally, two cases reported psychomotor slowing, ataxia, and dexterity impairments (Ballard et al., 1996; Saw et al., 2000).

Table 1. Review of Susac's syndrome case studies with neuropsychological test results

Citation	Patient description	Symptoms	Imaging/Studies/Laboratories	Neuropsychological results
<sup>1</sup> Assuras and Lacy (2011)	38-year-old female	<ul style="list-style-type: none"> <li>• Dizziness</li> <li>• Hearing loss</li> <li>• Dysarthria</li> <li>• Ataxia</li> <li>• Cognitive symptoms</li> </ul>	<ul style="list-style-type: none"> <li>• <i>MRI</i>: WM changes, prominent lateral ventricles, cerebellum volume loss</li> </ul>	<ul style="list-style-type: none"> <li>• <i>Deficits</i>: attention, nonverbal learning, and executive functioning;</li> <li>• <i>Intact</i>: language and memory</li> </ul>
Saw et al. (2000)	29-year-old male	<ul style="list-style-type: none"> <li>• Visual blurring</li> <li>• Headaches</li> <li>• Paresthesia</li> <li>• Olfactory aura</li> <li>• Confusion</li> </ul>	<ul style="list-style-type: none"> <li>• <i>MRI</i>: Multiple hyperintensive WM and GM lesions;</li> <li>• <i>EEG</i>: Triphasic waves consistent with encephalopathy</li> </ul>	<ul style="list-style-type: none"> <li>• <i>Deficits</i>: Attention and concentration, higher order language, psychomotor speed</li> <li>• <i>Follow-up</i>: Unspecific time, improvement in memory; stable deficits in attention, language, and psychomotor speed</li> </ul>
Ballard et al. (1996)	29-year-old male	<ul style="list-style-type: none"> <li>• Vertigo</li> <li>• Diplopia</li> <li>• Confusion</li> <li>• Spasticity</li> <li>• Hearing loss</li> <li>• Retinal microangiopathy</li> </ul>	<ul style="list-style-type: none"> <li>• <i>MRI</i>: multiple foci of increased T2 signal in bilateral hemispheric WM</li> <li>• <i>Brain biopsy</i>: Multifocal microinfarcts</li> </ul>	<ul style="list-style-type: none"> <li>• <i>Deficits</i>: Clear decline from premorbid, diffuse</li> <li>• <i>Follow-up</i>: 9 months later; deficits remained diffuse</li> </ul>
Heiskala et al. (1988)	21-year-old female	<ul style="list-style-type: none"> <li>• Headache</li> <li>• Vomiting</li> <li>• Unsteady gait</li> <li>• Hearing loss</li> <li>• Drowsiness</li> <li>• Memory decline</li> </ul>	<ul style="list-style-type: none"> <li>• <i>EEG</i>: diffuse delta</li> <li>• <i>CT Scan</i>: slight cortical and central atrophy.</li> <li>• <i>Otologic Exam</i>: bilateral sensorineural hearing loss (cochlear origin)</li> </ul>	<ul style="list-style-type: none"> <li>• <i>Deficits</i>: Diffuse, including: reasoning, memory, complex visual and language abilities, concrete, and perseverative, dementia level of functioning</li> <li>• <i>Emotional</i>: Immature, labile, and impulsive</li> <li>• <i>Follow-up</i>: Rapid improvement</li> </ul>

(continued)

Table 1. (Continued)

Citation	Patient description	Symptoms	Imaging/Studies/Laboratories	Neuropsychological results
Heiskala et al. (1988)	24-year-old female	<ul style="list-style-type: none"> <li>• Unilateral hearing loss</li> <li>• Dysarthria</li> <li>• Unsteady gait</li> <li>• Hyperactive tendon response</li> <li>• Positive Babinski</li> <li>• Emotional lability</li> <li>• Cognitive symptoms</li> </ul>	<ul style="list-style-type: none"> <li>• EEG: diffuse delta</li> <li>• CT Scan: slight cortical and central atrophy</li> <li>• MRI: small area of increased T2 in right frontal lobe</li> <li>• Otologic Exam: unilateral sensorineural hearing loss of cochlear origin</li> </ul>	<ul style="list-style-type: none"> <li>• Deficits: Diffuse, including: reasoning, memory, complex visual and language abilities, concrete, and perseverative, dementia level of functioning</li> <li>• Emotional: Immature, labile, and impulsive</li> <li>• Follow-up: 1 and 12 months later; continued cognitive impairment, behavior problems, visual/auditory hallucinations, and delusions</li> </ul>

Notes: MRI = Magnetic Resonance Imaging; EEG = Electroencephalogram; CT = Computerized tomography; WM = White Matter; GM = Gray Matter.

<sup>1</sup>“Possible Susac’s syndrome case.”

Cognitive trajectory as it relates to treatment response also varies among individuals with this syndrome, four cases report findings from initial and follow-up evaluations during the course of treatment, and another reported findings from only one assessment which took place several years after initial diagnosis. One case highlights that the course does not appear to be progressive and/or degenerative past the initial presentation (Ballard et al., 1996), while another identified regressive behaviors one year after diagnosis and treatment (Heiskala et al., 1988). Additionally, review of these cases suggests that severity of initial impairments does not necessarily appear to predict outcomes at follow-up. For example, two patients whose initial presentation was similar, characterized by diffuse and severe cognitive deficits and emotional/personality disturbance, had very different outcomes (Heiskala et al., 1988). One patient improved rapidly, while another was still demented one year later, and even demonstrated signs of increased behavioral changes. Cognitive recovery is again equivocal in the other two cases. That is, there is evidence for continued cognitive difficulties in one case (Ballard et al., 1996), but indication of partial cognitive improvement as a result of treatments in another patient (Saw et al., 2000). Finally, one patient with a one-time assessment several years after diagnosis and treatment evidenced moderate impairments in several areas (Assuras & Lacy, 2011).

Emotional (16%), behavioral (15%), personality (12%), psychosis (10%) are also common in this syndrome (Dörr et al., 2013), but as with the neurocognitive patterns described above, specific characteristics, severity, and course of patients' psychological presentation have been variable. Of the limited number of case studies providing descriptions of psychological clinical course, one individual presented with sadness, anxiety, anger, and ruminative thoughts (Ballard et al., 1996), while another two patients exhibited "immaturity" and emotional lability (Heiskala et al., 1988), as well as personality change, hallucinations, and paranoid delusions. Other cases either do not describe psychological changes (which may mean that they were not present, that they were not assessed, or that they were simply not reported) or deny clear evidence of hallucinations, delusions, or confabulations (e.g., Ballard et al., 1996). On a case-by-case basis, psychological disturbance has been shown to both continue and remit throughout treatment course (Heiskala et al., 1988). It is unclear how preexisting psychiatric diagnoses (e.g., Bipolar disorder) might impact presentation following the diagnosis. In one case, a patient experienced a severe episode of depression, which coincided with the acute stages of the syndrome and encephalopathy, however, years later symptoms did not recur (Assuras & Lacy, 2011).

Overall, review of the very limited literature describing cognitive and emotional functioning in individuals with Susac's syndrome supports the notion, at this juncture, of interindividual variability. As detailed above, there is no established "pattern" or typical cognitive sequelae associated with Susac's syndrome, and factors such as cognitive severity at onset of diagnosis do not appear to be contributory to outcomes. Rather, neurocognitive status appears to be mediated more directly by interindividual variability and possibly "other factors" not yet identified and examined. What can be taken away from the five cases described above is that *at least* during the acute stages of the condition diffuse cognitive impairment may be present (Ballard et al., 1996; Heiskala et al., 1988), and these deficits *may* (e.g., Assuras & Lacy, 2011; Ballard et al., 1996; Heiskala et al., 1988; Saw et al., 2000) or *may not* (Heiskala et al., 1988) persist after treatment. Finally, mood and personality changes are also certainly possible (Heiskala et al.,

1988), although not necessary for diagnosis. However, empirical and systematic interpretation of these data are not possible, given extremely limited number of patients, variability in test batteries, and a general lack of reporting neuropsychological measures administered and test scores.

## METHOD

### Case introduction

“WD,” a 42-year-old Caucasian, married, right-handed woman, was referred for neuropsychological exam in a neuropsychology clinic housed within a university medical center. The purpose of the evaluation was to assess her current cognition due to concerns of declines presumed to be secondary to a two-year history of Susac’s syndrome. She attended the evaluation unaccompanied. Background information was obtained from the patient and review of available medical records. Comprehensive neuropsychological evaluation was completed by two neuropsychology track predoctoral interns in an American Psychological Association accredited predoctoral internship. Supervision was provided by an experienced professor and neuropsychologist certified by the American Board of Professional Psychology-Clinical Neuropsychology specialty.

### Subjective complaints

Although aspects of WD’s physical and sensory symptoms had begun to subside by the time of the assessment, many of her cognitive symptoms were still present. She reported persisting problems with memory, problem-solving, and following directions. Specifically, she noted forgetfulness (e.g., turning off the oven, chronicity of events), problem-solving/organizational difficulties (e.g., simple mathematical calculations, writing checks, managing/keeping track of time, and attending to details), and word-finding deficits. She denied difficulties driving or with medication management. Despite reported problems with math and writing out checks, she remained involved in managing her family’s finances, without note of any errors. With regard to emotional functioning, WD described a number of life stressors that included the recent death of a family member, financial strife, and her cognitive and health problems. From a clinical standpoint, WD described her emotional functioning to be “good;” she reported generally euthymic moods, and denied episodes of depression and/or mania within the last five years. There was no evidence of hallucinations, delusions, behavioral problems, or personality changes.

### Previous medical/neurological examinations

Onset of WD’s symptoms was two years before this examination took place. She reported rapid onset of bilateral hearing loss, tinnitus, severe migraines, vision loss, photophobia, bilateral numbness in her hands and feet, and increased daytime fatigue despite adequate sleep; she denied changes in olfaction or appetite. Due to these problems, she underwent evaluation by a neurologist. Formal diagnosis of Susac’s syndrome was subsequently made by her neurologist following several confirmatory tests,

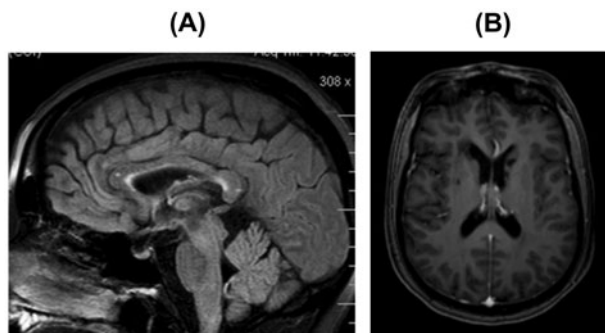


including as follows: (1) an MRI study identifying a solitary punctate microischemic lesion in the genu (central) of the corpus callosum and ischemic and microlacunar infarcts in the head of the left caudate nucleus and right globus pallidus, (2) an otologic exam positive for bilateral hearing loss, (3) a vision test identifying “unexplained” vision changes, and 4) a thorough neurological examination. Additional lab results (e.g., spinal tap, blood, and metabolic labs) for syndromes commonly presenting with similar symptoms (e.g., MS, ADEM, encephalitis, and lupus,) were negative, therefore ruling out alternative diagnoses. She began intravenous immunoglobulin (IVIG) treatments upon diagnosis, and responded positively to immunosuppression treatment. She has been consistently followed by her neurologist from diagnosis through the neuropsychological evaluation to monitor symptoms, progression of the condition, and treatment efficacy.

Her most recent neurological examination prior to our evaluation revealed that WD was still experiencing headaches (and occasional migraines), especially around the time of her IVIG treatments, as well as continued hearing loss (though bilateral hearing aids helped) and tinnitus; visual microangiopathy had subsided. Eye movements were most recently reported to be normal. In her medical records, her neurologist corroborated her report of continued problems with a variety of troubling cognitive concerns, including problems with word finding, forgetfulness, difficulty retaining information and details, and recalling the chronological order of events.

### Neuroimaging

As noted above, WD underwent neuroimaging (e.g., MRI) at the time of her diagnosis and a second time the year immediately preceding this evaluation. MRI images from her first scan revealed T2 cerebral WM abnormalities, as well as hemosiderin deposition in the basal ganglia, left parieto-occipital region, and cerebellum. Follow-up MRI revealed T2 microischemic WM lesions, involving the genu of the corpus callosum, the splenium, and anteromesial basal ganglia bilaterally, qualifying the findings as consistent with Susac’s syndrome. Notably, unusual hemorrhagic hemosiderin deposits were found in the basal ganglionic microischemic lesion and left temporal



MRI scan from 2012. (A) Solitary punctate microischemic lesion in the genu of the corpus callosum and splenium. (B) Ischemic and micro-lacunar infarcts in the head of the left caudate nucleus and right globus pallidus.

**Figure 1.** MRI of WD’s brain from 2012.

lobe; the pathogenesis of these lesions would be entirely atypical for MS, but have not been reported in Susac's syndrome either. Finally, the deep WM bilateral plaques that were identified on her first scan were unchanged and inactive at the time of the follow-up scan, and no new lesions were present. See Figure 1 for WD's most recent MR images.

### **Medical and psychiatric history**

Other medical/psychiatric history was significant for hyperlipidemia, arrhythmia, ganglion cysts, and bipolar disorder without associated hospitalizations. All medical/psychiatric conditions were described as stable and well controlled with medications (good adherence also noted). According to records, her bipolar disorder had been successfully managed pharmacologically for at least five years, with no recent changes in mood or episodes of mania or depression since her diagnosis of Susac's syndrome. Her medications at the time of the evaluation included the following: Imitrex, Zolof, Symmetrel, Crestor, Seroquel, CoQ 10, Calcium Carbonate-Vitamin, coenzyme Q10, Lortab, Ativan, CellCept, Phenergan 2, aspirin, vitamin B12, prednisone, and monthly IVIG treatments for Susac's syndrome. She denied recent changes in medications or dosage and did not report significant side effects at the time of the evaluation. She has a remote history of tobacco use (<1 pack per day); alcohol use was reported to be minimal. Family medical history is significant for scleroderma, arthritis, bipolar disorder, and depression.

### **Psychosocial, educational, and work history**

WD was born in Europe and relocated with her family several times during childhood, as her father was in the military. She and her family eventually settled in a southeastern state. WD graduated from high school earning average grades. She denied learning-related challenges or difficulties, describing herself as "lazy" and uninterested in school, which she felt accounted for "average" grades. Following high school graduation, she completed one year of college before she decided to go directly into the workforce, and began working as an administrative assistant. More recently, she and her husband started a finance-related business. At the time of the evaluation, she was not working, as she and her husband were beginning to transition into a different field of work. WD has been married for nearly 20 years; she has a teenage son and younger daughter.

### **Behavioral observations**

On the day of the neuropsychological assessment, WD's gait was unremarkable. She wore a hearing aid only in her right ear (left ear hearing loss had improved since her last neurological examination), which she reported also reduced tinnitus. She was fully oriented and alert. Spontaneous speech was of normal volume, rhythm, rate, and tone. She was articulate, with no evidence of word-finding difficulties or paraphasias. She independently initiated conversation with the examiner, and there were no observable difficulties with comprehension. Affect was generally euthymic, although at times

anxious during testing. For example, she became flustered and discouraged by her performance on certain tests (e.g., “This is so frustrating! Is the goal to make me cry?” comments made with some level of humor). Despite some frustration, she remained cooperative, pleasant, and engaged in the various tasks at hand.

### Test battery

This evaluation occurred at a neuropsychology clinic associated with a large university medical center in the southeast United States. A comprehensive neuropsychological test battery was administered, including the following tests (grouped by domain): *Embedded Effort Measures*: Reliable Digits Span (WAIS-IV; Wechsler, 2008) and California Verbal Learning Test-2nd edition Forced Choice (Delis, Kramer, Kaplan, & Ober, 2000); *Premorbid Estimate*: Wechsler Test of Adult Reading (WTAR; The Psychological Corporation, 2001) and Barona Index (Barona & Chastain, 1986); *Intellectual Abilities*: Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV; Wechsler, 2008); *Attention, Executive Functions, and Processing Speed*: Digit Span, Arithmetic, Coding, and Symbol Search subtests from the WAIS-IV, Trail Making Test parts A & B (Spreen & Strauss, 1998), Paced Auditory Serial Addition Test (Gronwall, 1977), and Stroop Color and Word Test (Golden, 1978); *Learning and Memory*: CVLT-II, Wechsler Memory Scales-Third Edition: Logical Memory and Visual Reproductions subtests (Wechsler, 1997), and Rey Complex Figure Test (RCFT; Rey, 1941); *Language and Language Related Skills*: Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983), Controlled Oral Word Association Test (Letter FAS; Spreen & Strauss, 1998), Category Fluency (Animals, see Lezak, Howieson, & Loring, 2004), Vocabulary and Information subtests from the WAIS-IV, Cookie Theft Picture from the Boston Diagnostic Aphasia Examination-Third Edition (Goodglass, Kaplan, & Barresi, 2001), and Sentence Repetition; *Visuoperceptual, Spatial, and Constructional Skills*: Benton Judgment of Line Orientation (JLO; Benton, Sivan, Hamsher, Varney, & Spreen, 1994), Benton Facial Recognition Test (Benton et al., 1994), RCFT, and Block Design and Visual Puzzles from WAIS-IV; *Problem Solving and Abstract Reasoning*: Matrix Reasoning and Similarities from WAIS-IV, and Wisconsin Card Sorting Test, Computerized Version (WCST; Heaton, 1981); *Frontal-Motor*: Grooved Pegboard (Spreen & Strauss, 1998), and Finger Tapping (Spreen & Strauss, 1998); *Mood Status*: Beck Depression Inventory—Second Edition (BDI-II; Beck, Steer, & Brown, 1996), and State-Trait Anxiety Inventory (Spielberger, 1977).

## TEST RESULTS

Neuropsychological results are provided in Table 2. Test data are considered valid, given adequate performances on embedded measures of effort (WAIS-IV Digit Span-Reliable Digit Span = 10; CVLT-II Forced Choice = 16/16). She denied pain, headache, fatigue, or problems with vision or hearing that might have affected testing. WD has no known vitamin or metabolic deficiencies that might have negatively affected testing. As noted above, there were no changes in medications or dosages immediately preceding the evaluation that may have influenced performance.

**Table 2.** Neuropsychological test results

Cognitive domain/test	Raw	SS	%ile
<i>Estimated Intelligence Quotient (IQ)</i>			
Wechsler Test of Adult Reading		114	82
Barona Estimate		103	58
<i>Intellect</i>			
<i>WAIS-IV full scale IQ</i>			
Verbal comprehension index		107	68
Vocabulary	–	110	75
Similarities	–	100	50
Information	–	110	75
Perceptual reasoning index		98	45
Block Design	–	95	37
Matrix reasoning	–	90	25
Visual puzzles	–	110	75
Working memory index		102	55
Digit span	–	100	50
Arithmetic	–	105	63
Processing speed index		120	91
Symbol search	–	120	92
Coding	–	115	84
<i>Attention and Executive</i>			
WAIS-IV digit span		100	50
Digits forward	8	85	16
Digits backward	10	105	63
Digits sequencing	11	115	84
Trail making test			
Part A	21" (0 error)	113	79
Part B	29" (0 error)	135	99
Stroop color word test			
Word	94 (0 error)	90	23
Color	82 (1 error)	101	53
Color-word	60 (1 error)	123	93
Interference	–	124	95
Paced auditory serial addition test			
Block 1	42	115	81
Block 2	31	–	–
Total	73	109	68
Wisconsin card sorting test			
Number of categories	6	–	>16
Perseverative responses	10	101	55
Perseverative errors	10	100	50
Total errors	22	98	42
Failure to maintain set	3	–	2–5
<i>Language</i>			
Boston naming test	58	113	79
Controlled oral word-FAS	50	110	76
Category fluency (Animals)	25	113	79
<i>Learning and memory</i>			
CVLT-II total learning	48	90	23
Trial 1	5	78	6
Trial 5	15	108	68

(continued)

**Table 2.** (Continued)

Cognitive domain/test	Raw	SS	%ile
Short delay-free recall	10	85	16
Short delay-cued recall	13	100	50
Long delay-free recall	10	40	16
Long delay-cued recall	13	100	50
<i>Wechsler memory scale-III</i>			
Logical memory-I	45	105	63
Logical memory-II	34	115	84
Logical memory discrimination	90%		
Visual reproduction-I	86	100	50
Visual reproduction-II	35	85	16
Visual reproduction-recog.	43	95	37
<i>Rey-Osterrieth complex figure test</i>			
Immediate recall	21	99	46
Delayed recall	21	99	46
<i>Visual</i>			
Benton judgment of line orientation	22		22
Benton facial recognition test	50		90
Rey-Osterrieth complex figure-copy	32		34
<i>Motor</i>			
Finger tapping dominant	32.4	75	4
Non-dominant	31.4	78	6
Grooved pegs dominant	68"	90	23
Non-dominant	66"	101	53
<i>Effort Measures</i>			
WAIS-IV Reliable Digit Span	10		
CVLT-II Forced Choice	16/16		
<i>Mood Measures</i>			
Beck depression inventory –II	3		
<i>State-trait anxiety inventory</i>			
State	34		53
Trait	33		50

Notes: SS = Standard Score; WAIS-IV = Wechsler Adult Intelligence Scale-4th edition; CVLT-II = California Verbal Learning Test-2nd edition.

**Table 3.** Recommendations following neuropsychological evaluation

- (1) Should WD experience progression in her cognitive symptoms, follow-up testing is recommended. Now that a patient-specific baseline has been established, it will be much easier to determine if there is measureable progression of symptoms warranting reconsideration of treatment options.
- (2) Although WD did not report clinically elevated symptoms of depression or anxiety on self-report measures, she did indicate life stressors. Given her psychiatric history, should she begin to experience mood symptoms or increased anxiety/worry, she is encouraged seek additional intervention beyond that of the psychotropic medication she is currently prescribed. Cognitive-behavioral therapy may be useful in developing coping strategies to deal with significant life stressors.
- (3) WD should continue to be followed by her neurologist for ongoing treatment.

Estimated premorbid intellect (WTAR and Barona Index) revealed WD to be a bright woman who was expected to perform in the average to high average range on measures of intellectual functioning. Performances on a measure of intellect (WAIS-IV)

were consistent with this estimate and placed her well within the average range. Direct assessment revealed performance on tasks of attention, speed of processing, language, visuoception and visuointegration, most aspects of executive functioning, verbal and nonverbal memory, bilateral motor speed and dexterity, and writing were within or above normal limits (ranged from low average to superior). In contrast, testing indicated inefficiencies on the following tasks: (1) visuoconstruction of a complex design, (2) first trial encoding of a list of words, and (3) bilateral speeded finger oscillations. In addition, she committed three set loss errors on a measure of novel problem-solving and cognitive flexibility, though the overall performance was deemed intact. Recommendations following neuropsychological evaluation can be found in Table 3.

Regarding mood, WD denied significant levels of depression or anxiety on objective self-report measures. This was generally consistent with her report during the clinical interview, as she noted a several “life stressors,” but no changes in mood or anxiety. Results suggest that medications may be effectively treating her mood and anxiety symptoms.

## DISCUSSION

Susac’s syndrome is a rare neurologically based autoimmune condition that produces acute encephalopathy and changes in vision and hearing. To date, there are only four articles that discuss neuropsychological profiles of five individuals with the condition. The existing literature on neuropsychological sequelae of the syndrome has not identified a “typical” cognitive pattern. Rather, deficits among these individuals have ranged from “diffuse cerebral dysfunction” to select impairments in attention/concentration, complex language and visual abilities, nonverbal learning, executive functioning, and psychomotor slowing (Assuras & Lacy, 2011; Ballard et al., 1996; Heiskala et al., 1988; Saw et al., 2000). Although the pattern may vary, impairment in cognitive functioning was noted in all cases (e.g., Assuras & Lacy, 2011; Ballard et al., 1996; Heiskala et al., 1988; Saw et al., 2000).

In this study, we presented test findings from a comprehensive neuropsychological evaluation of a 42-year-old woman with a two-year history of Susac’s syndrome and accompanying cognitive concerns, including difficulties with memory, problem-solving, managing/keeping track of time, and word finding. Other neurological symptoms described during the clinical interview included hearing loss/tinnitus, sensorineural vision loss, migraines, and paresthesias of the extremities. Diagnosis was confirmed with neuroimaging results and otologic and vision exams, as well as laboratory findings to rule out other diagnoses (e.g., MS). Her most recent (i.e., within one year of the neuropsychological assessment date) MRI revealed microischemic WM lesions in the corpus callosum and basal ganglia bilaterally—which is considered a hallmark feature of the condition (Heiskala et al., 1988; Monteiro et al., 1985). Otologic and vision examinations were also consistent with Susac’s syndrome. Comprehensive neuropsychological exam revealed a number of focal inefficiencies within the broader context of a generally “intact” profile. Specific areas of concern include the following: (1) poor visuoconstruction of a complex figure (RCFT), (2) inefficient initial encoding of a list of words (CVLT-II), (3) reduced speeded finger oscillations (Finger Tapping), and (4) three set loss errors on a cognitive flexibility/novel problem-solving task (WCST).

Premorbid estimate was average to high average, and, overall, her profile was consistent with these estimates. Although this seems to be consistent with her current functioning, it is unclear whether the various difficulties in visuoconstruction, executive functioning, encoding of new verbal information, and psychomotor speed pre-date her diagnosis of Susac syndrome. Also, it is unknown whether improvements in cognition have occurred since she was diagnosed and treatment was initiated. As such, the only logical conclusion to be drawn is based solely on the test data available, which revealed a number of relative inefficiencies in the context of a generally intact cognitive profile, despite subjective report of cognitive difficulties. Contextualized within the scope of existing literature, the findings from our exam were more subtle than the five neuropsychological case studies in the literature. Specifically, the level of cognitive dysfunction in these cases was characterized by descriptions such as “diffuse deficits,” “dementia-level of functioning,” and/or “clear patterns of deficit in specific cognitive domains” (Assuras & Lacy, 2011; Ballard et al., 1996; Heiskala et al., 1988; Saw et al., 2000). Additionally, her current profile is also in contrast to existing cases where treatment resulted in only moderate improvements, at best, during follow-up visits (Assuras & Lacy, 2011; Ballard et al., 1996; Heiskala et al., 1988; Saw et al., 2000); there is evidence for rapid improvement in cognition in only one case (Heiskala et al., 1988).

Regarding specific domains, only general comparisons can be made, given that most test names and scores have not been published. Such comparisons should also be interpreted with caution, given the limited number of cases available. WD’s visuoconstructional and psychomotor speed deficits are supported by two cases (Heiskala et al., 1988; Saw et al., 2000). Deficits in memory (Ballard et al., 1996; Heiskala et al., 1988) and higher order cognitive functions (Assuras & Lacy, 2011; Heiskala et al., 1988) have also been noted, which broadly align with her reduced list learning and set loss errors. Comorbid behavioral, personality, and psychiatric symptoms have been documented in at least 15% of patients Susac’s syndrome (Dörr et al., 2013). Despite these rates and WD’s predisposition to mood disturbance (i.e., history of bipolar disorder), she did not report significant changes in psychiatric status, nor were such symptoms observed during the clinical interview or testing. Though anecdotal, WD’s psychological presentation does align with another patient with probable Susac’s syndrome who also had a history of bipolar disorder and denied recurrence of psychiatric symptoms over the course many years (Assuras & Lacy, 2011).

There are several ways to conceptualize WD’s current cognitive profile. Firstly, as alluded to earlier, it is unclear the extent to which her cognitive inefficiencies represent “new” symptoms associated with the syndrome. While one could surmise such, based on the patient’s subjective complaints together with objective test findings, it could also be effectively argued that the variability relates to preexisting weaknesses/inefficiencies. Secondly, it is also plausible that WD had greater cognitive impairments at the time of her initial diagnosis prior to treatment for which we do not have data. Effective immunosuppression may have resulted in reduced difficulties at the time of our evaluation. Evidence for cognitive recovery is mixed and limited (Ballard et al., 1996; Heiskala et al., 1988; Saw et al., 2000). Specific factors, such as response to treatment type/course and premorbid intelligence, affecting cognition in the context of Susac’s syndrome certainly need further exploration to disentangle the effects of inter-individual differences.

Finally, while there may be a number of plausible reasons for interindividual differences, some of which have been described above, certainly one of the most parsimonious explanations is that the inconsistencies among patients may be a reflection of the variable pathology and lesion distribution. As initially described, individuals with Susac's syndrome typically demonstrate small, multifocal patterns of supratentorial WM lesions that involve the corpus callosum (Susac, 1994). However, other studies have implicated deep gray nuclei (Susac et al., 2003), while individual cases have found lesions in WM near the lateral ventricles (Assuras & Lacy, 2011), the right frontal lobe (Heiskala et al., 1988), and also in gray matter (Saw et al., 2000). Additionally, lesions have been found bilaterally (Ballard et al., 1996). Because of this, uniform cognitive presentation should not be expected.

## LIMITATIONS

This is only the sixth case of Susac's syndrome for which formal neuropsychological test scores have been presented. Most would agree that such rarity increases the inherent value and necessity of presenting the test findings; however, this does not minimize the presence of a number of limitations that must be acknowledged. Firstly, given the small number of case studies examining neuropsychological profiles of individuals with Susac's syndrome, one may expect the presence of "reporting bias," such that cases without significant clinical findings have not been deemed interesting and were less likely to be published. This would undoubtedly inappropriately skew knowledge of the "typical" cognitive presentation for the condition. Subsequently, this bias may have incorrectly affected the way in which we presented this case (i.e., as more "atypical" and "less severe"). Secondly, it is unknown whether WD's failure to report new onset of psychiatric symptoms relate to the genuine absence of change in mood or reflects "lack of awareness/insight" in this domain due to a preexisting psychiatric illness of bipolar disorder. While there was no evidence in her medical records to support recent psychiatric features, it is possible that symptoms were not appropriately reported and/or observed. Thirdly (and relatedly), it is unfortunate that collateral source information, beyond the written medical records, was unavailable for support of information during the clinical interview. Such information could have provided additional insights (and either corroborated or contradicted her report) into her cognitive and emotional presentation and trajectory over the last two years. Finally, though WD had extensive medical work-up prior to her diagnosis of Susac's syndrome, she did not undergo a brain or muscle biopsy, which could have provided additional confirmation of the diagnosis.

## CLINICAL CONSIDERATIONS

Recommendations for patient WD that were provided as part of her evaluation are depicted in Table 3. However, this case provides insight into clinical care and treatment of Susac's syndrome from a cognitive and psychological perspective beyond the scope of the individual. Several key components to treatment emerge. Firstly, more systematic monitoring of neurocognitive and emotional functioning by neuropsychologists and psychologists in individuals with Susac's syndrome is necessary, both for patient



care and to expand upon the limited literature. Should individuals present with neurocognitive changes that do not resolve with treatment, specific rehabilitation services (e.g., cognitive remediation with a psychologist, occupational therapy, physical therapy, speech therapy) may be warranted. Secondly, as with many conditions affecting cognitive functions, individuals may come to expect certain symptoms or misattribute “normal” or benign cognitive, physical, and emotional symptoms to the condition (e.g., Mittenberg, DiGiulio, Perrin, & Bass, 1992). In this regard, WD may have been hyper-vigilant and began attributing physical and cognitive symptoms to her diagnosis. Psycho-education may mitigate the effects of misattribution, which again highlights the importance of assessment and treatment of individuals with this syndrome by a neuropsychologist and/or psychologist. Finally, despite WD’s report of minimal psychological distress, emotional, behavioral, and personality changes are common in Susac’s syndrome. Appropriate assessment, diagnosis, and treatment recommendations for therapy at the onset of diagnosis may reduce impact of these psychological changes on later functioning. Taken together, individualized tailoring of medical, cognitive, and psychological treatment appears most appropriate given the variable presentation of Susac’s syndrome.

## DISCLOSURE STATEMENT

No potential conflict of interest was reported by the authors.

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