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USEFULNESS OF SLEEP-DEPRIVED EEG IN THE DIAGNOSIS OF SEIZURE DISORDERS IN CHILDREN

SEYYED MOHAMMAD RAFIEI, M.D.

From the Department of Pediatric Neurology, Shiraz University of Medical Sciences, Shiraz, Iran.

ABSTRACT

The provocative effects of sleep deprivation (SD) on patients with seizure disorder and on the electroencephalogram (EEG) are well known. The purpose of the study was to test its routine use and usefulness in the pediatric and adolescent age group with, or suspect of having, seizure disorder, especially those presenting with first unprovoked seizure.

Between September 2000 and November 2002, among patients referring to the author 's clinic and the Pediatric Emergency Department of Nemazi Hospital, Shiraz, 598 children and adolescents were randomly assigned to a 10-minute surface EEG, either routinely, or after a period of partial or total SD. Those who refused or could not tolerate the SD procedure entered the routine group. The EEG's were analyzed for the presence of epileptic abnormality.

Of 598 patients, 544(91%) had clinical seizures; the rest (54, 9%) were seizure suspects or had seizure "mimickers" (syncope, night terrors, pseudo-seizures, etc). Of seizure patients, 210 (38.6 %) suffered from a first unprovoked seizure, and the rest (334, 61.4%) had more than one seizure episode at the time of EEG performance.

Abnormal epileptiform EEG's were more frequently seen in the group of seizure patients who were sleep-deprived before performing the EEG, as compared to the routine group. Conversely, more normal EEG's were seen upon routine performance of EEG (p value <00001, $\chi^2 = 76.5$).

Similarly, more abnormal sleep-deprived EEG's were seen in patients with first unprovoked seizure than when EEG was done routinely in this subgroup of patients. Patients with complex partial seizure had significantly more abnormal EEG's when subjected to SD (p<00001).

Older patients could tolerate SD better than the younger age group; so more routine EEG's had to be performed in the younger age group. Younger children could only tolerate partial SD. There was no difference in the yield of EEG in patients with absence epilepsy between the two groups. In 5 patients with juvenile myoclonic epilepsy, SD precipitated a generalized tonic-clonic seizure which necessitated acute anti-epileptic drug administration to the seizure activity.

All patients with non-seizure episodes showed normal EEG's.

In conclusion SD can be safely applied in the work-up of selected pediatric patients with seizure disorder, especially in those with their first unprovoked seizure, in whom an abnormal EEG might dictate anti-epileptic drug therapy.

Not all children with seizure disorder need to undergo SD for EEG, as it may not

be necessary in some, and intolerable in others. In non-seizure episodes, if used in appropriate pediatric age groups, it can be very helpful to ensure that a seizure disorder is not present.

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INTRODUCTION

EEG is the most useful procedure in patients with suspicion of seizure disorder. Obtaining an EEG after a period of sleep deprivation (SD) is a well known procedure to increase the yield of EEG "positivity" and bring about the inter-ictal epileptiform activity.[1-10] It is sometimes used as an activation procedure in a patient with seizure disorder whose first EEG has been negative; it is also recommended to be used routinely in children and adults[11,26] for the diagnosis of seizure disorder, or to induce sleep in children for obtaining sleep EEG's.[11] Especially in a child with first unprovoked seizure, a positive EEG helps in determination of the risk of seizure recurrence, and the decision of drug therapy.[12] In children with "seizure mimickers"–syncope,breath holding spells, emotional problems, pseudo-seizures–[13] a negative EEG would be reassuring both to parents and physician, and obviates unnecessary anti-epileptic therapy. SD may activate interictal epileptiform discharges and provoke clinical seizures in susceptible individuals[14] and is inconvenient or not feasible in infants and small children.[15]

The aim of the study was to see which patients benefit most from obtaining an EEG with SD, and whether it should be part of a routine EEG in every infant or child with or suspect of seizure disorder in our region.

MATERIAL AND METHODS

From September 2000 to November 2002, 598 infants,

Table I. Patient characteristics.

Total no. 598	**Male 356**	**M/F 1.47 :1**		**Female 242**	
NL Exam 597	Abnormal. Exam 1				
Age (in year):	#			Age	#
< 5	68			5	38
>5 <10	157			10	88
>10 <15	175			15	26
>15	46				
Type of Seizure					
GTCS 364		Gen. tonic			34
Gen. atonic	26	Rol +/- 2 Gen.			34
GTCS/jerk (J.M.E.)	31	Absence +/- GTCS			25
CPS	30				
TOTAL					544
Non-seizure episodes		Total		54	
Faints	21	Pseudo-Seizure		12	
Night Terrors	7	Vertigo		6	
Anxiety Reaction	2	R/O Absence		2	
Depression	2	Sleep Jerks		2	

Table II. EEG abnormality vs. patient's condition at EEG performance.

Condition at EEG	No.	Normal EEG	Abnormal EEG
Routine			
Awake	253	154	99
Asleep	27	18	9
Awake—>Asleep	0	0	0
Total	280	172	108
Sleep-Deprived			
Awake	133	50	83
Asleep	61	8	53
Awake—>Asleep	70	6	64
Total	264	64	200
Total	544		

Table III. Frequency of EEG abnormality vs. number of seizures before EEG performance.

First Seizure	N= 210	Normal EEG	Abnormal EEG	>1 Seizures	N = 334	Normal EEG	Abnormal EEG
Routine							
Awake	91	64	27		162	90	72
Asleep	6	5	1		21	13	8
Awake —>Sleep	0	0	0		0	0	0
Total	97	69	28		183	103	80
Sleep-Deprived							
Awake	46	20	26		87	30	57
Asleep	42	6	36		19	2	17
Awake —>Sleep	25		25		45	6	39
Total	113	26	87		151	38	113

children, and adolescents, were randomly selected for the study from the author's private clinic patients, as well as those brought in to Nemazi Hospital Pediatric Emergency Room, Shiraz, with a chief complaint of one or more clinical seizure episode(s), or paroxysmal behaviors suspect of seizure disorder, for ruling out a seizure disorder. A thorough clinical evaluation, including detailed history and general physical and neurological examination was performed on each patient. Except for one case, patients with abnormal neurological examination were excluded from the study.

Patients were randomly advised to undergo either 1) a routine EEG, which according to the patient's age and cooperation, included: a wake, sleep, or awake -to-sleep tracing with or without a 3-minute hyperventilation and 1-30 Hz intermittent photic stimulation, or, 2) the same EEG after a period of SD.

The second group were advised to not go to sleep either for 24 hours before performing EEG (total SD),[9] or in the case of younger children, to be kept awake as much as possible in the night before EEG performance, and to sleep only for no longer than 3 hours, and then be awakened (partial SD), and be present for the EEG laboratory, to undergo the EEG procedure, exactly as mentioned above.

The EEG machine was a 10-channel Nihon-Codon (Japan) paper EEG machine, as was shown in our previous report[16] to be effective in showing epileptiform activity. Sleep was achieved either normally, or if needed, after a hypnotic, mainly promethazine syrup 0.5 mg/kg. In those who could not tolerate, or refused, the SD, the EEG was obtained routinely at a later time.

A 10-minute EEG was thus obtained. It was visually analyzed for the presence of: 1) epileptic abnormality, i.e., spikes

Table IV. Type of seizure vs EEG abnormality.

Seizure Type	Routine EEG		Sleep Deprived EEG	
	Normal	Abnormal	Normal	Abnormal
Absence +/- GTCS	2	13		10
Gen. Atonic	6	4	6	10
CPS	8	3		19
GTCS	139	67	42	116
J.M.E.	4	6	6	15
Rol +/- GTCS	3	8	3	20
Gen. Tonic	10	7	7	10

GTCS : Generalized tonic-clonic seizures

ROl.: Rolandic seizures

J.M.E. : Juvenile myoclonic epilespy

Table V. Seizure "mimickers' and EEG at routine vs sleep deprivation.

All EEG's taken were normal							
Condition	**No.**	**EEG: R1**	**R2**	**R3**	**SD1**	**SD2**	**SD3**
Faint	21	7			10		4
R/O Absence	2				2		
Anxiety	2						2
Pseudo-Seizures	12	5			2		5
Night Terrors	7				7		
Depression	2				2		
Sleep Jerk	2				2		
Vertigo	6	3					3

R1: Routine, awake; R2: Routine, asleep; R3: Routine, awake ——> sleep

SD1: Sleep-Deprived, Awake; SD2: SD, Asleep; SD3: SD, awake —> asleep

& waves, poly spikes and waves, sharp-&-slow waves, 2) non-epileptic abnormality, i.e., generalized or focal slowing.[17] A data analysis was done.

RESULTS

Table I shows patient's characteristics. Of 598 infants, children, and adolescents, 544(91%) had some form of clinical seizure activity, for the first time (210, 38.6%), or more than one seizure episode (334, 61.4 %), before being subjected to EEG procedure. 54 patients (9%) had non-seizure paroxysms, most commonly syncopal attacks. Except for one patient, all other patients had normal developmental and neurological evaluation. This

patient, a 14 year old boy with congenital hemiparesis and mild developmental delay with two episodes of nocturnal generalized tonic-clonic seizures(GTCS), underwent a sleep-deprived EEG, first awake and then went to sleep during the EEG procedure, and his EEG proved abnormal. Of all patients with seizure disorder, GTCS predominated (364,66.9%) (Tables I, IV).Other seizure types had equal frequencies.

Routine EEG's predominated somewhat over sleep-deprived ones; this was because some patients, especially those below 5 years, either refused, or could not tolerate sleep deprivation; so they underwent a routine EEG procedure.

As shown in Table II, the number of normal EEG's predominated in the routine group (172 vs. 64); conversely, in the sleep-deprived group, more abnormal EEG's were encountered (200 vs. 108) (p value <0.0001)

In the routine group, more EEG's had to be performed in awake state (253 vs. 133); in the sleep-deprived group,more sleep,and awake-to-sleep EEG's could be performed (131 vs. 27).

As shown in Table III, when patients with first seizure underwent a sleep-deprived EEG, more abnormal results were obtained (87 vs. 28); the same prevailed for patients with more than one seizure at the time of EEG performance (113 vs. 80). Slightly more sleep-deprived EEG's were performed on patients with first seizure (113 vs. 97); this may also partly account for more abnormal EEG's in this group.

When patients were sleep-deprived, more awake-to-sleep EEG's could be performed (70 vs. zero); the majority of these EEG's were abnormal (64 out of 70) (Table II). This procedure combines the "power" of sleep deprivation and sleep in provoking epileptiform discharges.[21]

When first-seizure group was compared to multi-seizure group regarding EEG abnormality, the second group had more abnormal EEG's whether or not sleep-deprived (80 vs. 28; 113 vs. 87).

When seizure type is tested versus frequency of EEG abnormality relative to condition at EEG performance, it seems that, a) for absence seizure it does not matter whether it is performed routinely or with SD; both show high percentage of EEG abnormality (Table IV); b) in patients with generalized seizures, SD did increase the yield of EEG, whether or not primarily or secondarily generalized (p< 0.0001). This is as well true for complex partial seizure (CPS), which showed high yield with SD (Table IV) (p< 0.0001); c) regarding juvenile myoclonic epilepsy (J.M.E.), although SD increased the yield, it provoked clinical GTCS in 5 patients, which necessitated acute anti-epileptic therapy, in the form of diazepam rectally or intravenously.

Regarding the age at which sleep SD could best be implemented, the older the child the easier it could be done, so most of the patients sleep-deprived were more than 5 years old. In younger children, only partial sleep deprivation could be performed.

SD – even partial - facilitated putting patients to sleep, and obviated the need to sedate the patients artificially.

Hyperventilation (H.V.) increased the EEG abnormality only in patients with absence seizure, equally in both groups; other patients in either group did not show any increase in EEG abnormality. This may reflect ineffective H.V. by the uncooperative or sleepy patients.

Early in the study, equal numbers of patients (n=4) in either group showed increase in EEG abnormality with photic stimulation (P.S.). Later, P.S.did not enhance any further EEG abnormality in either group. So the differential effect of P.S. in the two groups was not further studied.

All patients with "seizure mimickers" had normal EEG's when sleep-deprived (Table V).

DISCUSSION

Obtaining EEG's using sleep SD is not a recent procedure. Rodin et al. noted high voltage paroxysmal activity in the EEG's of 16 normal subjects following 120 hours of SD.[1] Cases of convulsion in normal subjects (pilots and soldiers) after SD were later reported.[2-5] SD has a very low false-negative rate (1.2-2.2 %).[2,4,6,7] SD has activating effects on interictal epileptiform discharges over and above the effects of sleep per se.[8,10,27,28] It may obviate the need for a second routine EEG when the first one is normal.[23,24,25]

SD may also provide a useful way of inducing sleep in children, avoiding sedative artifacts on the EEG background.[11] However, the effect of SD on EEG is independent of the effect of sleep itself.[10]

As is well known, sleep unravels or potentiates epileptiform activity on EEG.[14] Activating effects of SD may be more pronounced in children compared to adults.[20,22]

So it seems prudent to obtain a sleep deprived awake EEG followed by sleep, in children with clinical impression of seizure activity, or paroxysmal behavior for which seizure disorder is to be ruled out. This obviates the need to perform a second EEG in those whose routine EEG has been normal, and the suspicion of clinical seizure is still high. Potential "side effects" of SD include:[15] stress and inconvenience of SD, especially in children, potential accident to patient when *en route* to EEG laboratory due to sleepiness; this means that another person should accompany the patient, which implies loss of work or school for *two* persons, and minor chance of seizure provocation.

Patients with known seizure disorder experience increase in seizure frequency when sleep-deprived. Acti-

vation of seizure discharges, and increase in seizure after SD is a known phenomenon.[14]

Patients with juvenile myoclonic seizure may be particularly susceptible to the seizure-provoking effect of SD, and in them, GTCS activity may be precipitated if sleep-deprived,[30] as shown in this study. Therefore, a great precaution is advised when counseling these patients regarding obtaining an EEG with SD.

The EEG laboratory and parents should be provided with necessary information and guidance to abort the seizure, if one occurs in the sleep deprived patient before, during or after the EEG procedure. It is probably better to admit these patients at hospital, sleep-deprive them in the ward, and perform the EEG with close monitoring. Or, if the history is highly suggestive of juvenile myoclonic epilepsy, to perform a routine EEG, or start anti-epileptic drugs without performing EEG.

So based on our results, we recommend a sleep deprived EEG in children and adolescents who present with first unprovoked seizure.

Sleep deprivation may be inconvenient for children,[15] and may precipitate clinical seizure in patients with seizure disorder.[14,30] GTCS activity may be precipitated if the patient is sleep - deprived.[30] Children with absence seizures might not need a sleep–deprived EEG, as the routine awake EEG with hyperventilation usually unravels the typical EEG abnormality in this group of patients. Patients with juvenile myoclonic epilepsy may be exempted from SD before performing EEG, as it may provoke a clinical GTCS.

In infants and children and adolescents who are "seizure mimickers",[13] a negative sleep deprived EEG may be more assuring to the parents and clinicians, and obviates unnecessary and potentially harmful anti-epileptic administration.

Infants and children below 5 years of age may be partially sleep-deprived, merely to induce natural sleep and obviate the need for sedation, which may impart artifact on EEG tracing.

CONCLUSION

With minor exceptions, SD can safely be employed in the protocol for EEG recording in children. It is especially useful in children with first seizure episode, when an abnormal EEG result may dictate initiation of anti-epileptic therapy.

Patients with absence epilepsy may not need it; in patients with juvenile myoclinic epilepsy, it is advisable not to employ it for the potential danger of provoking a clinical GTCS episode. In younger children partial sleep SD is advised.

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