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Evaluation of Dry Sensors for Neonatal EEG recordings

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Abstract

Introduction—Neonatal seizures are a common neurologic diagnosis in Neonatal Intensive Care Units (NICUs), occurring in approximately 14,000 newborns annually in the US. While the only reliable means of detecting and treating neonatal seizures is with an EEG recording, many neonates do not get an EEG or experience delays in getting them. Barriers to obtaining neonatal EEGs include: 1) lack of skilled EEG technologists to apply conventional wet electrodes to delicate neonatal skin, 2) poor signal quality due to improper skin preparation and artifact, 3) extensive time needed to apply electrodes. Dry sensors have the potential to overcome these obstacles but have not been previously evaluated on neonates.

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Methods—Sequential and simultaneous recordings with wet and dry sensors were performed for one hour on 27 neonates from 35-42.5 weeks postmenstrual age. Recordings were analyzed for correlation and amplitude, and were reviewed by neurophysiologists. Performance of dry sensors on simulated vernix was examined.

Results—Analysis of dry and wet signals showed good time-domain correlation (reaching >0.8) given the non-superimposed sensor positions, and similar power spectral density curves. Neurophysiologist reviews showed no statistically significant difference between dry and wet data on most clinically-relevant EEG background and seizure patterns. There was no skin injury after 1 hr of dry sensor recordings. In contrast to wet electrodes, impedance and electrical artifact of dry sensors were largely unaffected by simulated vernix.

Conclusions—Dry sensors evaluated in this study have the potential to provide high-quality, timely EEG recordings on neonates with less risk of skin injury.

Keywords

Electroencephalography (EEG); dry sensor; neonatal neurology; Neonatal Intensive Care Unit (NICU); epilepsy; seizure

Introduction

Neonatal seizures are a common neurologic diagnosis in the Neonatal Intensive Care Unit (NICU), occurring in 1.8-3.5/1000 live births or 14,000 newborns annually in the US (Hall et al., 2006; Glass et al., 2009a). They contribute to injury after hypoxia-ischemia (Legido, et al., 1991; Wirrell et al., 2001; Miller et al., 2002; Glass et al., 2009b) and are frequently associated with long-term deleterious consequences including intellectual disability, cerebral palsy, epilepsy, and other neurodevelopmental disabilities (Clancy et al., 1991; McBride et al., 2000; Toet et al., 2005; Pisani et al., 2007; Nagarajan et al., 2010; Glass et al., 2011). Early detection and treatment can result in more effective seizure control (Painter et al., 1999; Castro Conde et al., 2005; Goodkin et al., 2005; Cornejo et al., 2007; van Rooij et al., 2010;), decreased rates of epilepsy (Toet et al., 2005) and may also lead to reduced morbidity and mortality after neonatal seizures (Castro Conde et al., 2005; Low et al., 2012; Srinivasakumar et al., 2013).

EEG is the only reliable means for detection and management of neonatal seizures (Shellhaas et al., 2011). In NICUs that do not obtain EEG, up to 12% of affected neonates go unrecognized (Helmers et al., 1997; Laroia et al., 1998; Clancy et al., 2005), and almost 75% of seizures are missed despite outward signs (Clancy et al., 1988; Bye et al., 1995; Murray et al., 2008). EEG can detect seizures up to 20 hours before any outward signs (Helmers et al., 1997; van Rooij et al., 2010), and can significantly reduce the likelihood of misdiagnosis (Murray et al., 2008). EEG monitoring is critical for assessment of treatment efficacy, since after seizure medication 58% of neonates continue to have seizures that are detected only on EEG (Scher et al., 2003).

Significant barriers currently exist in obtaining useful and timely EEGs in many NICUs. Skilled personnel are essential for properly applying conventional wet electrodes to delicate neonatal skin. Many hospitals lack EEG technologists trained specifically for this task and

others only have them available 8-15 hours per day, and thus EEG recordings cannot be initiated or properly maintained. Preparing a newborn for an EEG can take up to 60 minutes, which includes the process of gently cleaning the head of extensive birth related products including vernix, and application of electrodes. An additional step involves the elimination of sources of artifacts and electrical interference, which are numerous in the NICU setting and can corrupt signals. Recordings are thus not started until the infant is stabilized, often 9-10 hours after onset of hypoxia-ischemia (Nash et al., 2011; Wusthoff et al., 2011). This is a significant delay since therapy can be less effective within hours of the start of a seizure (Castro Conde et al., 2005; Goodkin et al., 2005) and seizures after hypoxia ischemia can start as early as 6 hours of life (Wusthoff et al., 2011). While subdermal needle electrodes can be applied more quickly than wet scalp electrodes, they have inferior recording characteristics and are not recommended for prolonged recordings (Herman et al., 2015). Finally, there is risk of skin injury and infection from skin abrasion and application of conductive paste, which is especially problematic for the fragile skin of premature and critically-ill term neonates. These barriers cause significant delay in initiating EEG monitoring, and in some cases at-risk newborns are not evaluated at all.

Dry sensors (QUASAR Inc., San Diego, CA) make a high-impedance electrical contact to the skin, and record EEG without the need for skin preparation of any kind (Matthews et al., 2006, 2007). Previous studies have demonstrated that these sensors record signals comparable to those obtained from wet electrodes attached by a technician, including a study on 19 adults (Estepp et al., 2009). Juxtaposed dry and wet sensors typically record signals with over 90% correlation (Matthews et al., 2008), and dry sensors are largely immune to electrical interference. Dry sensors' data quality is also suitable for diagnosing status epilepticus and seizure activity, and a 20-sensor montage can be put on adults by technicians in approximately one-sixth the time it takes for a wet montage (Slater et al., 2012). While the dry sensors have the potential to overcome many barriers to neonatal EEG recordings, there had been no prior studies using these sensors for neonates. In this study, we evaluated the signal quality and safety of dry sensors in neonatal EEG recordings in an NICU.

Methods

Data Acquisition

Dry sensor measurements were made using a prototype QUASAR EEG system (Fig. 1a), which uses sensors (Fig. 1b) identical to those in QUASAR's adult 20-channel headset. The system had 2 EEG sensors, a Common-Mode Follower (CMF) sensor which acts as a reference and dynamically removes the common-mode artifact on the body (Matthews et al., 2006), and a flat disc ground. Each sensor (3.3 × 3.3 × 2.5 cm) has foam around its circumference and double spring-loaded electrode pins, which retract into the sensor case and touch the skin with preset pressure. Signals from dry sensors were amplified with an analog gain of 64 prior to digitization (16-bit sigma-delta, resolution 0.3 μV) at a 300 Hz sample rate, and wirelessly transmitted by the data acquisition module to a PC. Dry sensors, CMF and ground were held against unmodified skin using elastic straps, tape or bandages. Wet electrode recordings were made with a Nihon-Kohden EEG 1100C, yielding 14

channels of data sampled at 200 Hz. Wet electrodes were applied conventionally in the International 10-20 positions (Fp1, Fp2, Cz, T3, T4, C3, C4, P3, P4, O1, O2) using skin abrasion with Nuprep (Weaver & Co., Aurora, CO) and LemonPrep™ (Madivon Corp., Lake Worth, FL), and filled with Ten20 (Weaver & Co., Aurora, CO) conductive paste. Details of separate measurements on adult subjects with simulated vernix are provided in the Appendix.

Subjects

Twenty-seven infants, postmenstrual age 35 to 42.5 weeks, from Children's National Health Systems in Washington, DC were enrolled in this study with parental consent under an IRB-approved protocol. Subjects were eligible if they were having EEG recording as part of routine care and were not actively having seizures or clinical deterioration. Approximately 1 hour of data was recorded with each system on 27 subjects (sequential: 3-15; simultaneous: 1, 2, 16-27). Sequential data were recorded first with wet electrodes, followed by dry sensors placed at T3 and T4 after removing the wet electrodes. Simultaneous data were recorded with wet electrodes and dry sensors at T5 and T6 (Fig. 1d). For all data, the CMF and ground were placed on the midline forehead inferior to the frontal wet electrodes and on the abdomen, respectively. Clinical reviews examined 20 datasets (sequential: 3, 5, 7, 9-15; simultaneous: 16, 19-27). Two datasets were excluded due to incomplete or interrupted recordings, and five due to high noise or artifact (one wet electrode recording and four early dry sensor recordings with poor skin contact prior to establishing a more secure attachment method). Quantitative analysis examined 15 datasets (sequential: 10-14; simultaneous: 16, 19-27), after excluding additional five sequential datasets due to high noise or artifact in either system.

Quantitative EEG Analysis

Pre-processing—A subset of the wet electrodes was used in quantitative analysis based on their proximity to the dry sensors (Fig. 1d). Differences between wet electrodes produced lateral bipolar channels O1-O2, T3-T4, P3-P4 and C3-C4, and the difference of dry sensors produced T5-T6. All data used in the time-domain analysis and shown in time-domain plots were filtered in a 1 Hz to 40 Hz bandwidth. Simultaneous recordings by both systems were synchronized in post-processing (see Appendix).

Correlation—Pearson's correlation, r, was computed on simultaneous data between the dry channel and one of the wet channels, as well as between all wet channels, yielding 4 dry/wet and 6 wet/wet combinations. The highest r for each set of combinations is reported here. The correlation was computed on selected data segments 60 sec or 600 sec in length with the quietest signal in each recording, which was determined by minimizing the sum of the average measured amplitude, V_{rms}, of all dry and wet channels.

Amplitude and Power—Each channel in a subject's recording was searched individually for a 10 second segment with the minimum measured amplitude, V_{rms}. The percent of data points in the entire recording that is above a threshold value was also determined. The amplitude and percent of data above a threshold are averaged across wet channels. Power

spectral density (PSD) curves were calculated using a Fourier transform with Hanning windowing, 2 sec segments and 75 % segment overlap.

Clinical Review

Two ABPN board-certified neurophysiologists independently reviewed data recorded by both systems. Paired data sets were blinded and randomly presented to reviewers in identical format on Persyst software (Persyst, Prescott, AZ). All data were digitally filtered from 0.5 Hz to 70 Hz and with a notch filter at 60 Hz. Reviewers identified relevant EEG patterns according to terminology and categorization in the most recent ACNS guidelines (Tsuchida et al., 2013), and scored the signal quality. Agreement between wet and dry data was assessed using kappa coefficients (stratified as 0-0.20 slight; 0.21-0.40 fair; 0.41-0.60 moderate; 0.61-0.80 substantial; 0.81-1.00 almost perfect, computed using IBM SPSS Version 21). Fisher's exact test was performed to compare ease of interpretation, presence of artifact and ability to interpret recordings, with $p<0.05$ deemed significant in two-tailed testing.

Results

Signal Quality and Correlation

Representative data recorded simultaneously with both systems are shown in Fig. 2. Time-domain signals for subject 20 show high quality EEG signal measured by dry sensors which is characteristically similar to wet electrodes. Corresponding PSD curves show minor differences between channels. Data for subject 26 shows distinct patterns recorded by both systems. Data in Fig. 2 for subject 20 has $r = 0.81$ between T5-T6 (dry) and O1-O2, while r between wet channels ranges from 0.43 to 0.78. For subject 26, $r = 0.77$ between T5-T6 and P3-P4, $r = 0.77$ between T5-T6 and T3-T4, while r between wet channels ranges from 0.43 to 0.83. Recordings on subject 23 exhibited a seizure seen by both systems (Fig. 3). T5-T6 and T3-T4 are highly correlated ($r = 0.84$) and show similar PSD curves with a distinct oscillatory pattern at 3.5 Hz.

Fig. 4 shows the highest correlation of any dry/wet and wet/wet channels. Data for subject 22 has been excluded due to a dry/wet correlation below 0.1, possibly due to error in sensor placement. The r values show that, for most subjects, the dry/wet and wet/wet correlations of similar magnitude and are statistically equivalent on average and show little dependence on the length and selection of the data segment (dry/wet $r = 0.61 \pm 0.13$, wet/wet $r = 0.70 \pm 0.12$ for 60 seconds and dry/wet $r = 0.58 \pm 0.16$, wet/wet $r = 0.72 \pm 0.11$ for 600 seconds).

Amplitude and Impedance

Dry and wet channels have similar amplitudes on a given subject (Fig. 5). Averaging the ratio of amplitudes across subjects, the dry system had average amplitudes 1.55 ± 0.43 times higher than the wet system. The percent of data in the entire dataset that is above a threshold is shown in Fig. 5b. Averaging the ratio of values across subjects, the dry system had 1.26 ± 0.54 times higher amount of data above the threshold than the wet system. The threshold was 3 times a channel's signal amplitude in the quietest 10 second segment.

Dry sensors generally recorded less external noise pickup at 60 Hz, which in Fig. 3b is 6 times smaller compared to wet. Eleven out of 15 subjects analyzed had less pickup in recordings with dry sensors over the entire recording, on average by a factor of ∼2,000. For the remaining subjects, the wet system had an average of ∼3 times less pickup compared to dry.

The impedance of dry sensors to the skin was monitored by injecting a small AC signal through the sensor electrode. Values were averaged across the two dry sensors and over the length of each recording. For datasets used in the quantitative analysis, the average impedance was 51 kΩ (95% CI [27, 90]), for sequential datasets, and 362 kΩ (95% CI [53, 947]), for simultaneous datasets.

Clinical Review

There is substantial agreement between wet and dry EEG recordings for continuous background (kappa 0.77, $p<0.001$). Two patients with seizures were identified by both reviewers in both recordings, resulting in perfect agreement (kappa 1.0, $p<0.001$). Similarly, two patients with excessively discontinuous background were identified with substantial agreement between recordings (kappa 0.84, $p<0.001$). Discontinuous background was identified by one reviewer in two patients and had a moderate level of agreement between recordings (kappa 0.64, $p<0.001$). There was fair agreement in the identification of spikes/sharps (kappa 0.35, $p=0.03$) in 16 patients and state changes (kappa 0.26, $p=0.1$) in 19 patients. Inactive/low voltage background, Rhythmic and Brief Rhythmic Discharge (BRD) were infrequent findings with poor agreement between reviewers as well as between recordings. There were no recordings with burst suppression.

In addition, there was no statistically significant difference in ease of interpreting either recording. Fifteen and five percent of the data segments were difficult to interpret for the dry and wet systems, respectively ($p = 0.26$). Artifact was present in 60% and 38% of the dry and wet recordings, respectively ($p = 0.073$). For the recordings with artifact, 17% and 8% were rated as not interpretable for the dry and wet systems, respectively ($p = 0.63$).

Performance on Simulated Vernix

Contact impedance of dry sensors was not significantly affected ($p>0.05$) by placement on simulated vernix compared to bare skin, while contact impedance of wet sensors increased from 8.4 ± 6.7 kΩ to 143 ± 77 kΩ. Likewise, the 60 Hz pickup of the dry system was not affected by vernix, while the wet system recorded a ∼40 fold increase.

Skin integrity

Skin redness and abrasion were documented for each patient. No infants had skin abrasion after recordings with either system. All infants had skin dimpling immediately after recording with dry sensors, and one infant had redness for 24-48 hours. A few infants had redness after 24 hours of recording with wet electrodes.

Discussion

We find a range of correlations (∼0.4 to 0.8) between wet/wet combinations consistent with a variation of the EEG signal over the subject's head. To account for the non-superimposed placement of dry and wet sensors, we thus compare the highest correlation of the dry/wet to wet/wet combinations (Fig. 4). Our correlation analysis is also impacted by the poor timing synchronization between the acquisition systems (see Appendix), which plausibly explains the slightly lower dry/wet correlation compared to the wet/wet correlation, the latter of which is not affected by synchronization.

Analysis of the amplitude in the quietest 10-second segment allows us to compare the noise of each system when a minimal EEG signal or artifact is present. The dry system on average measured slightly higher (∼1.5 times) average amplitude than the wet system. Since, in general, dry sensors have comparable noise to wet electrodes on adults, the increased amplitude could have resulted from the temporal lobe locations chosen for the dry system, making it more susceptible to EMG artifact. Indeed, we find that dry locations T5-T6 have signal power similar to T3-T4, which are both higher than power in P3-P4 above 20 Hz (Fig. 2b and 2d). The latter locations are generally less susceptible to EMG produced by the temporalis muscle (Goncharova et al., 2003).

The percent of data above a threshold indicates ∼1.3 times more artifact in the dry system compared to the wet, consistent with reviewer observations. However, importantly, this did not significantly affect the ability to interpret EEG background patterns. We note that the method of attaching dry sensors was not optimized in this study, leading to possible motion artifacts. We hypothesize that further improvements in headset design will reduce this artifact, much like similar improvements through successive designs of an adult EEG headset (Matthews et al., 2009). Higher powered studies on larger populations could help tease out more detailed advantages or disadvantages of interpretation between the two systems.

While wet electrodes placed on simulated vernix showed a large increase in contact impedance and 60 Hz pickup, dry sensors were largely unaffected. The dry system is much less susceptible to pickup of 60 Hz signals irrespective of skin condition, and showed less pickup on most recordings in this study than wet electrodes applied with skin abrasion. Pickup of 60 Hz is a surrogate measure for pickup of other sources of electrical interference present in the NICU environment that is rich with power lines and electronic equipment such as incubator heaters and ventilators (Neubauer et al., 2011; Tatum et al., 2011).

The impedance of the dry sensors to the skin was 5 to 40 times larger than what is typically the maximum acceptable for wet electrodes (Herman et al., 2015). This observation confirms that the design of the dry sensors used in this study does allow acquisition of high-quality signals with less electromagnetic interference, despite high impedance to the skin (Matthews et al., 2006, 2007). The smaller impedance of dry sensors in sequential vs. simultaneous datasets is consistent with the presence of conductive paste residue from the prior application of wet electrodes to the same locations during sequential data collection.

There was moderate to perfect agreement between wet and dry recordings of EEG background patterns continuous, discontinuous, excessively discontinuous and seizures with the given sample size. Agreement was negative to fair for other features. This may partly be due to the low frequency of some of these findings or to interobserver variability. Interpretation of single channel recordings is difficult since typical EEG pattern characterization utilizes spatial distribution of signal over several channels in order to distinguish artifact, background patterns and epileptiform abnormalities. In addition, pattern characterization is subjective and some features are known to have extensive interobserver variability. Studies of interobserver agreement in interpreting neonatal EEG found values of kappa ranging from 0.65-0.74 for background patterns (Tekgul et al., 2005; Shah et al., 2008) and 0.84-1.0 for seizures (Toet et al, 2002; Tekgul et al., 2005; Shah et al., 2008). In children, kappa ranges from 0.69 for continuity, 0.73 for burst suppression, 0.4 for spike wave, and 0.65 for overall interpretation (Abend et al., 2011). A larger study is needed to examine agreement between data from wet and dry systems while considering impact of differences in interobserver interpretation.

Finally, dry sensors do not appear to cause any skin injury after a one hour recording. Additional experiments are needed in order to evaluate safety after 24 hours or more of recording.

Conclusion

This study evaluated the signal quality and safety of dry sensors for use in neonatal EEG recordings in an NICU environment. Reviews by neurophysiologists found statistically significant agreement between dry and wet data on most clinically-relevant EEG background patterns and seizures, and no statistically significant difference in ease of interpreting recordings. This suggests that neurophysiologists rate the data quality of dry sensors as substantially equivalent to that of conventional wet electrodes. Data analysis showed an average correlation between the dry and wet systems of ∼0.6 for 60 sec of data, with some correlations reaching 0.84, consistent with the non-superimposed placement of sensors and suboptimal data synchronization between the two systems. Dry sensors were found to be much less susceptible to pickup of external electronic interference. Furthermore, in contrast to wet electrodes, dry sensors were largely unaffected by simulated vernix, which would facilitate rapid placement on neonates without skin preparation. No skin injury occurred after a one hour recording, and additional experiments are needed to evaluate their safety in long-term, continuous recordings. Based upon these results, we conclude that dry sensors appear suitable for neonatal monitoring in a NICU, and could have multiple advantages in application time, safety and long-term monitoring over conventional wet electrodes. Further improvements in sensor and headset design are expected to reduce signal artifacts. Future studies on neonates will examine the performance and safety of miniaturized dry sensors and new sensor mounting methods, as well as prolonged recordings with a larger sensor montage.

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Appendix

A. Measurements with Simulated Vernix

Contact impedance and EEG were measured with dry and wet electrodes on Aquaphor (Eucerin, Wilton, CT), a topical barrier with properties similar to natural vernix caseosa (Rissmann et al., 2009; Visscher et al., 2011). EEG was collected on 4 adult subjects. Four dry electrodes were placed without skin preparation, two on bare skin near Fp2 and two on Aquaphor (simulated vernix) near Fp1. Wet cup electrodes were subsequently attached to the same sites, with the bare skin sites abraded with Nuprep (Weaver & Co., Aurora, CO), simulated vernix sites were not abraded, and all cup electrodes filled with Grass EC2 paste (Astro-Med, West Warwick, RI).

B. Synchronization of Simultaneous Recordings by Both Systems

Simultaneous data were recorded independently by their respective data acquisition systems and were not synchronized in time. Alignment of data was found by maximizing the cross-correlation between the dry and one of the wet channels, while varying their relative time offset and the sampling rate of the dry channel in steps of 10 msec and 0.1 mHz, respectively. This yielded a value for time offset for each dataset, and a sample rate offset for all data of -15.9 ± 0.2 mHz.

This method did not yield perfect synchronization due predominantly to drift in sampling rate over the hour-long dataset, which in turn had a significant effect on the dry/wet correlation. For example, our algorithm yielded a 17.81 sec time offset between dry and wet data for subject 23, while a visual inspection of the data 15 minutes into the recording showed a misalignment by 38 msec. Manually adjusting for this time delay further improved the correlation in Fig. 2 from $r = 0.72$ to $r = 0.84$. This illustrates the sensitivity of the correlation metric on the precise time and sampling rate alignment between datasets, and plausibly explains the slightly lower dry/wet correlation compared to the wet/wet correlation, the latter of which is not affected by the alignment.

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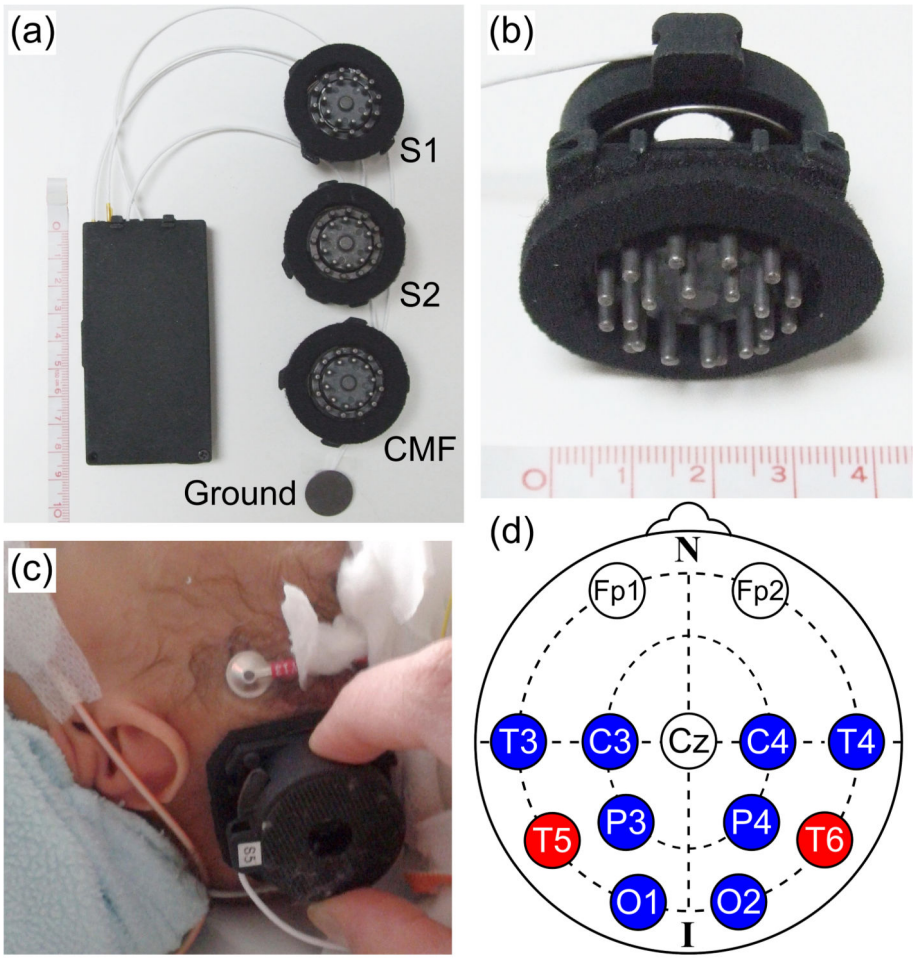

Figure 1.

(a) Prototype QUASAR dry EEG system with 2 adult-size sensors (S1, S2), common-mode follower (CMF) reference sensor, flat disc dry ground and wireless data acquisition module. (b) Close-up of the dry sensor with two sets of spring-loaded electrode pins and comfort foam. (c) Experimental setup showing wet electrode (T3) applied using conventional techniques, and dry sensor (T5) which was held against the scalp by a bandage. (d) Wet (blue and white) and dry (red) sensor positions during simultaneous recordings. A subset of wet electrodes (blue) was used in quantitative analysis due to their proximity to the dry sensors.

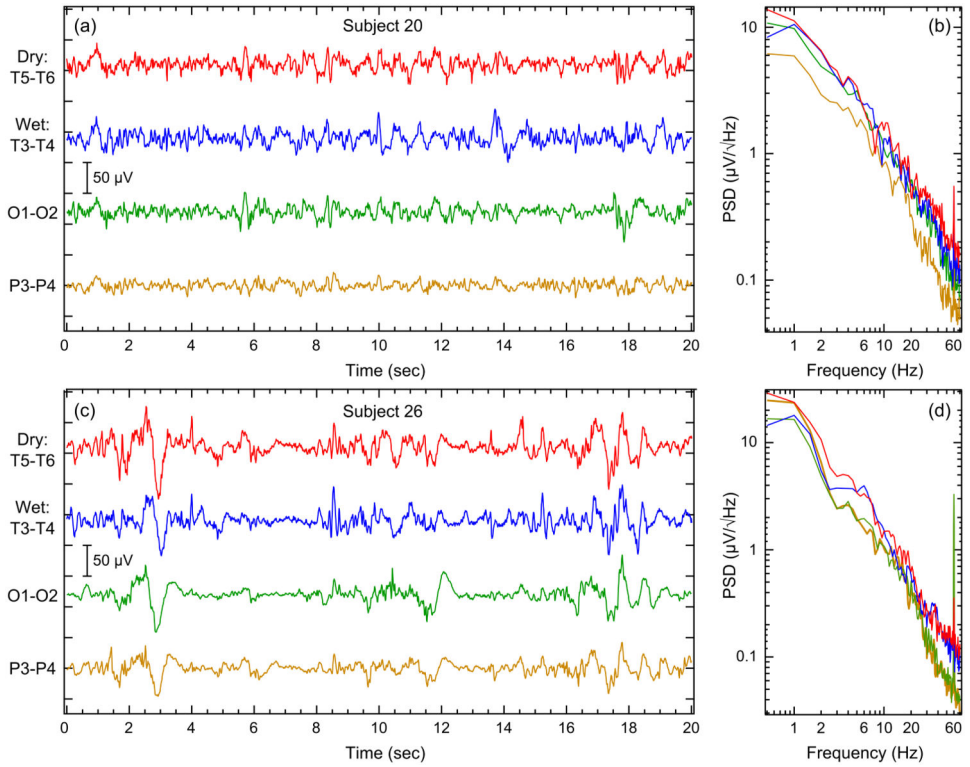

Figure 2.

Representative EEG signals recorded with dry and wet systems on subjects 20 (a)-(b) and 26 (c)-(d). Data with dry sensors shows EEG signal in the time-domain that is correlated with wet channels ($r = 0.81$ between T5-T6 and O1-O2 in (a), $r = 0.77$ between T5-T6 and P3-P4 in (c)). Corresponding power spectral density (PSD) curves show minor differences between the channels.

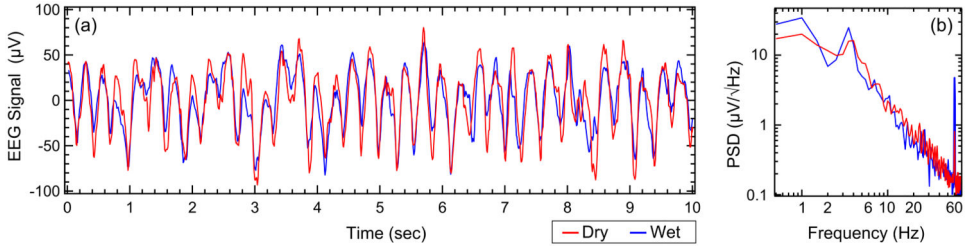

Figure 3.

Comparison of signals recorded during a seizure on subject 23, showing simultaneously-recorded EEG with adjacent dry (T5-T6) and wet (T3-T4) sensors. (a) Time-domain overlay of both signals shows high correlation ($r = 0.84$). (b) Power spectral density (PSD) curves are similar for both systems, with dominant peaks at 3.5 Hz. The power at 60 Hz is 6 times smaller for the dry system compared to the wet.

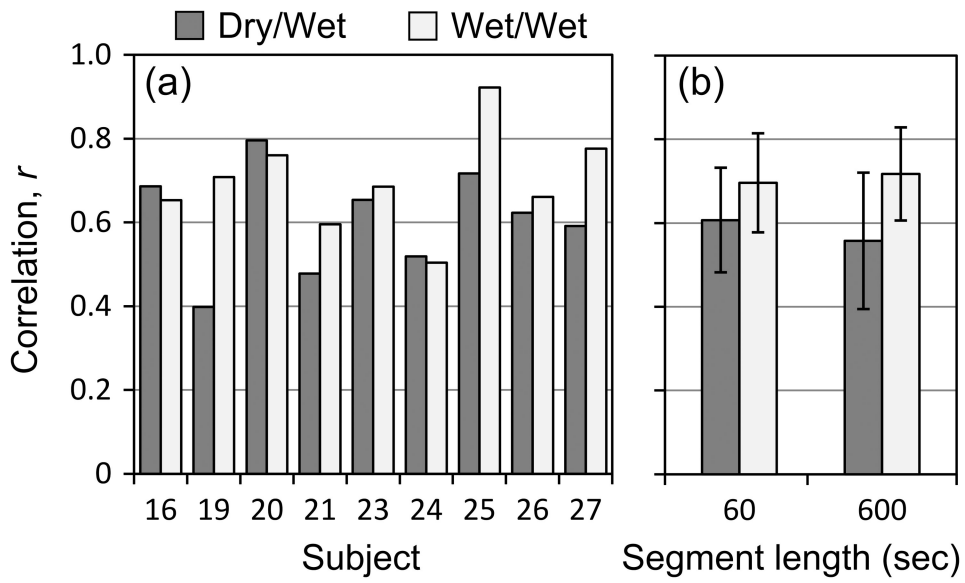

Figure 4.

(a) Highest correlation within the quietest 60 second segment between any dry/wet channel and wet/wet channels. (b) Correlations averaged across subjects and shown for different segment lengths.

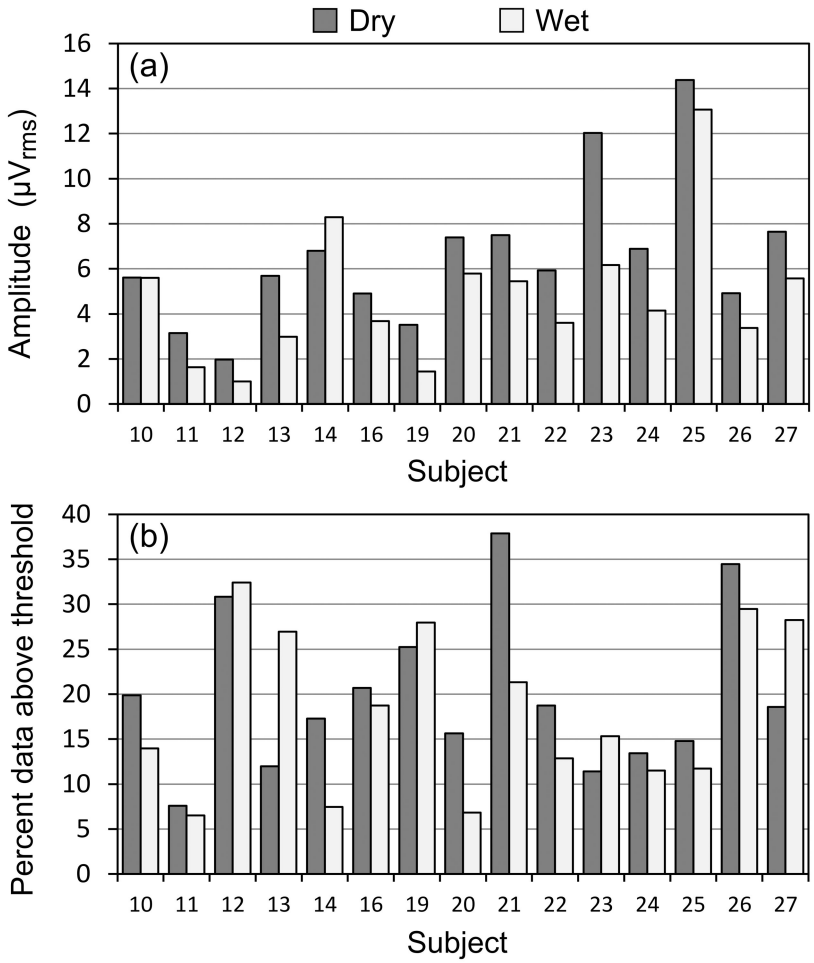

Figure 5.

(a) Average amplitude during the quietest 10 second segment measured by each system. (b) Percent of the data throughout the entire dataset (approx. 1 hr) with amplitude at least 3 times the level in (a). For the wet system, values in (a) and (b) are averaged across the wet channels.