SPECT Findings in the Kleine-Levin Syndrome

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Study Objectives: The Kleine-Levin Syndrome, is a rare disorder with onset during teenage years, but little is known on etiopathogenesis. Seven subjects with Kleine-Levin Syndrome accumulated over time had systematic SPECT studies during (n=5) and out (n=7) of the symptomatic period.

Subjects: Seven boys with symptom onset between 11 and 17 years of age and at least 2 episodes per year were followed for a mean of 6 years.

Methods: Electroencephalogram awake-asleep, computed tomography scan, and magnetic resonance imaging studies were performed before Tc-99m ECD single photon emission tomography (SPECT) obtained during day 4 or 5 (n=5) and at least 1 month away from the symptomatic period (n=7).

Results: All imaging tests except SPECT were normal. Hypoperfusion of both thalami were seen during the symptomatic period that completely disappeared during the asymptomatic period. Hypoperfusion in other regions were also noted in some, but not all subjects. They persisted during the asymptomatic period in 2 cases over the temporal lobe (2/7 cases), frontal lobe (1/7 cases), and basal ganglia (1/7 cases). The largest amount of persistent hypoperfusion was seen in the subject with longest clinical evolution.

Conclusion: Hypoperfusion of the thalamus is a consistent finding during the symptomatic period, but perfusion abnormalities may persist even during the asymptomatic period. The longer the duration of the syndrome, the more extended the hypoperfusion regions during the asymptomatic period.

Keywords: Periodic hypersomnia, Kleine-Levin Syndrome, cerebral hypoperfusion, thalamus, brain imaging SPECT

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INTRODUCTION

THE KLEINE-LEVIN SYNDROME (KLS) IS A RARE DISORDER WITH ONSET DURING TEENAGE YEARS.[1-4] IT IS SEEN MOSTLY IN MALES, BUT FEMALE AND MIDDLE-aged adult-onset cases have been reported.[4-7] The diagnosis of KLS is based on the clinical presentation, as no objective test affirming it has been described. The most common symptoms are periodic hypersomnia; hyperphagia; and various behavioral disturbances such as hypersexuality, social disinhibition, aggressiveness, irritability, and depressed mood.[8-12] When hyperphagia is absent, the term *periodic hypersomnia* or *atypical Kleine Levin* has been applied.[13-17] The different symptoms may not be seen with each recurrence.[1,10] This variability of the symptomatology, in addition to the absence of an objective diagnostic test, may inhibit proper diagnosis. The etiopathogenesis of KLS is still unknown. Hypothalamic dysfunction based on abnormal prolactin or growth hormone secretions[18-23] has been reported.

The presence or absence of serotonin and dopamine metabolism or neurotransmitter imbalance in the serotoninergic or dopaminergic pathways[19,24,25] remains controversial. Possible triggers for KLS include head trauma and viral infections.[10,26-28] Carpenter and Fenzi[28] performed histologic studies on brains of subjects who had KLS and found infiltrates of inflammatory microglia in the thalamus, the diencephalon, and the midbrain; the presence of a small locus coeruleus; and a decreased pigmentation in the substantia nigra. In another histologic case report, abnormalities in the hypothalamus, amygdala, and gray matter of the temporal lobes were identified.[29] Recently, the possible presence of an autoimmune process was investigated. Visscher et al[30] first studied the HLA-DR antigens in KLS. Since then, HLA-DR1, HLA-DR2, tryptophan hydroxylase, and catecholomethyl-o-transferase gene polymorphisms[31,32] have been studied. Based on the HLA findings, an autoimmune hypothesis has been elaborated.[32]

There are few articles on brain structural changes. Hypodense lesions in the suprasellar cistern, suggesting an infundibular lipoma, have been reported by CT scan.[33] SPECT has demonstrated hypoperfusion in the right frontal lobe;[34] left frontal lobe, temporal lobes, and right parietal lobe;[35] and left mesiotemporal structures.[36] This report presents 7 subjects with KLS on whom we performed systematic SPECT studies during (n=5) and out of (n=7) the symptomatic period.

SUBJECTS

The 7 subjects are all right-handed males and presented with onset of symptoms between 11 and 17 years (mean = 13.4 years). They had clinical follow-up and reevaluations to date between 14 months and 13 years (mean = 6 years and 2 months). They presented with a minimum of 2 and a maximum of 7 symptomatic episodes per year. The duration of each episode was variable within and between subjects, from 7 to 28 days. Table 1 presents the 7 subjects. All subjects presented with behavioral hypersomnia and hyperphagia, but this hyperphagia was not observed with each episode in 4 of 7 cases. Other symptoms included hypersexuality or sexual and social disinhibition (5/7) that included obvious masturbation with ejaculation (3 cases), irritability and burst of aggression (6/7), apathetic presentations (5/7), personality changes (7/7), depressive mood (1/7), de-realization (4/7),

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and questions of visual and auditory hallucinations (2/7). Subjects, particularly those with long-term follow-up, had received treatment trials that included lithium, imipramine, fluoxetine, moclobemide, risperidone, methylphenidate, modafinil, acetazolamide, carbamazepine, and influenza type A vaccine. None of the treatment trials had an impact on the duration of the episode or prevented a relapse. All subjects had imaging investigations several months to several years after treatment was discontinued; 1 subject had never been treated.

Prior to imaging studies, all subjects had normal urine and blood tests, including C-reactive protein. IgG and IgM antibodies in serum and cerebrospinal fluid were evaluated at the first symptomatic episode to rule out viral infection or immunologic disorders. Cerebrospinal fluid studies performed after imaging and during other occurrences were noncontributive.

METHODS

During a symptomatic (n=5) and an asymptomatic period (n=7), KLS subjects underwent an imaging investigation. After routine blood and urine tests, each subject had an awake and asleep clinical electroencephalogram; a brain computerized tomography (CT) scan; brain magnetic resonance imaging (MRI), and Tc-99m ECD single photon emission tomography (SPECT). Cerebral perfusion SPECT was performed using a triple-head gamma camera SPECT system (Multi-SPECT 3; Siemens, Hoffman Estate, Ill) equipped with fan-beam collimators. The acquisition was started 20 minutes after intravenous injection of 925 MBq (25mCi) of technetium-99m ethyl cysteinate dimer (Tc-99m ECD) in 120 projections, 3 degrees apart. The acquisition data were reconstructed using the filtered back-projection method with a Butterworth filter and Chang attenuation correction. The visual inspection reports of SPECT were performed by 2 experienced nuclear medicine specialists blind to the timing of the scan and the condition of the subject. Subtraction was performed. The quantitative analysis of SPECT was done based on the level of cerebellum and analyzed by using the same machine a. All data were normalized, and a Wilcoxon signed rank test was used to perform statistical analysis that included all patients and all affected regions during the symptomatic period compared with the asymptomatic period.

RESULTS

The 7 subjects had a typical clinical presentation of symptoms during the symptomatic period selected for imaging studies. The mean time in bed had been 19.5 hours (± 1 hour) for at least 4 days, associated with hyperphagia (from moderate to severe n=2); apathetic presentation (n=7) when not behaviorally in bed with eyes closed; bursts of irritability when asked to do something with aggressive language (n=6) and sexual disinhibited behavior (n=3) (Table 1). Electroencephalogram awake and asleep, CT scan, and MRI were all read as normal. Two out of the 7 subjects who underwent SPECT during the asymptomatic period withdrew consent for further imaging study during the symptomatic and aggressive period during wakefulness. The last 5 patients showed a hypoperfusion covering both thalami in all cases (5/5). The thalamus was the only brain structure that was consistently affected during the symptomatic period. Furthermore, hypoperfusion was seen in the basal ganglia (4/5 cases) and cortex (3/5 cases), specifically, the temporal cortex (3/5 cases), occipital cortex (3/5 cases), and frontal cortex (3/5 cases). These 5 cases had a follow-up SPECT study at least 1 month after the end of the symptomatic period. Complete resolution of the perfusion problems involving the thalami was seen in all 5 cases, and the thalami of the last 2 subjects who had refused imaging during the symptomatic period showed normal perfusion. As shown in Tables 2 and 3, after normalization of the data, the SPECT studies were analyzed quantitatively, and the relative perfusion comparing asymptomatic to symptomatic test was obtained. A right-to-left analysis was also performed. A more than 30% difference in thalamic perfusion was seen in all SPECT when comparing the 2 studies. The difference was the most dramatic in patients #2 and #6 (see Table 2), in whom there was a very important difference also noted between the left and right thalami. An important cortical perfusion decrement (more than 30%) was also observed

Table 1—Demographic and Clinical Data of 7 Male Subjects with Kleine-Levin Syndrome

Patient #	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Current age, y	27	12	13	27	23	18	13
Age at onset, y	17	11	12	14	14	15	11
Episodes, no./y	2-3	4-5	4-5	3	5-6	1-2	6-7
Triggering factor	URI,	URI, fever	URI, SE: exam	URI, SE: conflict with friend	SE school stress	URI	URI, fever
Duration of episodes, d	10-14	14-20	7-10	7-14	7-14	14-21	21-28
Behavioral TST per day, h	20	18	20	20	18-20	18	18
Hyperphagia	+	+++ BW gain	+	++	++	+	+
Hypersexuality	++	+	+	+++	+++	_	_
Other psychiatric symptoms	Irritable, fearful, sad, personality change, derealization	VH+, irritable, fearful, personality change, derealization	Irritable, personality change, derealization, apathy	Irritable, sad, personality change, derealization, hot temper	Irritable, personality change, uncooperative attitude, apathy	Psychotic symptom (AH,VH, delusion), apathy	Irritable, fearful, personality change, apathy, mutism

VH refers to visual hallucination; AH, auditory hallucination; SE, stress event; URI, upper respiratory infection; TST, total sleep time. +Mild increase, ++moderate increase, +++severe increase; (-)no increase

during the symptomatic period in patients #5, #6, and #7, but this decrement involved different lateral cortical regions depending on the subject. For example hypoperfusion was predominant on the right in patient # 6 and the left cortical regions in patients #5 and #7; the basal ganglia changes were limited in patient #6 but were much more marked in patient #7, as indicated by the pixel count. Some decrement (<30%) was noted in the frontal, temporal, and occipital areas in subject #3, and no decrement in cortical perfusion was not noted in the last subjects. Similarly, decrement was noted in the basal ganglia, but, again, it was completely absent in 1 subject (#2), and it was limited in 2 patients (#3 and #6). The consistent finding during the symptomatic period in all subjects was the thalamic hypoperfusion (Tables 2 and 3 and Figures 1 and 2) This hypoperfusion was always more marked on the left thalamus when a right-left difference was noted. All 7 patients had SPECT performed during an asymptomatic period. Perfusion of the thalami was shown to be appropriate in all cases when asymptomatic, but 2 patients had persistent areas of brain hypoperfusion. Patient #1 had hypoperfusion in the left anterior temporal cortex. Patient #4 had decreased cerebral perfusion over the temporal lobe, the right posterior frontal lobe, bilateral parietal and occipital lobes, and the left basal ganglia. This patient had the longest syndromic evolution, with symptoms present over 13 years. In summary, a persistent decreased cerebral perfusion was seen over the temporal lobes in both subjects and over the frontal, parietal, and occipital lobes and the basal ganglia in the patient who had the longest evolution. The Wilcoxon rank signed test that included the 5 subjects submitted to SPECT during the symptomatic period

Table 2—Quantitative Analysis of Single Photon Emission Computed Tomography

Normalized data		**Pt #2**			**Pt #3**			**Pt #5**			**Pt #6**			**Pt #7**		
		R	L	R/L	R	L	R/L	R	L	R/L	R	L	R/L	R	L	R/L
Cortex:	SMP	5.20	5.15	1/0.99	3.06	3.06	1/1	1.72	1.64	1/0.95	4.32	4.00	1/0.93	2.50	2.75	1/1.1
frontal lobe	ASMP	5.25	4.95	1/0.94	3.82	3.82	1/1	2.92	3.00	1/1.03	6.25	6.04	1/0.97	5.00	4.71	1/0.94
	SMP/ ASMP	0.99/1	1.04/1		0.8/1	0.8/1		0.59/1	0.55/1		0.69/1	0.66/1		0.5/1	0.58/1	
Cortex:	SMP	4.85	4.90	1/1.01	3.06	2.94	1/0.96	1.52	1.76	1/1.16	4.08	4.04	1/0.99	2.81	2.63	1/0.94
temporal lobe	ASMP	5.10	5.00	1/0.98	3.88	4.00	1/1.03	2.68	3.20	1/1.19	6.16	6.56	1/1.06	4.65	4.47	1/0.96
	SMP/ ASMP	0.95/1	0.98/1		0.79/1	0.74/1		0.57/1	0.55/1		0.66/1	0.62/1		0.6/1	0.6/1	
Cortex:	SMP	4.68	4.95	1/0.93	3.06	2.94	1/1.04	1.88	1.72	1/1.09	4.48	4.12	1/1.09	2.75	2.81	1/0.97
parietal	ASMP	5.15	5.00	1/1.03	3.88	4.00	1/0.97	3.16	2.92	1/1.08	6.88	6.72	1/1.02	4.71	4.82	1/0.98
lobe	SMP/ ASMP	0.91./1	0.99/1		0.79/1	0.74/1		0.59/1	0.59/1		0.65/1	0.61/1		0.58/1	0.58/1	
Cortex:	SMP	5.10	5.20	1/1.02	3.12	3.12	1/1	1.96	1.88	1/0.96	4.68	4.44	1/0.95	2.88	2.94	1/1.02
Occipital	ASMP	5.20	5.30	1/1.02	3.94	4.00	1/1.02	3.48	3.14	1/0.9	7.32	7.36	1/1.01	5.71	5.47	1/0.96
lobe	SMP/ ASMP	0.98/1	0.98/1		0.79/1	0.78/1		0.56/1	0.6/1		0.64/1	0.6/1		0.5/1	0.54/1	
Basal	SMP	5.80	5.85	1/1.01	3.24	2.94	1/0.91	2.20	1.96	1/0.89	7.08	7.12	1/1.01	3.50	3.44	1/0.98
ganglion	ASMP	5.10	5.25	1/1.03	4.82	4.41	1/0.91	3.96	3.68	1/0.93	4.68	4.32	1/0.92	7.12	6.82	1/0.96
	SMP/ ASMP	1.14/1	1.11/1		0.67/1	0.67/1		0.56/1	0.53/1		1.51/1	1.65/1		0.49/1	0.5/1	
Thalamus	SMP	5.15	4.40	1/0.85	3.00	2.94	1/0.98	1.88	1.76	1/0.94	4.56	3.92	1/0.86	2.94	2.94	1/1
	ASMP	4.55	4.95	1/1.09	4.24	4.06	1/0.96	3.68	3.32	1/0.9	6.72	6.88	1/1.02	6.59	6.35	1/0.96
	SMP/ ASMP	1.13/1	0.89/1		0.71/1	0.72/1		0.51/1	0.53/1		0.68/1	0.57/1		0.45/1	0.46/1	

Measurement unit: count per pixel. Pt refers to patient; SMP, symptomatic period; ASMP, asymptomatic period; R, right; L, left; R/L, the relative perfusion of right to left side area; SMP/ASMP, relative perfusion during symptomatic compared to asymptomatic period. The quantitative data are based on the level of cerebellum. Normalization of data for each brain region was done before calculation.

Table 3—Symptomatic Versus Asymptomatic Single Photon Emission Computed Tomography: Statistical Analysis

Brain structure		**Cortex: frontal lobe**	**Cortex: temporal lobe**	**Cortex: parietal lobe**	**Cortex: occipital lobe**	**Basal ganglion**	**Thalamus**
SMP	R	3.36	3.26	3.55	3.39	4.36	3.51
(count per pixel)		(1.40)	(1.27)	(1.17)	(1.30)	(2.01)	(1.33)
	L	3.32	3.25	3.31	3.34	4.26	3.19
		(1.33)	(1.23)	(1.25)	(1.28)	(2.15)	(1.02)
ASMP	R	4.65	4.49	4.76	4.79	5.14	5.16
(count per pixel)		(1.30)	(1.31)	(1.41)	(1.43)	(1.19)	(1.40)
	L	4.50	4.65	4.69	4.75	4.90	5.11
		(1.15)	(1.26)	(1.40)	(1.39)	(1.21)	(1.50)
Wilcoxon	R	0.043*	0.043*	0.043*	0.043*	0.500	0.080
Test, *P* value	L	0.080	0.043*	0.043*	0.043*	0.500	0.043*

Data are shown as mean (SD) with Wilcoxon signed-rank test used due to the small sample size. SMP refers to symptomatic period; ASMP, asymptomatic period; R, right side; L, left side. *P<.05

Figure 1a—Patient #3 (Symptomatic) Hypoperfusion of right temporal (left arrow), left thalamus and basal ganglion (right arrow).

Figure 1b—Patient #3 (Asymptomatic) : Negative finding

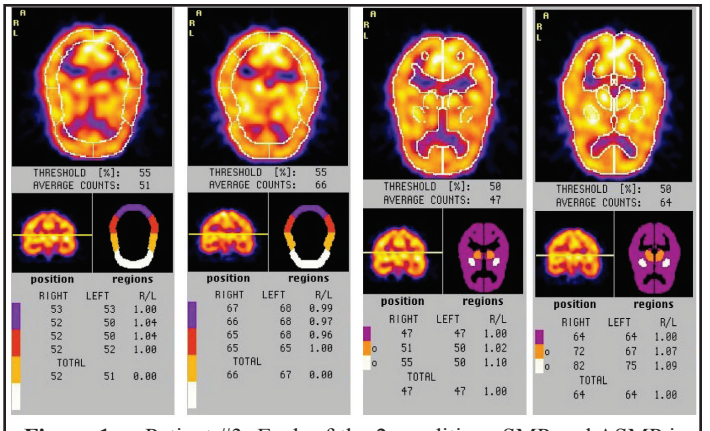

Figure 1c—Patient #3: Each of the 2 conditions SMP and ASMP is represented by 2 photos, the figures are axial sections going through basal ganglia and thalamic planes. The same section is presented for the SMP and for the ASMP period on left and right side of the figure, and the same colors are used to represent the different brain area in both conditions. In the first (left) section of the SMP cut and the 1st (left) section of the ASMP cut, purple identifies occipital cortex, orange: parietal cortex, yellow: temporal cortex, white frontal cortex. On the right section of SMP and ASMP cut, yellow identifies the thalamus and white, the basal ganglia. The extreme right 2 photos show that perfusion of the thalami is significantly decreased during SMP (left thalamus to 50 count/ pixel) and right thalamus to 51 count/ pixel). The basal ganglia also present hypoperfusion (left with decrease to 50 count/ pixel and right to 55 count/ pixel).

showed significant differences compared with the asymptomatic period in the right frontal lobe, right and left temporal lobe, parietal lobe, and occipital lobe and in the left thalamus (Table 3). The comparison of the basal ganglia was nonsignificant; this was related to opposite perfusion changes in different subjects during the symptomatic period, with increased perfusion, for example, in patient #6.

COMMENTS

This is the first and largest systematic study on brain imaging in KLS patients. Our patients had a typical clinical presentation for KLS. They all had been followed for several years, and

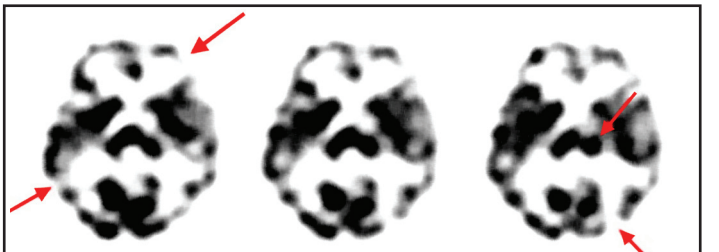

Figure 2a—Patient #5 (Symptomatic) The arrows demonstrated hypoperfusion in the right temporal and occipital junction;the left frontal cortex, left occipital cortex, left basal ganglion and left thalamus.

Figure 2b—Patient #5 (Asymptomatic) : Negative finding

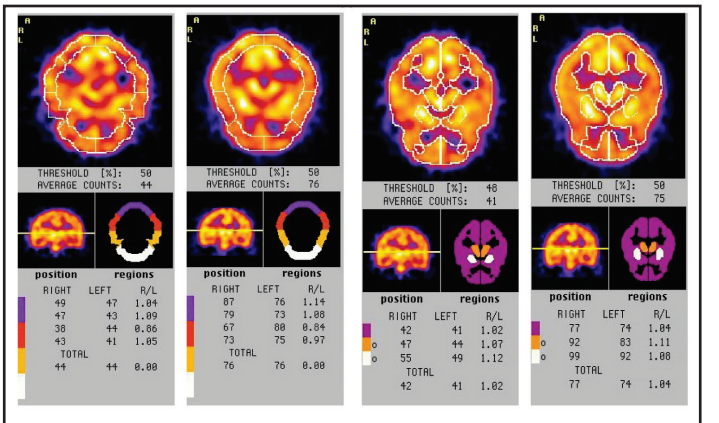

Figure 2c—Patient #5: The photos are similar to those from patient # 3 (figure 1c) with a similar color legend.each of the 2 conditions, SMP and ASMP, is presented again by 2 photos, with the axial sections through basal ganglia and thalamic planes. The left 2 photos showed the perfusion of frontal, parietal, temporal, and occipital cortices decreased during SMP to 44 count/ pixel. The 2 photos on the right show the perfusion of the left thalamus is significantly decreased during SMP to 44 count/ pixel as was the right thalamus, to 47 count/ pixel There is a simultaneous hypoperfusion of the basal ganglia with a decrease on the left to 49 count/ pixel and to 55 count/ pixel in the right basal ganglion.

the repetitive nature of the hypersomnic episodes had been well documented. The other symptoms were also clearly related to the syndromic symptomatology and associated with the hypersomnic phase. As frequently mentioned, none of the medications tried over time had any influence either on the repetitiveness of the periodic hypersomnia or on the duration or severity of any of the episodes. There was variability in the severity of the hypersexuality and hyperphagia from episode to episode within patients; however, behavioral hypersomnia, apathy, and aggressiveness triggered by environmental demands were seen with each episode. The aggressiveness during the symptomatic period precluded performance of SPECT at that time in 2 cases, despite prior agreement and full cooperation of all subjects out of the symptomatic period.

None of the studied subjects presented imaging abnormalities on CT scan and MRI independent of the time of the study. SPECT studies, however, were abnormal in all 5 cases during the symptomatic period. The thalami demonstrated normal perfusion during the asymptomatic period in all 7 cases. Thus, the consistent difference between the symptomatic and asymptomatic periods is the presence of thalamic hypoperfusion only during the symptomatic period. Furthermore, the thalamic hypoperfusion always resolved in all studied subjects during the asymptomatic period. Also, the longer a patient had a recurrence of episodes, the more likely abnormalities in SPECT were to be seen during the asymptomatic period. With 13 years of recurrent periodic hypersomnia, patient #4 had the largest amount of hypoperfusion in both hemispheres.

The explanation for the acute hypoperfusion, particularly in the thalamus, is unclear. Primarily based on the presence of HLA-DQB1-0601 in a group of well-documented Caucasians with KLS, a suggestion has been raised that an autoimmune process is involved in the occurrence of KLS as noted by Dauvillier et al.[32] Only 2 of 6 of our Asian patients were positive for HLA-DQ B1*02 (Huang, Tafti, Guilleminault; personal communication). The distribution of the HLA-DQB1*02 haplotype has been reported to be common in Taiwanese individuals. A recent study identified this haplotype in 28% of a 540-subject control group.[37] Despite the limited number of subjects with the HLA DQB1*02 haplotype, the autoimmune hypothesis is still the most plausible and is supported by the evolution of the clinical syndrome, the SPECT thalamic hypoperfusion, and its resolution. KLS patients present with symptoms that are seen in psychiatric disorders, including sexual disinhibition, aggressiveness, and mood disorders. The clinical manifestations are of very short duration compared with psychiatric disorders, and none of our subjects fulfill the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* diagnostic criteria for these disorders. There have been neuroimaging studies performed in these psychiatric conditions, but the results are still controversial, with articles indicating that the frontal lobe, temporal lobe, and basal ganglia may play roles in the pathophysiology of mood disorders. It will be of interest to perform further comparisons, when the field is more advanced, that investigate some of the behavioral changes associated with hypoperfusion of the overlapping cortical regions.[38,39]

The most interesting finding with our study is the involvement of the thalamus during the hypersomnic period. It was the only brain structure consistently involved during the symptomatic period and free of hypoperfusion during the asymptomatic one. Catsman-Berrevoets and von Harskamp[40] reported a case of bi-thalamic lesions leading to persistent apathetic behavior. In 1993, we reported 2 cases of behavior hypersomnia, hypersexuality, and aggressiveness when disturbed; all were related to bilateral lesions of the paramedian nucleus of the thalamus. These results in 2 young adults were secondary to vascular lesions of terminal arteries after smoking "crack" cocaine.[41] Continuous polysomnography showed that the "behavioral hypersomnia" was, in reality, a "pseudohypersomnia." The subjects were unable to develop stages 2, 3, and 4 non-rapid eye movement and rapid eye movement sleep during the daytime at a circadian time away from their normal sleep period. During the daytime, subjects presented hypersynchronic alpha and electroencephalogram figures of stage 1 sleep. Two to 3 months after their bi-thalamic stroke, subjects presented a persistent apathetic syndrome without pseudohypersomnia. Years later, however, 1 subject with long-term follow-up would still close his eye and assume a "nap posture" when idle. With persistent apathy as the major sequelae, he was unable to take any initiative. The clinical presentations during the acute phase of our 2 thalamic-stroke patients with very localized lesions and the acute phase of the KLS are very similar. SPECT cannot give as accurate a localization of vascular lesion as angiography can, but a clear hypoperfusion of the thalamus was seen in our patients. Even if the hypoperfusion were more extensive in our KLS than in the stroke patients, it would still involve the arterial territories impacted by the thalamic stroke in our previous 2 cases. Because these arteries are terminal arteries, the hypoperfusion would not be compensated, and clinical symptoms related to them would be dominant. As in our stroke patients, KLS was associated with a behavioral aspect of sleep. These patients can be easily pulled out from this behavioral state; at this time, they display disinhibited behavior and aggressiveness.

It is interesting to note that Villablanca's athalamic cats showed a complete loss of the behavioral sleep presentation without elimination of sleep. This indicates that the thalamus plays many roles in the sleep-wake regulation and is also involved in the "behavior" associated with sleep.[42]

Finally, our study shows that SPECT abnormalities may be seen during the asymptomatic period of patients, particularly those with numerous recurrences of symptoms over many years. It is interesting that some of the regions (including temporal, frontal, and occipital lobes and basal ganglia) that were hypoperfused during the asymptomatic period matched the regions already mentioned with SPECT studies (including the right frontal lobe,[34] left frontal lobe, temporal lobes,[35] and left mesiotemporal lobe[36]). Some of the hypoperfused structures correlate with histologic lesions found in the amygdala, the temporal lobe, and the thalamus[29,30] of KLS patients. This should lead to more systematic investigation of patients with long KLS evolution and search for more, even if subtle, permanent deficits in these subjects. Considering the location of hypoperfusion and histologic reports, neuropsychometric evaluation should be undertaken; there should be particular emphasis on the search for memory, cognitive, attention, and/or emotional problems.[36,43] Finally, the fact that the hypoperfusion of the thalamus resolves with disappearance of the hypersomnia-apathetic presentation suggests that there is direct involvement of this structure in the acute clinical presentation. SPECT has been a very positive tool in the investigation of KLS; further investigation of this type is warranted in the occurrence of this syndrome.

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