

Chapter 2

What Constitutes a Normal EEG

Introduction

The usefulness of the routine standard (i.e., visually inspected) electroencephalogram (sEEG) in psychiatric practice and research is significantly hampered by the reported prevalence of EEG abnormalities in “normal” adult populations, ranging from 4 % to as high as 57.5 % (Struve 1985). This wide range likely reflects the lack of clear and rigorous standards for choosing subjects for healthy comparison groups. Blanc et al. (1964) documented that the inclusion of psychiatric patients in healthy comparison samples contributes to increased prevalence of EEG abnormalities in the examined sample. This observation was reported as early as 1939 (Davis and Davis 1939) and remains unchallenged today. In order for this technique to be reliable and useful, the boundaries of normality should be well defined.

The danger of reliance on a subject’s self-report of normalcy was highlighted by Halbreich et al. (1989) who showed that in a sample of self-proclaimed “normal volunteers,” 16.5 % met criteria for diagnosis of a current mental disorder and of the subjects without a current mental disorder, as many as 35 % had past histories and 39 % had family histories of mental illness. This is particularly important because physiological differences have been found between “normal subjects” with and without family histories of mental disorders (Schuckit 1984; Wiesel et al. 1982). Inclusion and exclusion criteria used for patient selection have also been progressively more restrictive, particularly for imaging and physiological studies. The presence of general medical or neurological conditions that may influence particular measurements are routinely used as exclusion criteria. Whether a subject is receiving medications that may affect brain functions is either exclusionary or well controlled for in the majority of studies published in psychiatric peer-reviewed literature during the last decade or longer and is an essential requirement for most granting agencies. Furthermore, issues of drug abuse and dependence, presence of Axis-I and Axis-II disorders are crucially important. In order to assess the actual usefulness of currently established boundaries of normality for psychiatric investigations, an extensive search of the literature included in Medline and PsychInfo databases for all articles listing EEG as a keyword was

Table 2.1 Normality criteria used to evaluate published chapters

Number criterion	Historical or current absence of
1	Systemic disorders with CNS involvement (e.g., endocrine or metabolic disorders)
2	Neurological disorders including traumatic brain injury ^a , history of childhood neurological disorders, and dementing illnesses
3	Psychiatric disorders including all Axis-I disorders except alcohol and drug abuse or dependence
4	Alcohol and drug abuse or dependence
5	Receiving CNS active medications including any psychotropic medications
6	First-degree relatives with family history of Axis-I psychiatric disorders
7	Axis-II disorders including personality disorders and mental subnormality

^a History of head injury is particularly problematic as definition of what is a “significant head injury” is not known or agreed upon. Most current research groups require at least a momentary loss of consciousness but different studies do require varied length of loss of consciousness

performed (Boutros et al. 2005). Textbook chapters discussing “normal EEG” were also examined for references (Niedermeyer 1993). These two sources were the primary sources for references. The reference lists of each chapter or book chapter were searched for older relevant chapters. Articles pertaining to quantified or spectrally analyzed EEG, articles examining evoked responses or sleep EEG, and articles that did not include normal subjects or did not study humans were excluded from the study. Additionally, review articles and abstracts were excluded. Seven criteria that are commonly used in contemporary neuropsychiatric research for selecting healthy comparison subjects were chosen as the bases for this review (Table 2.1).

Criteria were ranked as present or absent for each article. If a criterion could not be confidently rated as present, the criterion was marked as absent. As the majority of studies identified by this search were performed prior to the publication of the DSM criteria, the simple mention of a diagnosis was credited as correct.

A notably large number of studies simply stated that subjects were “healthy.” The simple assurance of normality was considered inadequate for our purpose, and they were marked as lacking all seven normality criteria. While this is unlikely to have been the case, we elected to err on the side of rigorous reporting. Among the seven criteria were: presence of a general medical condition that may affect the EEG, any neurological conditions including history of head injury leading to any length of loss of consciousness, and history of any psychiatric disorders. History of drug dependence or abuse (excluding tobacco or social use of alcohol), receiving any CNS active medications, family history of psychiatric disorders, and presence of an Axis-II disorder were also used as criteria for normality. The inclusion of family history as an exclusionary criterion is based on data showing increased EEG abnormality in family members of psychiatric patients (Chamberlain and Russel 1952).

A total of 39 articles examining the EEGs of “normal” individuals were included. Articles either examined EEGs in “normal subjects” as the sole purpose of the study or included a “normal” comparison group as a comparison for a pathological group (Boutros et al. 2005).

A history or presence of a general medical condition, a neurological disorder, or a major psychiatric disorder were three conditions considered to be most important in determining the exclusion of normal subjects. All three criteria were considered to have been met in a total of four studies. Five additional papers limited exclusion criteria to medical and neurological disorders. Excluding subjects solely based on history or the presence of a systemic disease that is likely to affect CNS functions (e.g., hypo or hyperthyroidism) was indicated in two more studies. Exclusion based solely on the presence or history of a neurological problem was seen in one study (White et al. 1977). In this study, the criterion for excluding subjects based on receiving CNS active medications was also met. Another study excluded subjects based on psychiatric history but without specific criteria for neurological or medical conditions (Chamberlain and Russel 1952). In this study, a family history of a psychiatric problem was also an exclusionary criterion. A single study screened for drug abuse (Buchtal and Lennox 1953). In two studies, subjects receiving psychotropic medications were excluded (White et al. 1977; Nowak and Marczynski 1981). None of the studies excluded subjects receiving such non-psychotropic medications as steroids or centrally acting antihypertensive medications. Two papers reported collecting family history data and one other paper reported screening for personality disorders, but these were not considered exclusionary criteria. This is important, as the EEG literature is replete with reports of abnormalities in association with different personality disorders, particularly antisocial, and borderline types. Standardized psychiatric scales (e.g., The Structured Clinical Interview for the DSM-SCID) (Spitzer et al. 1992) were not administered in any of the studies. Studies relied mainly on historical denial of psychiatric symptomatology.

The most recent relevant paper we were able to find is that by Jabbari et al. (2000). In this paper, the authors report on the EEGs of 100 male subjects ranging in age from 18 to 45. These subjects were healthy controls for a number of neurological studies. They were all active duty soldiers. History of seizures, head injury (specifics of any loss of consciousness duration not provided), and history of drug abuse (not specified if meeting DSM-III criteria), were the exclusion criteria. It is worth noting that what would be a current day minimal requirement to exclude psychiatric disorders (a structured or semi-structured diagnostic interview like the SCID were not administered), nor a family h/o psychiatric disorders reported. The results of this study are none the less very important as they found significant abnormalities like focal or generalized slowing or unequivocal epileptic discharges to be completely absent while 12 % had positive spikes and 11 % had small sharp spikes. These EEG phenomena are discussed in much detail in later chapters.

Discussion and Conclusions

The literature review described above indicates that the overwhelming majority of EEG normative studies were performed prior to the advent of normality criteria currently applied by most research institutions in research endeavors involving psychiatric or neuropsychiatric populations. In general, our search indicates that the criteria for normality taken into consideration in currently available literature for “normal” analog EEG range from poor to absent. A neurological history and systemic pathologies impinging on the central nervous system were only implicitly excluded in the majority of studies. The specific exclusion of significant head injury was also lacking. Traumatic brain injury has an annual incidence of 370 per 100,000 (Kurtzke 1984). Traumatic brain injury can lead to personality changes (McKinlay et al. 1981), affective disorders (Rutherford et al. 1977), or even psychotic syndromes (Lishman 1987). Medications or psychoactive substances contaminating the picture were not considered as a factor.

The largest studies establishing normality of EEG were conducted on Navy candidates. These studies specifically addressed personality disorders. While subjects were not excluded, data on personality disorders were collected but not reported in the publications. The importance of rigorous exclusionary criteria was demonstrated by Buchthal and Lennox (1953). In their sample, 5.4 % of candidates who were refused admission to the Navy on psychiatric grounds had paroxysmal EEG abnormalities, while only 2.2 % who were admitted and completed the training had paroxysmal abnormalities.

A number of additional factors that contribute to the diminished value of currently existing norms also emerged from our search (specifically, small sample sizes in a number of studies, lack of established criteria for EEG normality, and disagreement among electroencephalographers regarding the significance of the so-called controversial waveforms).

Based on the above findings, we conclude that the boundaries for normal sEEG are not well defined for the purposes of neuropsychiatric clinical or research endeavors. In order to be able to better define and study sEEG abnormalities in neuropsychiatric populations, well-designed normative studies are needed. Specifically, future studies should not rely on a single normal routine EEG to conclude lack of abnormalities. Similarly, the value of securing sleep tracings cannot be overemphasized.

A major role of EEG is to reduce the heterogeneity of research studies (e.g., depression with or without localized abnormalities, aggression with or without spikes). In Table 2.1, we have delineated what we consider adequate factors to be taken into consideration for the inclusion of a subject as normal in a study. Obviously, different types of studies will require different exclusion criteria. For example, studies attempting to develop normative databases or criteria for general use should observe the most stringent criteria. If a person or a group then deviates from such norms, the cause or causes of the deviations can then be investigated in subsequent studies specifically designed to isolate specific possible contributing

factors. On the other hand, studies comparing specific patient populations to normal comparison groups may wish to allow some of the factors (e.g., history of drug abuse or head injury) based on study design or be more stringent (e.g., studies examining genetics of an EEG pattern may extend the family history exclusion beyond first-degree relatives).

Blanc et al. (1964), highlighted the problem of cross-sectional studies. Via case examples, they pointed out that EEGs may change its characteristics at different time points. They related these changes mainly to change in psychiatric status. Additionally, Chamberlain and Russell (1952) pointed out that first-degree relatives (particularly siblings) of schizophrenia patients may have higher prevalence of EEG abnormalities. This finding suggests that family history of Axis-I disorders (at least in first-degree relatives) should be an additional exclusion criterion for normative studies.

The above review indicates that the high prevalence of abnormal EEGs in normal populations, ranging from 5 to 20 %, is based on inadequate inclusion and exclusion criteria for healthy comparison subjects. We conclude that the boundaries for EEG normality are poorly defined as they currently stand and are invalid for drawing any conclusions regarding prevalence or significance of EEG abnormalities in psychiatric populations. The EEGs of large samples of well-characterized healthy individuals meeting the criteria specified in Table 2.1 need to be examined in order to provide more clearly defined boundaries of normality and to establish more uniform criteria for abnormality. While all efforts were made to obtain all published papers and book chapters addressing the development of normative EEG criteria, it is unavoidable that a number of such publications were not securable (most of this literature dates back 40–70 years). Similarly, it was not possible to contact the individual investigators to verify normality criteria used (for the same reason). Nonetheless, the data presented above strongly suggest the need for new research to help define the normal boundaries of the unquantified EEG.

Supported Findings

- (1) The exact boundaries of normality of the sEEGs are currently not well defined for the purposes of psychiatric EEG research.
- (2) There are no normative studies in healthy subjects with repeated testing over time.

Open Research Questions

- (1) What is an adequate EEG work-up in order to determine normality or deviations?
- (2) What are the boundaries of EEGs obtained from well-characterized healthy children, adults, and elderly individuals?

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