Physiological and Pathological Study on Sudden Infant Death Syndrome (SIDS): Physiological definition of arousal reaction - from arousals to arousability-

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Summary of the Research

It has been suggested that a defective arousal reaction is implicated in the development of sudden infant death syndrome (SIDS). The American Sleep Disorder's Association (ASDA) has edited definitions for the scoring of arousals in adults. These definitions, however, do not apply adequately to the description of arousal reactions at the pediatric age. A pediatric "Wake-up Club" was therefore established to define definitions suitable for infants and children. The first international conference of the pediatric "Wake-up Club" was held in November 1998 in Brussels (Belgium). A second conference was held in June 1999 in Paris (France), and a third conference was organized in Dresden (Germany) a few months later. The methodology and definitions of arousal reactions in children are still being refined. At the present time, a consensus was reached on the following points:

1. The arousal response is not a discrete state, but a continuous process,
2. An "arousal reaction can be scored in the presence of a partial or a complete arousal response,
3. Definitions must be adapted to the age of the subject (premature infants, newborns, infants, toddlers, children, adolescents),
4. Arousal reactions are classified into two major categories: spontaneous arousals (endogenous) and provoked reaction (exogenous),
5. The following EEG signals are associated with arousal reactions: rhythmic theta waves, increased EEG frequencies, flattening of the EEG signals and arousal followed by delta waves,
6. Arousals can be scored by taking into account EEG or non-EEG signals (autonomic or behavioral changes),
7. An arousal is rated when at least 2 of the following 4 criteria are met: the presence of augmented breathing signals, a change in heart rate, a change in EEG frequency and/or amplitude, and body movements. These changes should occur simultaneously for at least one second.

A. Aim

A defective arousal reaction was implicated in the development of sudden infant death syndrome (SIDS) almost 20 years ago. At the moment, the hypothesis of a defective arousal reaction has been widely recognized as the main hypothesis for the mechanism of SIDS. However, the relation between SIDS and arousal reaction is still unknown. There are still many basic problems and steps which should be clarified to understand the mechanism of the hypothesis with respect to SIDS and arousal reaction. The aim of this research is to define...
the physiological definition of arousal reaction and its methodology.

B. Research Method

In this report, the pediatric physiological definition of arousal reaction and its methodology are described. The content is mainly the result of the meaningful discussion at the European Pediatric Wake-up Club mainly.

A pediatric "Wake-up Club" was therefore established to define definitions suitable for infants and children in addition to the edited definition for the scoring of arousals in adults by the American Sleep Disorder's Association (ASDA). The first international conference of the pediatric "Wake-up Club" was held in November 1998 in Brussels (Belgium), a second in June 1999 in Paris (France), a third in June 1999 in Paris (France), and a fourth in Dresden (Germany). The discussion of these definitions and the methodology are still being.

C. Research Results

Arousal theory as the medical hypothesis of SIDS

The hypothesis regarding defective arousal reaction in SIDS has been suggested and well-known after reconsideration of the apnea theory in SIDS as the causal theory of SIDS1-9). The arousal reaction after the sense of some abnormality and danger during sleep is one of the important mechanisms for the system of protection in a living body. Normal babies and infants have a short interruption of respiration during sleep. However, they immediately recover their normal respiration. In such a case, the short stop of their respiration does not cause their death. In the hypothesis of arousal reaction in SIDS, it has been surmised that the recovery of respiration after apnea is disturbed by defective arousal reaction in SIDS. Franciosi RA has suggested the possibility that a disorder of entrainment of the sleep-arousal cycle causes the defective arousal reaction in SIDS3).

The interpretation of arousal theory in SIDS has come to be discussed in a broader sense than before. At the moment, it is understood that a defective arousal reaction can possibly increase some risk of SIDS. On the other hand, when some risk factors of SIDS are applied to the normal healthy babies and infants, arousability becomes decreased. In such a case, prone position10) and maternal smoking during pregnancy11) are recognized as such kinds of risks. For example, auditory arousal thresholds are higher when infants sleep in the prone position12)13).

Necessity of definition of a pediatric arousal reaction

In the above-mentioned process and discussion, it has become necessary to define an arousal reaction and gain a consensus of the definition in order to understand clearly the arousal reaction. As for the physiological definition of an arousal reaction in adults, ASDA has already been reported14). However, a consensus of the physiological definition of an arousal reaction in babies and infants has not been obtained at the moment. Therefore, to obtain this necessary consensus, the European Paediatric Wake-up Club was organized and several meetings of this organization have been held to discuss the definition of the pediatric arousal reaction.

Arousals and awakenings

There seemed to be a problem with the use of confusing words to define an arousal reaction. As examples of these confusing words, there are "arousal" and "awakening". Despite the publication of a tentative consensus on the scoring of arousals in adults14), the recent literature still offers a wide range of terminologies15). Terms such as arousals or awakenings are often used to describe changes from sleeping to waking states16). In the ASDA report, brief or transient arousals are opposed to behavioral awakenings14). In EEG patterns, we sometimes find K complexes which characterize arousals without awakenings16). To be summarized, " arousal" includes...
both polygraphic or electric changes and behavioral or clinical changes, while the latter refers to "awakening". Recognition of latter is relatively easy. However, the defective arousal reaction in recent SIDS research refers to the former, particularly early stages of the former.

Definition of an arousal reaction in adults 14)

The report from ASDA is already known as the physiological definition of an arousal reaction in adults. This defines an arousal reaction by measuring the change of electroencephalography (EEG). In this report, a concrete rule and some examples have been shown for scoring. The assumption of this definition is the following:

1. Arousals can be scored from either central or occipital derivation EEG,
2. An abrupt shift in EEG frequency, which may include theta, alpha and/or frequencies greater than 16 Hz but not spindles, is subjected to the following rules and conditions.

The EEG arousal scoring rules consist of the following,
1. Subjects must be asleep, defined as 10 continuous seconds or more of the indications of any stage of sleep, before an EEG arousal can be scored,
2. A minimum of 10 continuous seconds of intervening sleep is necessary to score a second arousal,
3. The EEG frequency shift must be of 3 seconds or greater in duration to be scored as an arousal,
4. Arousals in non-REM sleep may occur without concurrent increases in submental EMG amplitude,
5. Arousals are scored in REM sleep only when accompanied by concurrent increases in submental EMG amplitude,
6. Arousals cannot be scored based on changes in submental EMG amplitude alone,
7. Artifacts, K complexes or delta waves are not scored as arousals unless accompanied by an EEG frequency shift of at least one derivation. If such activity precedes an EEG frequency shift, artifacts or delta wave activity are included in meeting duration criteria,
8. The occurrence of pen blocking artifact should be considered as an arousal only if the EEG arousal patterns are contiguous. The pen blocking event can be included in meeting duration criteria,
9. Noncurrent, but contiguous, EEG and EMG changes, which are individually less than 3 seconds but together greater than 3 seconds in duration, are not scored as arousals,
10. Intrusion of alpha activity of less than 3 seconds duration into nonREM sleep at a rate greater than one burst per 10 seconds is not scored as an EEG arousal. Three seconds of alpha sleep is not scored as an arousal unless preceded by a 10-second episode of alpha free sleep,
11. Transitions from one stage of sleep to another are not sufficient of themselves to be scored as EEG arousals unless they meet the criteria indicated above.

Comparison of an arousal reaction between adults and infants

It is necessary to know the difference of the characteristics of an arousal reaction between adults and infants for the definition of a pediatric arousal reaction. With respect to this point, Busby et al. has suggested that incongruences between EEG and other polygraphic parameters have resulted in the definition of arousals as incomplete awakenings in newborns and young infants 17). Therefore, the scoring of pediatric arousals relies largely on non-EEG changes. These include autonomic and behavioral responses, such as abrupt changes in respiratory or cardiac rhythm, muscular tone or galvanic skin values. In older infants, a polygraphic arousal is scored when the child appears to be asleep but simultaneously manifests abrupt non-EEG or EEG changes.

Definition of a pediatric arousal reaction

As mentioned above, the definition of a pediatric arousal reaction has been discussed in the European
Pediatric Wake-up Club. According to the results of the discussion of the European Pediatric Wake-up Club, the following seven consensuses have been gained:

1. The arousal response is not a discrete state, but a continuous process. The change in sleep-wake behavior can be partial, as witnessed by changes in physiological variables, or lead to a complete behavioral awakening.

2. An "arousal reaction can be scored in the presence of a partial or a complete arousal response. Actually it can be sometimes described as the combination of partial reactions. As above-mentioned, "arousal" and "awakening" should be distinguished. When stable and concordant changes are seen in the recording of sleep for at least 2 minutes, an "awakening" is rated. An awake state is then scored.

3. Definitions must be adapted to the age of the subject (premature infants, newborns, infants, toddlers, children, adolescents). To evaluate sleep-wake scoring techniques, it was suggested that children be classified as: premature infants (from 25 weeks of gestation to 4 weeks after birth); infants and toddlers (1 month to 2 years old); and children (2- to 10 years old). The arousal reactions of premature infants are divided into the following three groups: spinal arousal including an augmented breath and a startle; brain stem arousal including an increase in heart rate and/or respiratory amplitude and/or rhythm and increase in blood pressure; and cortical arousal including a change in behavior.

4. Arousal reactions are classified into two major categories: spontaneous arousals (endogenous) and provoked reaction (exogenous). In addition, spontaneous (endogenous) arousals are divided into system-related arousal and non-system-related arousal. Non-system-related arousals are those occurring spontaneously and for no known cause. Some of these may be associated with specific behavioral changes, such as changes in sleep stages, often accompanied by body movements. These arousals may be classified as non-system related, associated with sleep-stage changes. System-related arousals may be classified according to the suspected cause of the arousal, such as respiratory-related arousals associated with apnea or hypopnea or other respiratory changes with increases in breathing efforts and other system-related arousals such as cardiac, digestive, and muscular arousals. The provoked (exogenous) reaction includes arousal reactions that follow changes in the sleep environment of the child such as noise, light and temperature.

5. The following EEG signals are associated with pediatric arousal reactions: rhythmic theta waves, increased EEG frequencies, flattening of the EEG signals and arousal followed by delta waves.

6. Arousals can be scored by taking into account EEG or non-EEG signals (autonomic or behavioral changes).

7. An arousal is rated when at least 2 of the following 4 criteria are met: the presence of augmented breathing signals, a change in heart rate, a change in EEG frequency and/or amplitude, and body movements. These changes should occur simultaneously for at least one second.

D. Consideration

The following matters and questions remained unanswered:

1. The specific changes by age, How should we estimate quantitative changes?

2. The duration of baseline periods with which to compare "changes",

3. The % of cardiac rates and respiratory rates required to be scored as "a change",

4. The duration of sleep periods between two successive" arousal reactions".

No consensus exists on the type of challenge that best fits the determination of thresholds.

Furthermore, it is not clear as to how a threshold...
should be determined.

E. Conclusion-From "arousals" to "arousability"

In the process of the above-mentioned discussion, "arousability" has been gradually given attention. "Arousability" seemed to be the word which expresses the total potential ability for arousal reaction. So, how should we define the definition of arousability? The measuring of arousal thresholds is actually equal to the concrete description of arousability. In addition, arousal thresholds can then be determined by measuring the intensity of the stimulus needed to induce arousals.

The determination of arousal thresholds is complicated by various factors. Some are maternal and some are infantile such as age and conditions before measurement. Experimental conditions such as the time of administration of the challenge, the infant’s sleep stage, body position, temperature of the room, the use of a pacifier or the type of feeding, and the situation of bed-sharing are significantly important as stimuli. Also the kinds of stimuli such as hypoxic or hypercapneic stimuli or other auditory stimuli influence arousal thresholds. In addition, other endogenous factors also influence the level of arousal thresholds.

The discussion to define arousals has gradually changed to a discussion to define arousability. The significance of the defective arousal theory with respect to SIDS might be transformed by this change.

F. Research Presentation

1) Presentation by publishments

Original articles:


Letters and abstracts :


Books chapters :


2) presentation in academic meetings

Sawaguchi T. The Moebius strip and the sudden death of an infant during sleep. The sixth SIDS International Conference. New Zealand. 2.8-11,2000.3.29

References


7) Harding R, Jakubowska AE, McCrabb J. Arousal and cardiorespiratory responses to airflow obstruction
in sleeping lambs: effect of sleep state, age, and repeated obstruction. Sleep, 1997;20:693-701.