

Introduction

Autism Spectrum Disorders (ASD) are characterized by persistent impairments in reciprocal social interaction and communication. Sleep problems in ASD have significant impact on daily function, social interaction, academic achievements. The genetic factors underlying autism interact in the genesis of the higher percentage of sleep disturbances in children's autism. Pediatric melatonin with extended release is intended specifically for pediatric population with sleep disorders. Melatonin XR ensures physiological sleep pattern.

Methods

We have enrolled 35 ASD children from our Sleep lab (25 males, and 10 females, average age 6.4 years, range 2.5-17.5). Inclusion criteria were a diagnosis of ASD using the Diagnostic and Statistical Manual of Mental Disorders IV-R/5 criteria.

In 12/35 children we have introduced oral pediatric melatonin with prolonged release (XR), 2 mg or 5 mg, or 10 mg, respectively, with the follow up to 1.5 years, while 23/35 continued with sleep hygiene and other therapy. Polysomnographic parameters included: EMG, EOG, 6-16 channel EEG, nasal pressure, oronasal thermistor, chest and abdominal belts for respiratory effort, oximetry with waveform, snoring microphone, EKG, body position, video and audio. Parents filled in the sleep questionnaire and sleep diary.

Characteristics of 12 ASD children under the melatonin XR therapy		
Gender 4 girls 8 boys	Age 2,5-16 yrs	High AHI in 2/12 (2.77, 2.38) Central apnea
EEG changes 5/12 Mostly focal CFTP	Epilepsy 3/12 Valproic acid oxcarbazepine phenobarbiton	Other therapy risperidon clonazepam melatonin rapid

Sleep disturbances on PSG studies	PSG findings of ASD children before and after introduction of melatonin	
Increased sleep latency	9/12	5/12
Decreased REM quantity	8/12	5/12
Increased REM latency	12/12	7/12
Increased NREM1	4/12	2/12
Sleep fragmentation	10/12	5/12
Early wake after sleep onset (<25 min)	5/12	4/12
High microarousal index (> 7)	4/12	2/12
Poor sleep efficiency	6/12	3/12

Results

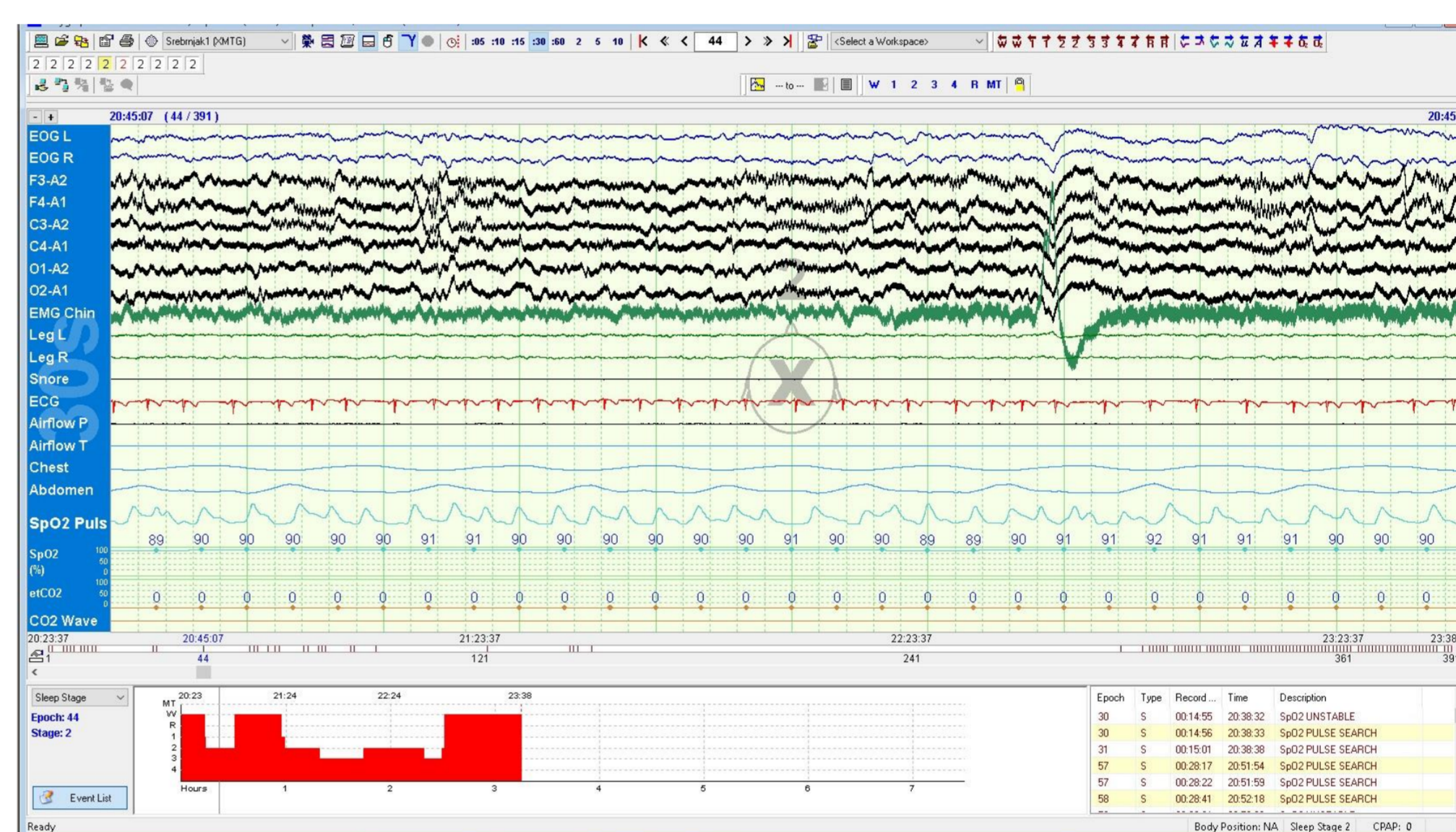
Fatigue, mood swings, headache, irritability, and aggressiveness were daily problems in the majority.

The first PSG analysis revealed sleep disturbances in both groups: decreased total sleep time, REM and NREM3 sleep quantity, longer sleep and REM latency, increased proportion of NREM1 sleep and immature sleep organization. Sleep fragmentation was higher in children with psychomotor delay.

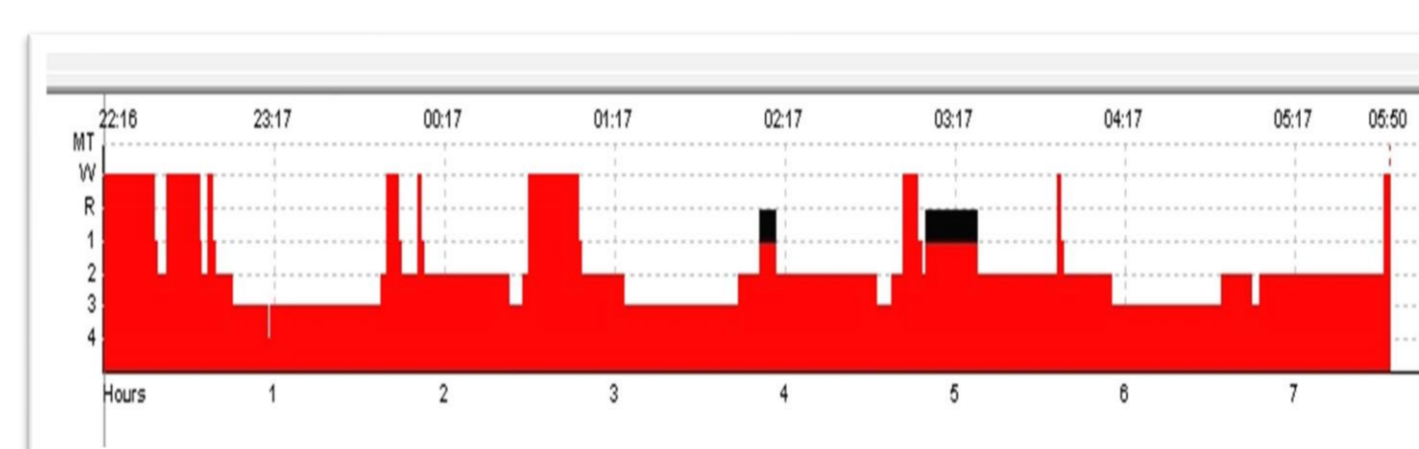
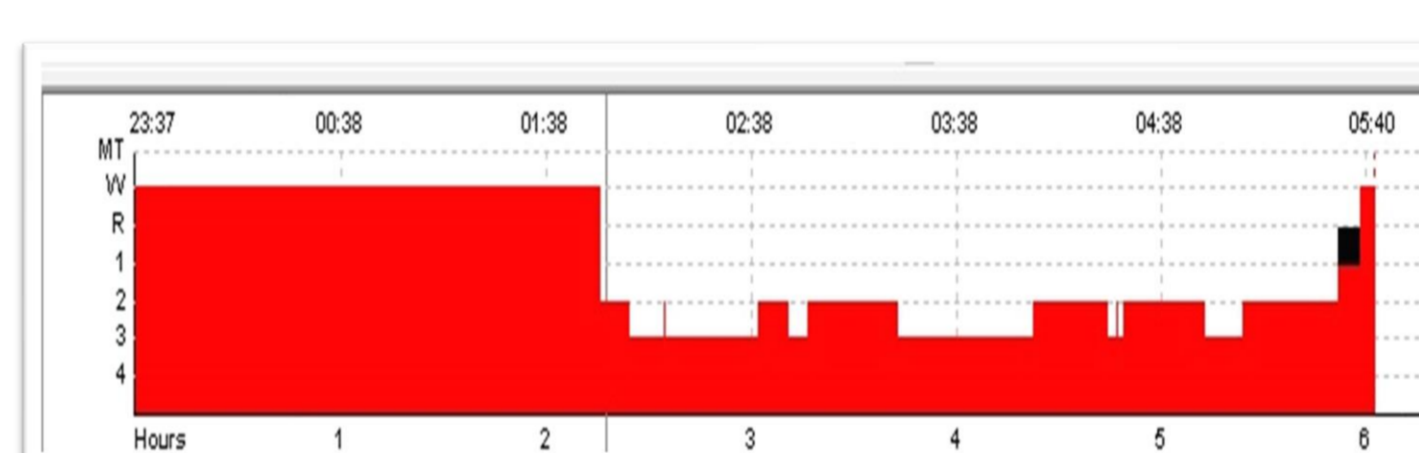
There was a higher percentage of sleep disruption in the subgroup with focal or/and generalized discharges on EEG, with or without epilepsy. If treated, the mostly used antiepileptic drugs were valproic acid and levetiracetam. Second /third PSG study in the melatonin XR group revealed the shortened sleep and REM latency, increased total sleep time and reduced arousals and sleep fragmentation.

The benefits of melatonin XR on daily functioning were also evident. No serious side effects of melatonin XR therapy were noted even after 1.5 years of therapy.

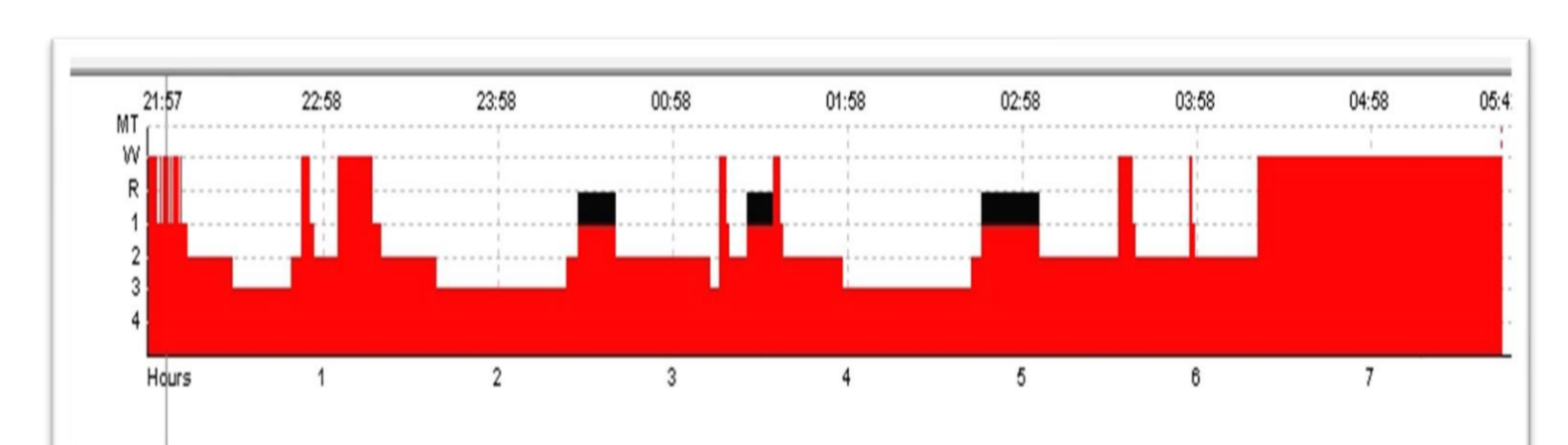
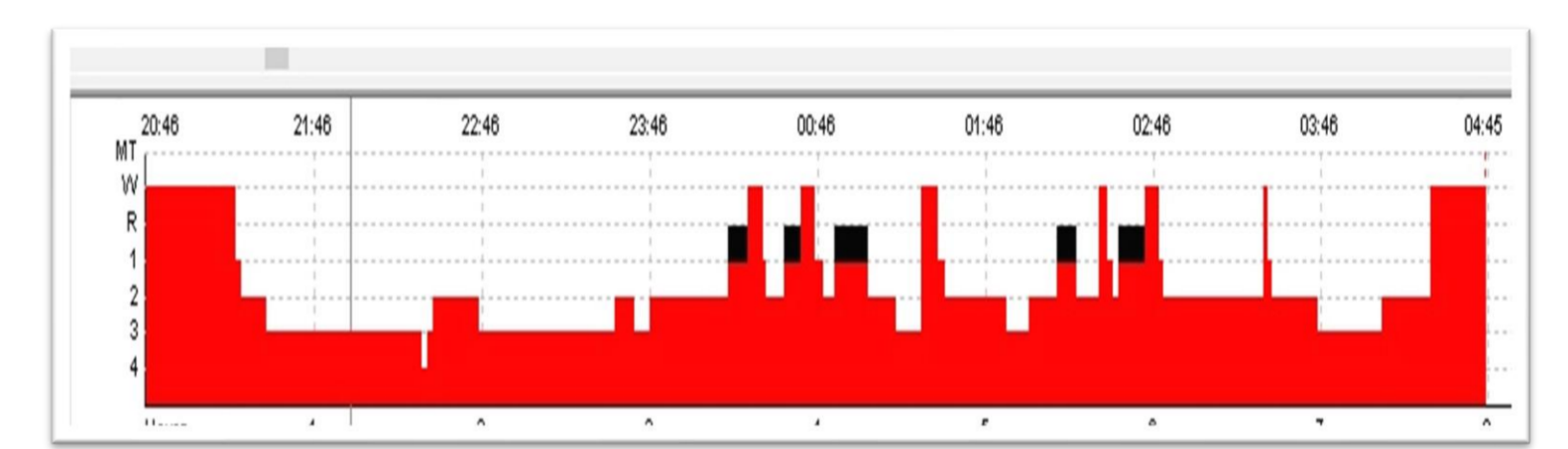
In the group without melatonin therapy, only 5/23 had the evident benefit of sleep hygiene.



Polysomnographic study – 30 s epoch -10-yr-old autistic child with insomnia



Hypnograms of 8yrs-old autistic girl, before, and after 3 months under melatonin XR (Slenyto), 2 mg



Hypnograms of 7yrs-old autistic boy, before, and after 6 months under melatonin XR (Slenyto), 5 mg

Conclusion

Polysomnography and sleep questionnaires are useful in identifying sleep disorders in autistic children, but also in demonstrating the benefits of treatment strategies with pediatric melatonin XR when bedtime routines and sleep sleep-wise approach are not successful. This 1.5 years long therapy with melatonin XR proved to be safe and efficacious in children with the autistic spectrum and sleep disorders. There is a need for further studies- long term and multicentric investigation.

REFERENCES

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