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European Paediatric Translational Research Infrastructure

An assistive device for patients with CCHS : clinical study on usability and efficacy

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A magnifying glass in the world of medical device development – 20/01/2022

CVBF Consorzio per Valutazioni Biologiche e Farmacologiche

Eugenio Medea | Associazione la Nostra Famiglia | Astrolab

What is CCHS?

Congenital Central Hypoventilation Syndrome (CCHS), or Ondine's curse, is a **rare genetic disease** (estimated prevalence 1/200000) , caused by a mutation in the PHOX2B gene.

It **affects the autonomic nervous** system and it is mainly characterized by **hypoventilation episodes** occurring especially during sleep.

This appears to be caused by an anomalous functionality of the respiratory control system made by the chemoreceptors.

Treatment

Treatment focuses on providing breathing support.

All Patients with CCHS require **lifelong ventilatory support during sleep** and, in some cases, 24 hours per day.

To prevent significant and sustained hypoxia and hypercapnia and their physiologic and neurocognitive sequelae, it is suggested to **monitor oxy-hemoglobin blood concentration (SpO2)**, especially during sleep.

Main issues

Patients, especially in the case of young children, have to be supervised by a **caregiver**.

The only **alarm systems** available for patients with CCHS are the ones integrated in the ventilators and monitor devices (e.g. pulse-oximeter).

Most **subjects with CCHS did not awaken** to ventilator or monitoring alarms and a majority of these patients did not have nighttime nursing *(Mathur et al., 2021)*.

An adequate domiciliary assistance is still not present!

Issues raised by A.I.S.I.C.C.

Habituation problem: both patients and caregivers can become less responsive to frequent and repeated alarm stimuli.

Alarms can be activated both for severe situations and for borderline or less severe ones, interrupting the sleep of both caregivers and patients. Thus, there is the tendency in **setting lower and lower alarm-threshold values**, to prevent false alarms and the related increase of stress and anxiety.

Achieving **independence** is a big problem for adolescents and young adults with CCHS that are always dependent on their caregivers.

The awakening device

How can we improve the assistance of patient with CCHS?

Assistive device, coupled with a pulse-oxymeter, which provides multisensory stimulations based on the patient condition and his oxy-hemoglobin (SpO2) blood concentration level

The awakening device

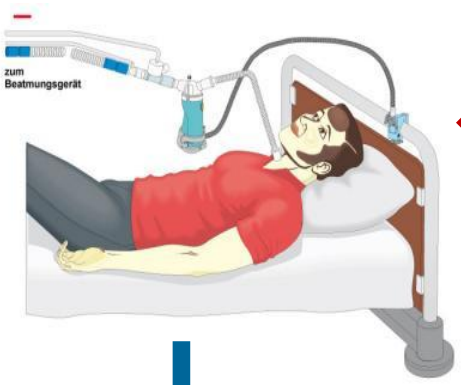
Main aim:

1. To **wake up** the patient or the caregiver in case of real danger

Secondary aims:

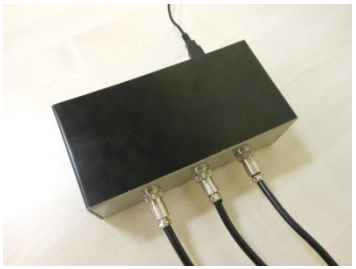
2. To get **gentle awakenings** in case of slight danger
3. To **foster a spontaneous recovery of the SpO2** basal level
4. To obtain a more **personalized monitoring**
5. To reduce the number of **false alarms**
6. To reduce the **habituation** problem
7. To increase the **independence** of adolescents and young adults

The awakening device



SpO_2

Pulse-oxymeter



Hardware

Software

Vibrating pillow

Air fun

Buzzer

Fire alarm

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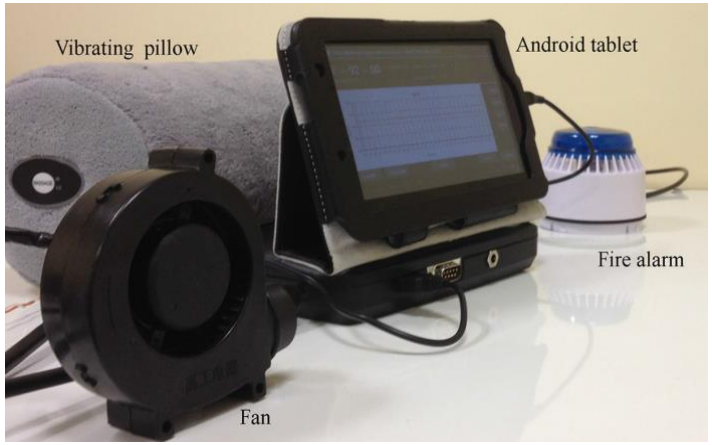
The awakening device

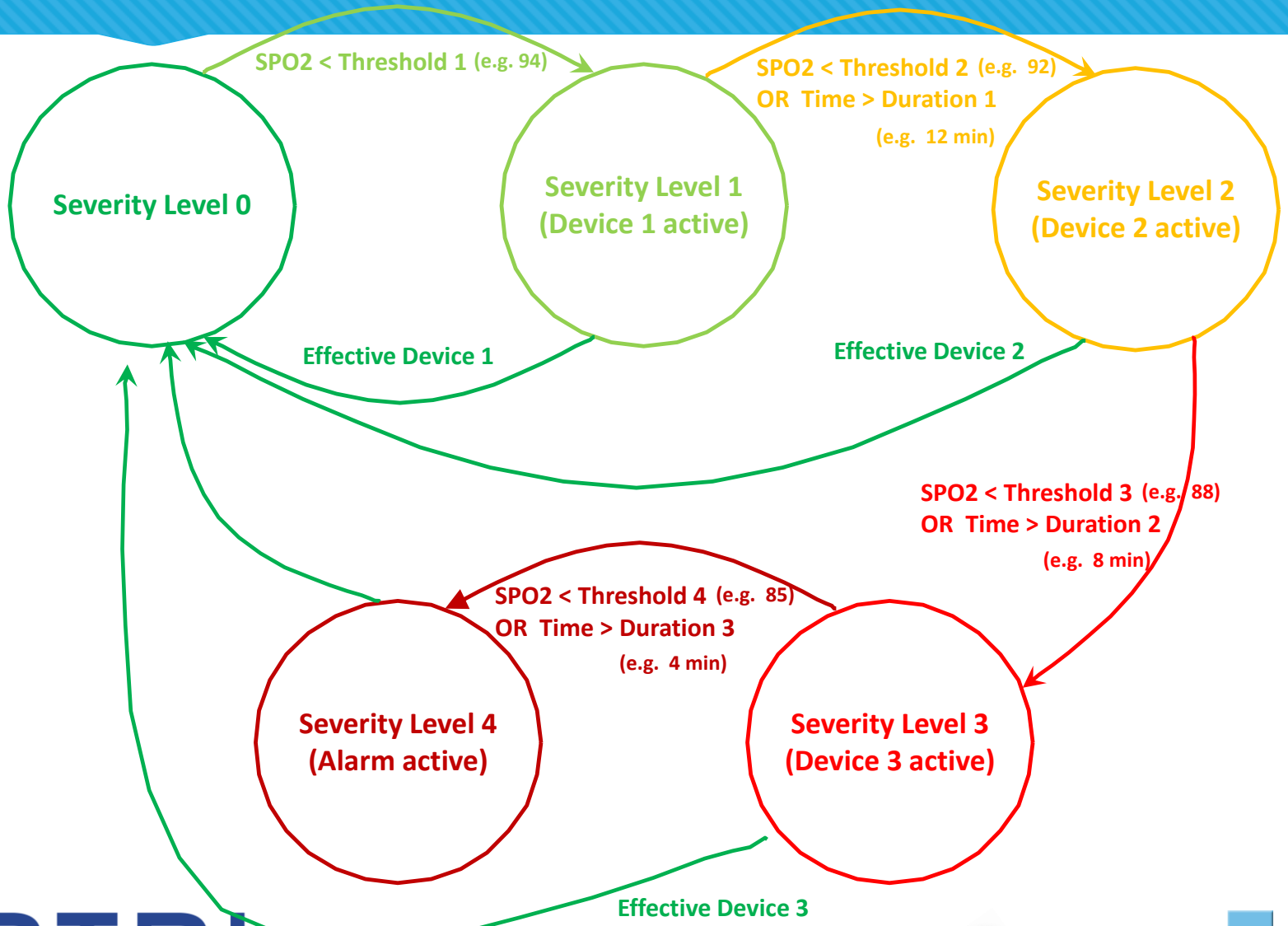
How does it work?

Definition of different and custom severity levels (SLs) based on SpO2 threshold and time below that threshold.

Each SL activates one or more actuators that stops when there is a recovery of the SpO2 basal level.



The awakening device



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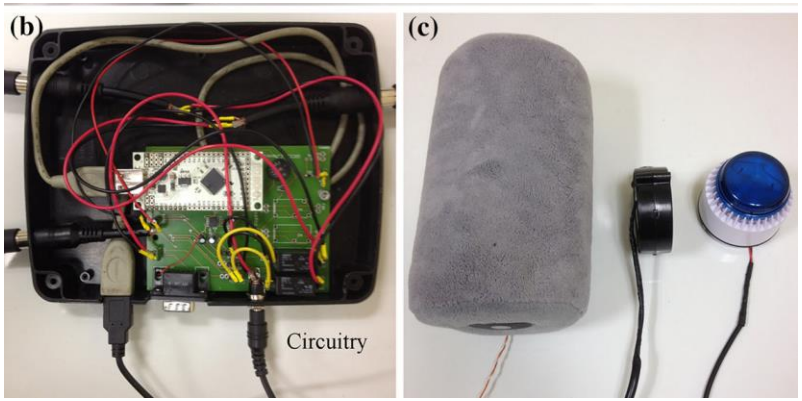
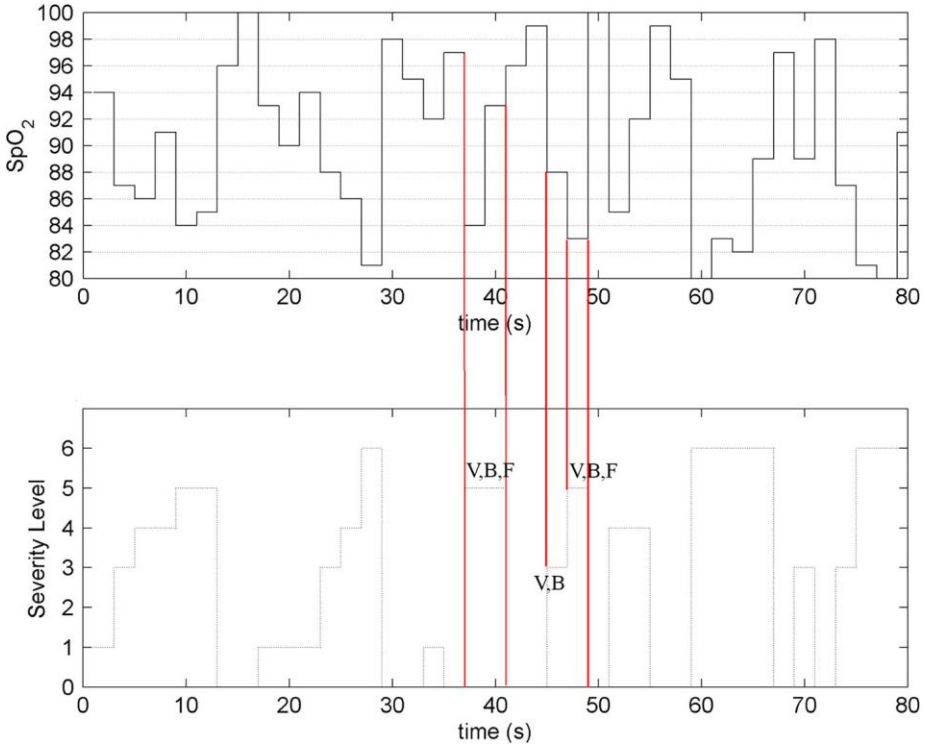
The awakening device

What we did?

1. Development of the device and laboratory tests with simulating signals





The awakening device

What we did?

2. Italian Patent (Application n° MI2011A002324) «Apparecchiatura per il ripristino della ventilazione particolarmente in soggetti affetti dalla sindrome da ipoventilazione centrale congenita (CCHS)"

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The awakening device

What we did?

3. Validation of the device on healthy subjects *(Biffi et al 2014, Annals of Biomedical Engineering)*

Annals of Biomedical Engineering (© 2014)
DOI: 10.1007/s10439-014-1068-7

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An Assistive Device for Congenital Central Hypoventilation Syndrome Outpatients During Sleep

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The awakening device

What we did?

4. Approval by the Italian Ministry of Health of a multicenter clinical trial on the efficacy of the device in a population of patients affected by CCHS (preliminary results in *Biffi, Piazza et al, IFMBE proc 2016*)

IFMBE Proceedings Vol. 57

Preliminary Data on the Usability and Efficacy of an Assistive Device for the Congenital Central Hypoventilation Syndrome: An Observational Study

E. Biffi[1,*], C. Piazza[1,2,*], F. Morandi[3], P. Avantaggiato[1], F. Formica[1], A. Carcano[4], R. Borgatti[1], and G. Reni[1]

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The clinical trial

Involved centers:

- Scientific Institute Eugenio Medea, Bosisio Parini (LC), Italy

- Pediatric Pain and Palliative Care Service of the University of Padua, Italy

- Meyer children's hospital, Florence, Italy

The clinical trial

Patient recruited: **15 subjects**

Subject	Gender	Age (years)	Gene Mutation	Type of ventilation
S01	F	18.1	PHOX2B 20/27	NIV
S02	M	5.2	PHOX2B 20/27	tracheo
S03	M	5.8	PHOX2B20/26	NIV
S04	F	18.5	PHOX2B frame shift	NIV
S05	F	19.8	PHOX2B 20/26	NIV
S06	F	15.8	PHOX2B 20/27	tracheo
S07	M	17.4	PHOX2B 20/26	NIV
S08	F	11.4	PHOX2B 20/29	tracheo
S09	M	28.9	PHOX2B 20/26	NIV
S10	F	27.0	PHOX2B 20/25	pacing
S11	F	22.7	PHOX2B 20/26	NIV / pacing
S12	F	12.2	PHOX2B 20/32	tracheo
S13	F	26.0	PHOX2B 20/26	pacing
S14	M	39.3	PHOX2B 20/25	NIV
S15	F	24.0	PHOX2B 20/25	NIV

The clinical trial

Study protocol

	REFERENCE NIGHT	TEST NIGHT 1	TEST NIGHT 2
Devices used	• PSG • Actigraph	• **Awakening device** • PSG • Actigraph	• **Awakening device** • Actigraph
Evaluated events	• Spontaneous desaturations	• Spontaneous desaturations • Induced desaturations	• Spontaneous desaturations

Randomized order

Only one actuators was associated to each SL in a random way

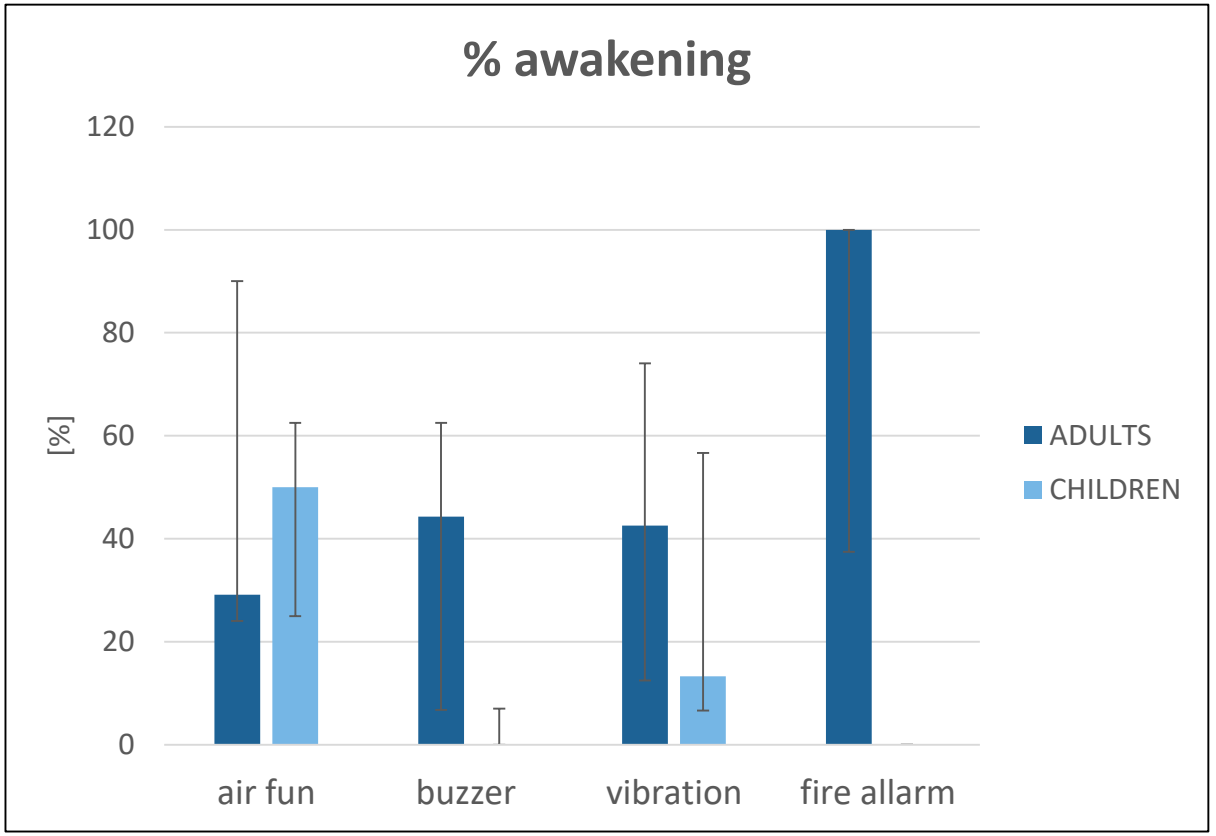
The fire alarm was always associated to SL4

The clinical trial

Results

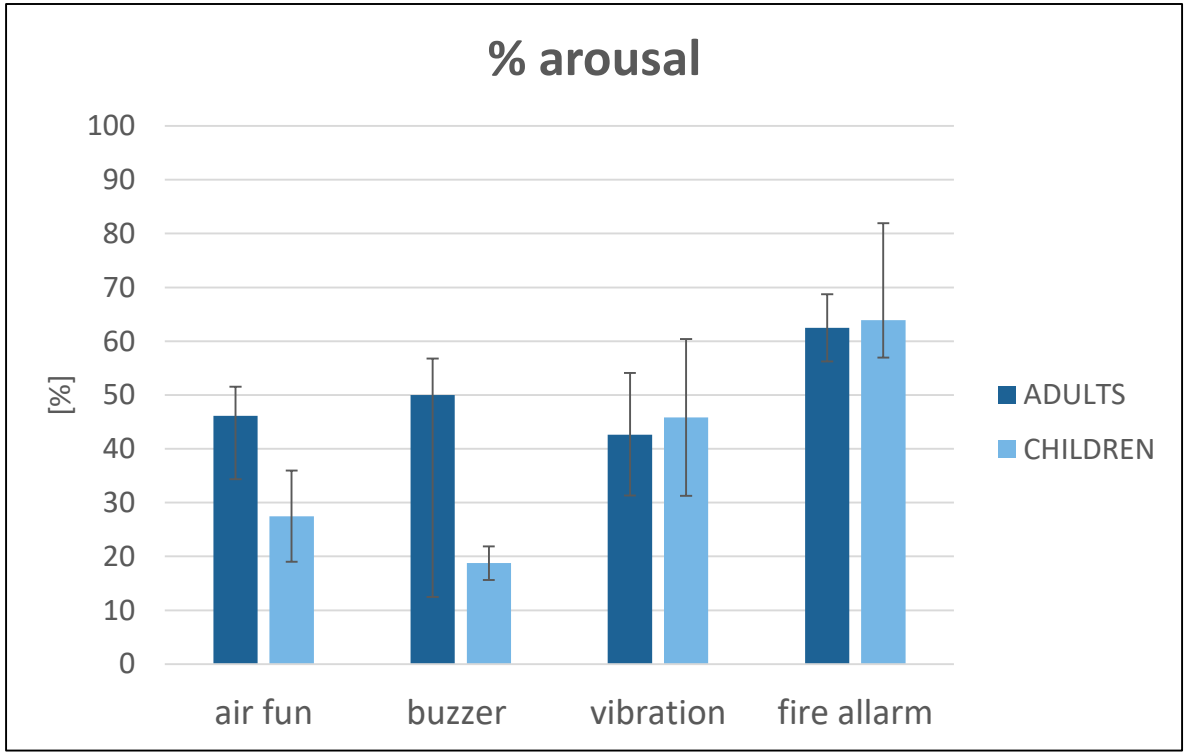
Number of activation per subject		
	Median	IQR
Air fun	4	28
Buzzer	4	28
Vibration	14	10
Fire allarm	1	2

- 4 children (2 females, 2 males)
  mean age: 8,7 years (sd = 3,7)
- 11 adolescents and young adults (8 females, 3 males)
  mean age: 23,4 years (sd = 6,8)



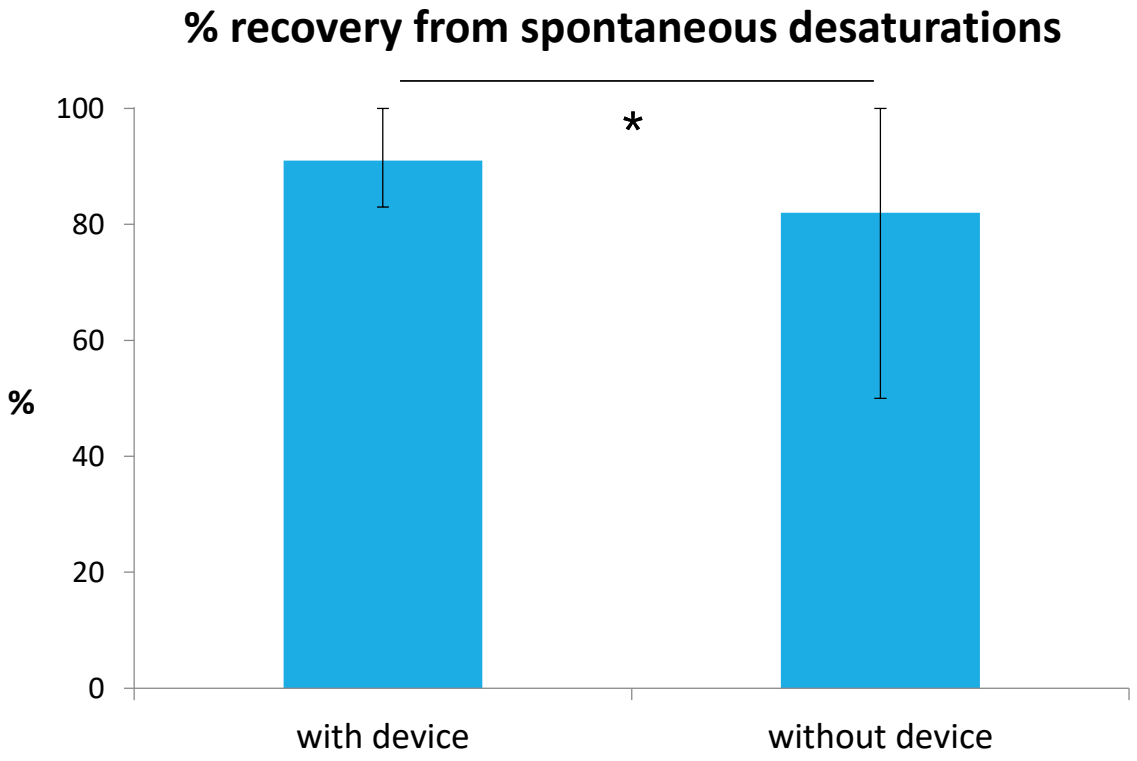
The clinical trial

Results



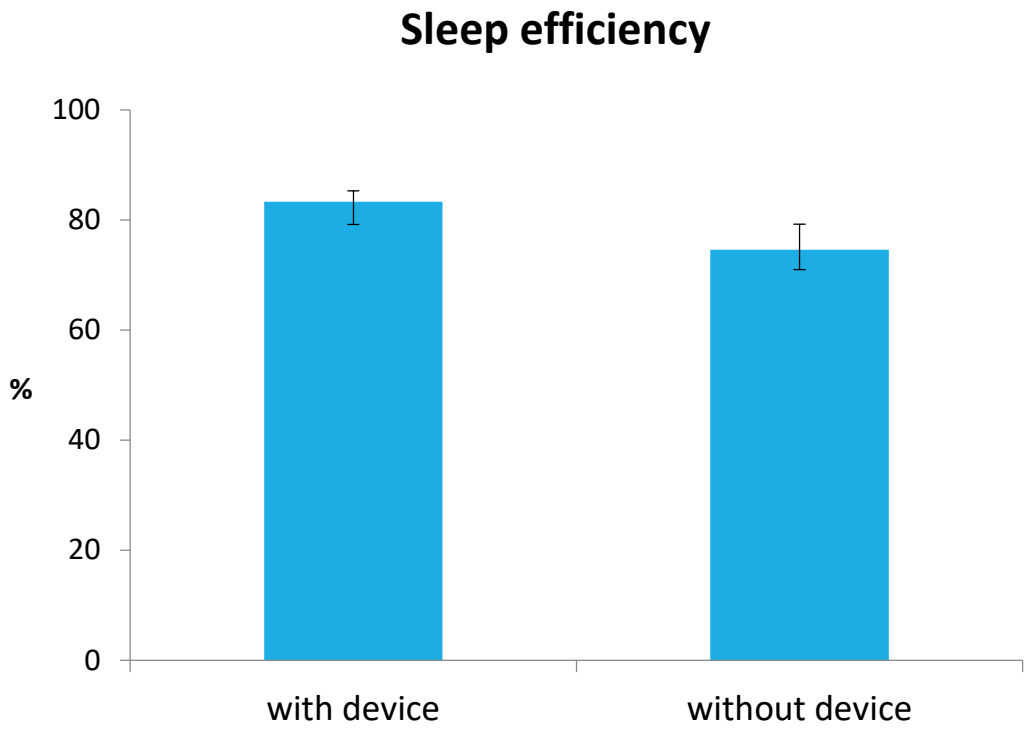
The clinical trial

Results



The clinical trial

Results



The clinical trial

Conclusion

- Promising results in awakening adolescents and young adults
- Low efficiency in awakening children
- The multisensory stimulations foster the spontaneous recovery
- The device didn't affect the sleep efficiency

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Thanks for your attention!

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