

Sleep and gastric function in irritable bowel syndrome: derailing the brain-gut axis

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Abstract

Background—Recently, several studies have shown an alteration in bowel function during sleep in patients with irritable bowel syndrome (IBS), and a recent study also suggests a remarkable increase in rapid eye movement (REM) sleep. These studies have suggested that an alteration in CNS function may play an important role in the pathogenesis of IBS.

Aims—To confirm the presence of an alteration in REM sleep in patients with IBS and to assess the relation between sleep and a non-invasive measure of gastric functioning, the electrogastrogram (EGG).

Patients—Ten patients with IBS and 10 age and sex matched normal volunteers.

Methods—All subjects slept one night in the sleep laboratory and underwent polysomnographic monitoring to determine sleep patterns, and recording of the EGG from surface electrodes.

Results—The IBS group had a notable and significant increase in the percentage and duration of REM sleep ($p < 0.05$). The control group had a decrease in the amplitude of the dominant EGG frequency from waking to non-REM sleep ($p < 0.05$), and a subsequent increase in the amplitude from non-REM to REM sleep ($p < 0.05$). No such changes were noted in the patients with IBS.

Conclusions—Results confirmed the enhancement of REM sleep in patients with IBS and suggested an intrinsic alteration in autonomic and CNS functioning in patients with IBS.

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Keywords: sleep; irritable bowel syndrome; gastric function; brain/gut

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between stressful stimulation and alterations in bowel function.^{1-3,4}

More recent studies have tended to mitigate the notion of IBS as a "psychosomatic" disorder, or that psychological stimuli play a major role in the pathogenesis of this condition. Several studies have determined that the symptom complex which defines IBS is present in a substantial portion (25-33%) of "normal" individuals, and that psychological measures distinguish only those individuals who seek medical care for their symptoms.⁵⁻⁹ Furthermore, Camilleri and Neri have recently reviewed studies attempting to relate stress and alterations in gastrointestinal motility and have concluded that definitive evidence is lacking to establish definitively a relation between stress, motility abnormalities, and IBS¹⁰; another recent study has shown no consistent relation between daily life stressors and symptoms in patients with IBS.¹¹

Recently, several studies have shown an alteration in bowel function during sleep and specific sleep disturbances in patients with IBS, suggesting that altered CNS function may be playing an important role in the pathogenesis of IBS. In a series of studies, Kellow *et al* demonstrated a relation between small bowel motor abnormalities and symptoms in patients with IBS; they showed that differences in small bowel motility patterns in patients with IBS and controls are confined to the waking state.^{12,13} They interpreted these findings to implicate CNS arousal in both the symptoms and abnormal motor patterns associated with IBS. Subsequently, Kumar *et al* described rather remarkable increases in rapid eye movement (REM) sleep in patients with IBS.¹⁴ In the discussion, the authors note that, "these findings inevitably raise the question of whether IBS is a consequence of abnormal function of the CNS. . .". Increases in REM sleep of the magnitude described in this study are extraordinary, and we are unaware of any medical condition, or even pharmacological intervention, which has been documented to produce comparable changes in REM sleep.

Several aspects of this study beg the question of replication and extension. Firstly, there were only six patients and six controls studied. These individuals were not age or sex matched, they were studied at the end of the day and underwent invasive monitoring of the gastrointestinal tract via a duodenal catheter. These factors certainly produce an extraordinary and abnormal circumstance for sleeping, and the very small number of patients increases the possibility of a spurious finding. Furthermore,

It has been a popular notion for many years that the manifestations of irritable bowel syndrome (IBS) include emotional and perceptual components which are suggestive of the involvement of not only peripheral but also central nervous system (CNS) mechanisms. Perhaps the most popular conceptualisation of IBS is that it is a "stress related" disorder and that symptoms are generally manifest in the face of intense emotional or psychological stimuli.^{1,2} Furthermore, a wide variety of psychological abnormalities have been described in patients diagnosed with IBS, and several investigators have shown a relation

the predominance of relatively young women with a diagnosis of IBS would argue strongly in favour of age and sex matching in the experimental design.

The present study further tests the hypothesis of enhanced REM sleep in patients with IBS. In addition, we test the hypothesis that the diminished cortical activation associated with non-REM sleep will decrease the amplitude of the gastric basic electrical rhythm as measured by the surface electrogastrogram (EGG).

Methods

SUBJECTS

Subjects were 10 women diagnosed with IBS according to the Rome criteria.¹⁵ Their mean age was 38.6, with a range of 26–54 years. All patients were obtained via public advertisements for patients with chronic abdominal pain or irritable bowel syndrome, and only one was diarrhoea predominant. In addition, 10 age and sex matched controls were recruited via public solicitation. All were without symptoms of gastrointestinal disease or evidence of other medical or emotional disorders. We were able to obtain SCL-90 data on seven of the patients, none of whom had abnormal elevations on the depression, anxiety, or somatisation scales. None of the subjects was taking any medications known to alter sleep or gastrointestinal function. This study was approved by the Institutional Review Board of the Baptist Medical Center of Oklahoma.

PROCEDURES

All subjects slept one night in the sleep laboratory and underwent complete polysomnographic monitoring to include the electroencephalogram (EEG), electrooculogram (EOG), electromyogram (EMG), electrocardiogram (ECG), and electrogastrogram (EGG). The EGG was acquired by placing three silver/silver chloride ECG electrodes on the abdominal skin: one at the midpoint between the xiphoid process and the umbilicus, one 5 cm to the left and 3 cm above, and the third 20 cm to the left of the first electrode. The two epigastric electrodes were connected to yield a bipolar EGG signal. The other electrode was used as a reference. The EGG signal was amplified using a portable EGG recorder (Digitrapper EGG, Synectics Medical Inc., Irving, TX, USA) with low and high cut off frequencies of 1 and 18 cpm, respectively. On line digitisation with a sampling frequency of 1 Hz was performed using an analog/digital converter installed on the recorder and digitised samples were stored on the recorder. All subjects ate a standardised meal between 1700 and 1800 hours and were fasted until leaving the laboratory following the polysomnographic recording.

DATA ANALYSIS

Sleep stages were determined according to a computer assisted program utilising standard criteria of stages one, two, three, four, and REM sleep.¹⁶ Total sleep time was determined by the time from lights out until awakening in the morning, less periods of waking. EGG analysis was accomplished via a spectral analy-

TABLE 1 Polysomnographic data

	Patients with IBS	Normal controls	p Value
Total recording time	498.7 (9.5)	489.8 (12.0)	NS
Total sleep time	448.4 (9.7)	427.7 (15.1)	NS
Sleep latency	8.3 (1.6)	12.0 (2.6)	NS
Sleep efficiency	89.9 (1.5)	87.5 (2.8)	NS
WASO	40.7 (6.7)	50.1 (15.1)	NS
Total SWS	83.4 (7.6)	82.0 (8.3)	NS
Percentage SWS	18.5 (1.5)	19.2 (1.9)	NS
Total REM	96.5 (7.0)	64.7 (4.5)	<0.005
Percentage REM	21.5 (1.3)	15.2 (0.9)	<0.004

All values are expressed as mean (SEM). All values are in minutes, except %SWS and %REM. Abbreviations: WASO, spontaneous waking after sleep onset; SWS, slow wave sleep (stages 3 & 4); %SWS, per cent of total sleep time spent in SWS; REM, rapid eye movement sleep; %REM, per cent of total sleep time in REM.

sis of 20 minute segments of EGG data during different sleep stages. The power (or amplitude) of the dominant 3 cpm frequency during each recording period was computed using the smoothed power spectral analysis technique which has been described in detail previously.^{17, 18} Non-parametric analysis was used to detect differences between matched subject pairs via the Wilcoxon signed rank test for matched samples.

Results

SLEEP MEASURES

Table 1 presents sleep parameters for both groups. There were no significant differences in sleep onset latency, total sleep time, or sleep efficiency (total sleep time/total recording time). Only two sleep parameters distinguished the two groups. The IBS group had significantly ($p < 0.05$) greater time and percentage of REM sleep.

EGG MEASURES

The dominant frequency did not change significantly from waking to non-REM sleep, or from non-REM sleep to REM sleep, remaining between 2 and 4 cpm in both study groups. Figure 1 shows typical spectral plots from a normal individual. The dominant frequency remains between 2 and 4 cpm. In addition, it can be seen that there is a decrease in the amplitude of the dominant frequency from waking to non-REM sleep, and a subsequent increase in the amplitude from non-REM to REM sleep.

Figure 2 shows the average amplitude of the dominant frequency for both groups. The comparison here is a within subjects comparison, as EGG amplitude (power) cannot be assessed across subjects due to differences in body morphology and electrode skin preparation.¹⁷ Here, it can be seen that in the control subjects, there is a significant decrease in the amplitude of the dominant 3 cpm frequency from waking to non-REM sleep. There is a significant increase in the amplitude of the dominant frequency during REM sleep compared with non-REM. In contrast, no significant differences were noted in the IBS group in the amplitude of the dominant frequency comparing waking to non-REM sleep or non-REM to REM sleep.

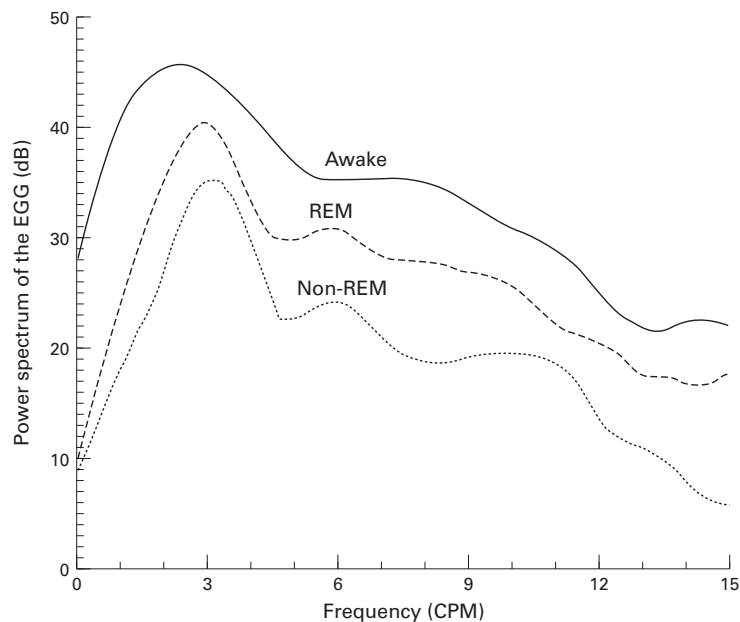


Figure 1: Typical EGG spectral plots of a normal subject during waking, non-REM and REM sleep.

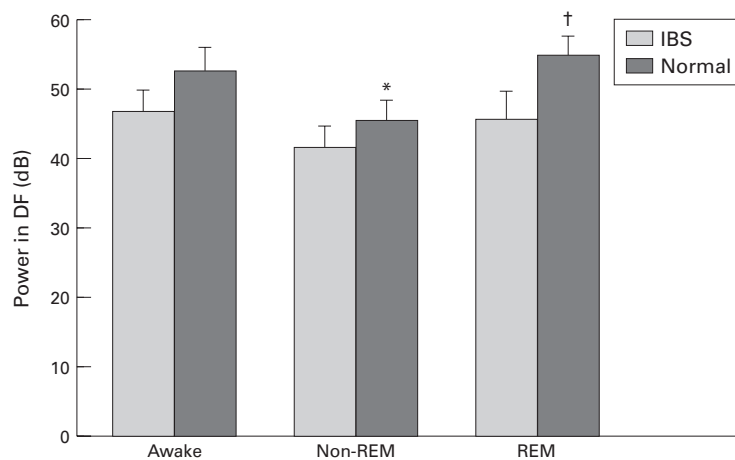


Figure 2: Average amplitude of EGG dominant frequency (DF) power across waking and sleep stages in normal subjects and patients with IBS. * $p < 0.05$ v awake; † $p < 0.05$ v non-REM.

Discussion

The results of this investigation have confirmed an important preliminary observation which suggested that REM sleep is increased significantly in patients with IBS.¹⁴ Our results have also shown REM sleep to be significantly increased in a group of women with IBS compared with a group of age and sex matched controls. In addition, a fundamental measure of intrinsic gastric functioning was found to be significantly altered during sleep when compared with controls. These results raise questions concerning the pathophysiology of IBS: Do these results reflect a fundamental alteration in brain function in patients with IBS? Are the alterations in the EGG noted during sleep a reflection of an intrinsic alteration in control mechanisms of REM sleep?

With regard to the alterations in REM sleep, our results and those of Kumar *et al* would have to be considered extraordinary.¹⁴ These studies represent the first description of any medical

condition associated with an increase in the percentage of REM sleep. Parameters of REM sleep have been described extensively in depression. For example, numerous studies have shown a decrease in the latency to the first REM period, as well as an increase in the percentage of REM sleep in the first half of the night without necessarily resulting in an overall increase in the percentage of REM sleep for the entire sleep period.¹⁹ Furthermore, the usual response to REM deprivation in the form of the rebound of REM sleep has been shown to be an accurate predictor of antidepressant treatment response.^{20, 21} On the other hand, schizophrenics seem to be somewhat impervious to alterations in REM sleep, but they fail to show the characteristic rebound of REM sleep subsequent to REM deprivation.^{22, 23} These results are of particular interest in view of the numerous studies documenting the presence of psychological abnormalities, particularly depression, in patients diagnosed with IBS.¹ Thus, the fact that REM sleep is controlled by a variety of complex brain stem mechanisms, alterations in REM sleep associated with neuropsychiatric conditions such as depression and schizophrenia, and the notable increase in REM sleep in patients with IBS described in the present investigation would argue strongly in favour of some CNS dysfunction characterising patients with IBS.²⁴

The change in the amplitude of the dominant EGG frequency during sleep deserves further comment. Our data unequivocally document amplitude decreases with the onset of non-REM sleep with a subsequent significant increase during REM sleep. EGG amplitude changes have been noted to be associated with phase III of the migrating motor complex (MMC), as well as with gastric contractile activity.^{25, 26} Similar increases in the EGG amplitude have been noted postprandially.²⁷ Some have interpreted these amplitude changes to be secondary to gastric distention which brings the stomach wall closer to the surface of the abdominal wall. Others have attributed amplitude increases to gastric contractility.²⁶⁻²⁸ However, a recent study by Satake *et al* reported no correlation between postprandial EGG amplitude and the proximity of the EGG electrodes to the stomach wall.²⁹ Certainly, the amplitude changes noted during sleep in this study could not be attributed to any alteration in gastric distention or the relation in the distance between the stomach wall and the recording electrodes. These patients had been fasting for several hours by the time of sleep onset; in addition, there are no data to suggest that there is any alteration in MMC activity associated with REM sleep.¹⁴ The latter data would suggest that it is no more likely that phase III MMC activity would be associated with increased contractility during REM versus non-REM sleep. Again, these data lend support to the notion that the EGG amplitude changes during sleep are most likely secondary to alterations in cerebral activation.

The second issue with regard to the findings of this study relates to the failure of patients with IBS to increase the amplitude of the

dominant frequency of the EGG during REM sleep. In general, an increase in the amplitude of the EGG is noted postprandially and studies have shown that it is very likely to be vagally mediated.³⁰ However, in the present study, it was several hours since the subjects had eaten, and meal stimulation cannot be invoked as a stimulus for enhancing the amplitude of the dominant frequency during REM sleep in the normal group. As the dominant amplitude diminishes from waking to non-REM sleep, it may be speculated that it is related to some level of cortical arousal, and as REM sleep has been shown to be a period of increased cortical arousal, this may explain the REM related resurgence in the dominant frequency amplitude.³¹ Support for an influence of CNS arousal mechanisms on smooth muscle contractile activity can be obtained from the study by Kellow *et al* in which the small bowel contractile responses associated with abdominal pain in patients with IBS were absent during sleep.¹² The inference with regard to the data presented here would be that there is some disturbed modulation of cortical arousal during REM sleep in patients with IBS. Thus, the failure of symptoms which awaken patients with IBS from sleep may be related not only to the decreased cortical arousal during sleep as suggested by Kellow *et al*; the failure of patients with IBS to increase the amplitude of the EGG dominant frequency during REM sleep may also be due to diminished cortical arousal.

Adding additional support to the relevance of sleep to the pathogenesis of IBS is a recent study showing a relation between subjective reports of good sleep quality and diminished IBS symptoms.³² Similarly, a study recently reported by Furukawa *et al* describes a pattern of colonic motor function during sleep identical to that which we have described with the EGG during sleep in our normal subjects.³³ That is, in both studies, there is a notable decrease from waking to non-REM sleep followed by an increase in activity during REM sleep. In both instances, the results suggest a diminution of intestinal activity associated with decreased higher cortical input, and a corresponding increase during a phase of sleep associated with increased cerebral arousal.³¹

In summary, these results have confirmed the enhancement of REM sleep in patients with IBS and have documented alterations in normal gastric functioning during sleep. These data suggest the presence of both intrinsic autonomic and CNS dysfunction in patients with IBS.

A preliminary report of these data was presented at the 1995 meeting of the American Gastroenterological Association in San Diego, California, USA.

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