

Insights from a very large EEG+Eyetracking dataset

Master Thesis Proposal

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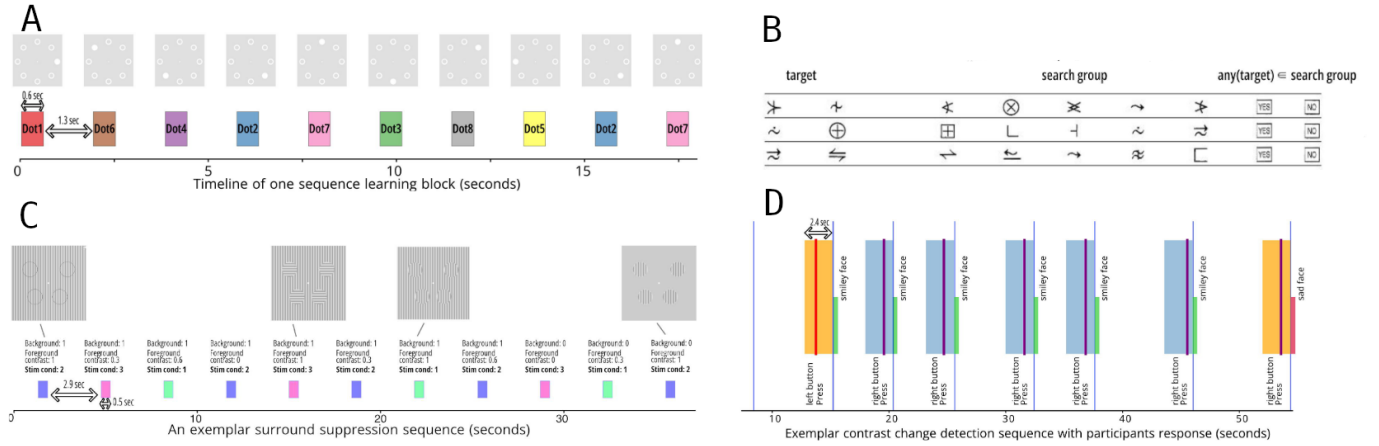


Fig. 1: Exemplar runs of paradigms that were performed for the Healthy Brain Network (HBN) dataset. Images are modified from [1]. Each paradigm is described in detail in 1

Abstract—Electroencephalography (EEG) offers an accessible and non-invasive way to record and thus study the brain and its reactions to various stimuli [2]. The Healthy Brain Network (HBN) dataset contains EEG and Eye-Tracking (ET) data of over 4000 subjects (ages 5-21) with diverse health conditions [3]. The HBN-EEG dataset is an effort to curate and convert the EEG of this dataset into the standardized Brain Imaging Data Structure (BIDS) format [1]. In this thesis, the HBN-EEG dataset will be firstly augmented with the ET data, which is still a work-in-progress of the HBN-EEG project. Afterward, the central analysis will attempt to determine whether the response of the brain to eye movements changes as a person ages or varies in health. Further reaching analyses may also take additional variables into account, such as the motifs that were looked at. As a stretch goal, the HBN will be utilized to verify or challenge previous findings of previous smaller-scale studies. The resulting software package will be primarily based on Unfold.jl and EYE-EEG.

1 INTRODUCTION

Electroencephalography (EEG) is one of the oldest, tried and tested methods to measure brain activity, having recently turned 100 years old [2]. It allows recording the electrical activity of the brain in a non-invasive (unlike Electrocochography) and accessible manner with relatively cheap setup (unlike e.g. MEG), while also maintaining high temporal resolution

(unlike e.g. fMRI) [4]. The main difficulty in interpreting EEG data lies in distinguishing true neural signals from a high level of background noise and artifacts, which is even further complicated by the variability in brain responses across different individuals [2] [5]. The methods to achieve this goal are subject to rapid ongoing development, with recent trends including the exploration of ever-growing datasets as well as the integration of artificial intelligence techniques into analysis pipelines. Both have shown promising results in addressing the aforementioned challenges [6] [7].

1.1 Healthy Brain Network

The Healthy Brain Network (HBN) is an initiative by the Child Mind Institute with the goal being ”to collect data from and provide diagnostic consultations to thousands of children and adolescents” [8]. As part of this effort, one subset of their collected and publicly released data contains the EEG (128 channels at 500 Hz), ET (Eye position and pupil dilation at 120 Hz) and behavioral data of more than 4000 subjects (ages 5-21), making it one of the largest research-grade, coherent EEG datasets available [3] [1]. They have also highlighted the importance and effectiveness of analyzing such large-scale EEG datasets for robust scientific results, naming this as part

of their motivation [3]. Numerous studies have already been conducted using the HBN EEG data [9] [10] [11] [12], but only few make use of the available ET data [13] [14], one reason possibly being the lack of BIDS integration.

The HBN dataset itself encompasses six different paradigms that each of the subjects were tested on (with exceptions). Three of the tasks were active (i.e. required participant interaction) and three were passive. Since these tasks are the foundation of our analyses, each paradigm is described in closer detail here:

1.11 Contrast Change (Figure 1D): Two circular overlapping gratings (black and white striped patterns) are shown on a screen. One is flickering at 20 Hz and is tilted 45° to the left, the other one is flickering at 25 Hz and tilted 45° to the right. The subjects were asked to maintain fixation on the center of the gratings. At some point, the contrasts of the two gratings gradually (within 1.6s) go from each being 50% to being of 0% and 100% contrast respectively, after which they go back to normal within 0.8s. The participants had to monitor which of the two gratings is beginning to fade and press a corresponding button as soon as they can identify the correct side. Feedback is given by flashing a sad or happy face.

1.12 Sequence Learning: A random visual stimulus representing a number between 1-8 (Figure 1A) is flashed on a screen and immediately fades out within 0.2s. After a 1.3s pause this process repeats, resulting in a 10-item sequence (8 items for ages 8 and below). Again, the subjects were asked to maintain fixation on the center of the visual stimuli. The sequence is then recalled (with indefinite time limit and without feedback) using a computer mouse. This "Observe → Recall" cycle is repeated five times with the exact same sequence.

1.13 Symbol Search: Participants are shown 15 rows of geometric symbols (Figure 1B). Each row contains two target symbols and five search symbols. For each row, the participant must decide if either of the target symbols is present in the search group and indicate their choice by clicking a "yes" or "no" checkbox with a computer mouse. When done, the participants clicked a "next page" button to view the next group of rows. The task has a 2 minute time limit to complete as many rows as possible. In a brief training session participants received feedback on their performance, but not in the main task.

1.14 Resting-State: Participants focus on a fixation cross shown on a screen. They alternate between keeping their eyes open for 20 seconds and keeping them closed for 40 seconds, following auditory instructions. This cycle of eyes-open and eyes-closed is repeated five times.

1.15 Surround Suppression: Participants focus on a fixation cross shown on a screen. For each trial, the participant is shown a full-screen "surround" grating that

has four circular "foreground" gratings overlaid within (Figure 1C). Each trial randomizes the contrast of the foreground (0%, 30%, 60%, or 100%), the surround (0% or 100%), and the surround orientation (vertical or horizontal). Each trial takes 2.4 seconds and the experiment took place in two blocks of 64 trials each.

1.16 Naturalistic Viewing: Participants are asked to view and enjoy 4 video clips: "E-How video: How to Improve at Simple Arithmetic: Lessons in Math" (1:40), "MIT K-12: 'Fun with Fractals'" (4:40), Diary of a Wimpy Kid Trailer (2:00) and "Despicable Me" (2:50).

1.2 Unfold toolbox

The Unfold toolbox is a family of tools relating to EEG processing and analysis. It has been used successfully in analyzing fixation-related potentials (FRPs) from combined eye-tracking/EEG experiments similar to e.g. the naturalistic viewing paradigm of the HBN dataset [15]. This thesis will use the Unfold toolbox, in particular its (non)linear deconvolution capabilities for its main analysis.

1.3 Brain Imaging Data Structure

The Brain Imaging Data Structure (BIDS) is a specification for formatting and describing neuroimaging experiments in a unified and standardized way, mitigating the necessity of tailoring tools to a specific format. Tools such as Unfold.jl as well as the MNE-BIDS-Pipeline already fully support BIDS. The standard is constantly evolving, with an integration of an Eye-Tracking data specification currently in the works [16]. BIDS also supports HED (Hierarchical Event Descriptors) annotations which allow detailed, machine-readable descriptions of the experimental events, making it easier to perform automated analyses. Part of the HBN data such as the imaging data (MRI) is already in BIDS format, but most of the dataset is in currently in the process of being converted over 2.

2 RELATED WORK

2.1 An open resource for transdiagnostic research in pediatric mental health and learning disorders [3]

Alexander et al. produced the original paper pertaining to the HBN dataset. It provides a detailed insight into the project rationale and execution, as well as descriptions on which types of quality assessment measures were taken, e.g. the usage of EEGLAB's `pop_rejchan.m` for EEG channel rejection. This allows for a clear understanding of the actual data that is being worked with in the thesis.

2.2 A resource for assessing information processing in the developing brain using EEG and eye tracking [17]

This paper developed and explored the paradigms before they were then later deployed in large-scale for the HBN dataset. Each paradigm together with their intended purpose is described in detail, together with plots of some fundamental

analyses. The exact processing steps and quality assurance checks of the EEG and ET data is given, such as the usage of the MATLAB toolbox "automagic". All of this information is crucial to know, so it can be understood which analyses make sense to perform on the dataset.

2.3 HBN-EEG: The FAIR implementation of the Healthy Brain Network (HBN) electroencephalography dataset [1]

HBN-EEG is an effort to convert the HBN dataset to BIDS, which the authors describe as "starting point in providing a large, transparent dataset in a form that will assist researchers in easily identifying the information they need to pursue their research [...]". The EEG data from all 11 Releases of the HBN dataset has already been converted. Each subject run was labeled with either "Available", "Caution" or "Unavailable", corresponding to usable runs, runs that need cleaning up (failed at least one consistency test), and runs that failed to convert. A total of 525 subjects did not have a single usable run, resulting in "available" data from 3613 subjects. Some further results include:

- Some behavioral data has already been integrated and synchronized as events.
- Events have been annotated using HED (Hierarchical Event Descriptors).
- Phenotypic data has been summarized for easier analysis (P-factor, Attention, Internalizing, Externalizing).
- An open-source automated electrode localization toolbox is being developed for digitizing electrode positions of the 2270 HBN participants who have had their electrode locations scanned

Finally, while the full integration of the Eye-Tracking data is currently bottlenecked by the unfinished Eyetracking-BIDS specifications, the tools to perform the conversion to BIDS are currently in beta [18] and will be used in this thesis.

2.4 Automated EEG mega-analysis II: Cognitive aspects of event related features [6]

This paper further highlights the importance of using HED tags for annotation and temporal overlap regression modeling in large datasets. Furthermore, they use t-SNE (t-distributed stochastic neighbor embedding) to visualize whether EEG patterns that are in similar HED categories cluster together (e.g. whether EEG responses of correct feedback can be clearly clustered separately from negative feedback EEG responses). This could be a further exploratory analysis for the HBN dataset as well, even though the dataset is not as diverse as in this paper.

2.5 Regression-based analysis of combined EEG and eye-tracking data: Theory and applications [15]

The authors demonstrate a state-of-the-art methodology in overcoming the difficulties posed by the analysis of FRPs (especially in free-viewing conditions), which they have broken down to

- 1) the synchronization of data streams
- 2) the removal of ocular artifacts

- 3) the condition-specific temporal overlap between the brain responses evoked by consecutive fixations
- 4) the fact that numerous low-level stimulus and saccade properties also influence the postsaccadic neural responses

The task is further complicated by the fact that:

- target stimuli are often fixated on for longer timespans than non-targets, creating a spurious effect between conditions
- a similar bias occurs when the conditions have different average saccade amplitudes (e.g. target conditions consistently require a bigger shift in gaze)
- many paradigms flash in a visual stimulus at the beginning, causing a long lasting potential that distorts the following signals (stimulus-onset ERP)
- factors like the saccade amplitude have a nonlinear effect on the FRP
- for active tasks, movements like button presses will further distort the signal
- involuntary miniature saccades are produced even when subjects are asked to fixate on one point

The authors argue that a framework combining linear deconvolution with nonlinear regression can effectively address and mitigate most of these issues. By modeling the continuous EEG signal as a sum of overlapping individual brain responses, it is possible to account for confounding variables by making sure they are part of the regression formulae. For example:

ERP \sim 1 addresses the stimulus onsets

FRP \sim 1 + spl(fixation_position_x, 5) + spl(fixation_position_y, 5) + spl(sacc_amplitude, 5) + circspl(sacc_angle, 5, 0, 360) addresses

(among others) the nonlinear effect of saccade amplitude and the effect of saccade direction.

The effectiveness is demonstrated in three different experiments: Face perception, scene viewing, and reading. Synchronization was done using EYE-EEG [19] and for the deconvolution and regression, the Unfold toolbox [20] was used.

Each of the three experiments highlights a different use case or strength of the approach in combatting the issues mentioned above:

- Face perception: Subjects were instructed to classify the emotional expression of a face using a button press. Despite being asked to fixate on a single point, 99% of trials had subjects perform miniature saccades (microsaccades or small exploratory saccades). The deconvolution model was able to isolate the (brain and muscle) potentials caused by these miniature saccades, and in turn was able to lead to a cleaner ERP
- Scene viewing: Subjects searched for a small, but constantly growing, gray dot inside various grayscale photographs. When they found it, they would press a button.

This free-viewing experiment contained multiple nonlinear confounding variables, as well as stimulus onsets and button presses. Still, the deconvolution model managed to successfully separate these effects.

- Natural reading: Subjects read two sentences with one containing a "target word". In some trials, this target word was static. In other trials, the target word was instead a random but visually similar string, and was only replaced with the correct target word during a saccade just before reading the target word. This manipulation causes shorter fixations on words with valid preview. The challenge is to determine whether there was an actual neural difference in the two conditions (valid or invalid preview), or whether differences in the signal are just caused by difference in fixation length. Using their framework, it could be confirmed that there is an actual neural difference between the two conditions.

In their analyses of each paradigm, the authors employ a two-stage statistical approach:

- 1) Individual Level: The deconvolution regression model is computed separately for each participant using `Unfold`. This results in the regression coefficients (betas, as noted by the β vector in the regression model), which can be understood as the separation of the various confounding factors and the cleaned FRP waveforms. These waveforms can now be treated like a regular subject-level ERP.
- 2) The betas are compared in within-subjects analysis to test for effects across all participants. The specific test that is used to identify significant effects in the EEG data is threshold-free cluster-enhancement (TFCE), and it has the advantage of controlling for multiple comparisons across all time points and electrode channels.

This paper will be a major guideline for the saccade amplitude analysis in this thesis, whose structure will be outlined in the following.

3 COURSE OF THE THESIS

Month 1-2

Due to the large nature of the dataset, a first step that allows for getting a feeling of the dataset could be to create a simple grand average ERP of the most recent HBN Release 11. This would also allow getting familiar with the `bwUniCluster` or `VISUS` cluster.

The analysis will only be focused on the two free-viewing paradigms present in HBN – symbol search and naturalistic viewing. These are the only paradigms where subjects were not instructed to fixate on a point. Going forward, only this subset of the HBN paradigms will be considered (e.g. when synchronizing it to the EEG). An analysis of miniature saccades as it is done in [15] is not possible, as the Eye-Tracker used in the HBN paradigms is unsuitable for reliable capturing of miniature saccades. This is in large

due to its low sampling rate of 120 Hz and gaze position accuracy of 0.5° , which are both of insufficient resolution for these kinds of saccades.

The free-viewing paradigms of the HBN will feature similar difficulties to those showcased in [15]. For example, in the symbol search there will be a spurious effect between conditions, as the target symbols will be fixated on for longer timespans.

Before any analyses can be done, the ET data has to be first curated, then synchronized to the EEG dataset and exported in a BIDS compliant format. A potential tool for synchronization includes the EYE-EEG toolbox [19], which has already been used in combination with `Unfold.jl` and is compatible with the Eye-Tracking data format present in the HBN dataset. EYE-EEG also has numerous functions for quality checking, like `checksync.m` for synchronization quality, or `rej_eyecontin.m` for rejecting segments with too many out-of-range gaze values (e.g. caused by blinks) — these would have to be set to 0 in the time-expanded design matrix. Potentially, a custom script by Prof. Ehinger will also assist in ET synchronization. The quality of the accompanying EEG also needs to be ensured. In [15] this is done by checking extreme peak-to-peak voltage differences in a shifting window. It will have to be tested whether this is also suitable for the HBN dataset. Additionally, the 5-point calibration check performed before each paradigm (look into center and four corners of the display) can be used to verify the quality of the ET data. If it seems appropriate, a visual summary of overall ET quality of the HBN dataset could be created.

For the BIDS export, EEG-BIDS [18] features a beta implementation for converting the `.set` output of EYE-EEG into a BIDS compliant format. In case there are difficulties in any of these steps, e.g. in curating suitable ET data, there is the option of a consultation session with Seyed Shirazi, who is the corresponding author of the HBN-EEG dataset and a contributor of EEG-BIDS.

Before the main analyses are performed, the two key papers relating to the saccade amplitude effect [15] [21], as well as other related papers (e.g. [22]) are summarized in a "Related Work" section. The purpose is to get a sense of which methodologies have been used in the past for similar analyses or for the same dataset, and why. Some focus points might include the eye-tracker-guided method [23] or Multiple-Source Eye Correction [24] mentioned in [15].

Month 3-5

Once the BIDS dataset is ready, it can be imported into `UnfoldBIDS.jl` [25], which seamlessly integrates with `Unfold.jl` (the updated version of the `Unfold` toolbox used in [15]). Some of the previously researched preprocessing steps can be applied directly using MNE. This will include

bandpass filtering and some type of ICA [5] (such as Infomax which was used in [15], or AMICA). It may be necessary to use different preprocessing steps for the two paradigms.

Finally, it will be checked whether deconvolution is actually suitable and effective for the dataset we have now. One precondition for deconvolution to work is sufficient variation in fixation duration, saccade amplitude and event sequences (saccade rate). These distributions will be plotted as histograms, to confirm that this necessary variation is given.

With filtered and cleaned EEG data, Unfold.jl can start fitting a model. First, the relevant articles in the Unfold docs will be read [26], and fitting parameters will be prototyped using a subset of the full HBN data. The local time (τ) window parameter (-400 to 800 ms) will be taken from [15].

Some sanity checks to perform during this phase may include

- Creating an `erpimage` plot as described in [15], with single trials sorted by the duration of the current fixation. Here it can be checked whether the brain response from the subsequent fixation actually starts earlier for trials with shorter fixations
- Use `erpimage` to plot the residuals (EEG activity not covered by the model) like in [15]. This can highlight whether saccade-related activity from neighboring fixations is properly filtered
- Comparing the un-corrected, raw FRP with the deconvolved rERP output by Unfold as intercept should show how the baseline becomes cleaner/more accurate.
- Checking whether the timings of the visually evoked lambda response of saccades matches the 110 ms after saccade onset as given in [15]
- Verifying that saccade amplitude actually has a nonlinear effect on the lambda response. There should be a graph similar to [15] Figure 5A, where the effect of saccade amplitude on the EEG potential is not linear

Once the model shows satisfactory results, the deconvolved FRPs will be used to compare neural responses between subjects of different age and health status. This analysis will likely be done with Threshold Free Cluster Enhancement (TFCE), as in [15]. The algorithm is implemented in MNE [27]. By avoiding arbitrary cutoffs and thresholds, it should be possible to identify significant effects more reliably, if there are any. All these analyses will be documented visually where possible, and the full analysis and pipeline will result in a standalone documented program package.

Depending on the time left over at this point, there are some stretch goals that could be aimed for:

- Experiment with different regression formulas. As mentioned in [15], saccade direction, the fixation location on the screen, local luminance and contrast may all impact the signal significantly

- In the HBN-EEG paper, the authors suggest some further improvements that could be made to the HBN-BIDS dataset other than the integration of ET data, for example the annotation of movies with detailed event sequences.
- After this, it would be easy to add a categorical variable `is_face()` to the regression model
- The ET data from the remaining paradigms could be curated and synchronized to their EEG
- The ICA algorithm could be fine-tuned to only specific segments of the EEG data for better performance [15]
- Besides age and health conditions, the performances for various paradigms could be used as a variable to compare under. For example, faster detection of contrasts in the contrast change paradigm could correlate with higher neural potentials for visual stimuli.
- Heatmaps of gaze positions could be interesting for all kinds of paradigms. For sequence learning it might also reveal some exploratory saccades similar to those observed in the face paradigm.
- Papers that have used datasets with the same paradigms as the HBN dataset, could be attempted to be challenged/verified by using a much larger sample size.
- As an ambitious goal, it could be compared how well AI techniques perform in the same analyses vs. the established methodology

Month 6

The last month will be used to finalize figures, writing, and the code with documentation. Ideally there will be some buffer room for revisions.

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