TECHNICAL COMMENTARY

EEG

NeuRA Discover. Conquer. Cure.

POST-TRAUMATIC STRESS DISORDER LIBRARY

Introduction

Electroencephalography (EEG) uses electrodes on the scalp to measure electrical activity from the brain. Quantitative spectral EEG investigates several waveforms, and so the activity can be measured, but EEG also gives rise to event related potentials (ERP), which measure the EEG activity directly evoked by a stimulus, often using cognitive or perceptual stimuli. P300, also referred to as P3, may be the ERP most suitable for the assessment of PTSD, given that it is well documented, and, with the appropriate stimulus paradigm used, can convey information about attention and working memory processes.

P300 refers to a spike in activity approximately 300ms following presentation of a target stimulus, which is alternated with standard stimuli to create an 'oddball' paradigm, which is most commonly auditory. In this paradigm, the subject must respond only to the infrequent target stimulus rather than the frequent standard stimulus. The amplitude of the P300 response is proportional to the amount of attentional resource devoted to the task and the degree of information processing required, while the latency is considered a measure of stimulus classification speed, unrelated to behavioural response time.

Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2010 that report results separately for people with PTSD. Reviews were identified by searching the databases MEDLINE, EMBASE, and PsycINFO. When multiple copies of review topics were found, only the most recent and comprehensive version was included. We prioritised reviews with pooled data for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis[1]. Reviews with less than 50% of items checked have been excluded from the library. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large or if there is a dose dependent response. We have also taken into account sample size and whether results are consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)[2]. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

Results

We found one systematic review that met our inclusion criteria[3].

- Moderate quality evidence found large increases in P3a (involuntary attention) amplitude with trauma-related distractors in people with PTSD compared to people without PTSD but with trauma exposure. Medium-sized effects showed P3b (voluntary attention) amplitude was also increased with trauma-related distractors in

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frontal and central regions, but not in parietal regions, in people with PTSD compared to people without PTSD but with trauma exposure.

- There were medium-sized reductions in P3b amplitude with neutral distractors in people with PTSD compared to healthy controls, and there were small reductions in P3wm (working memory) amplitude with neutral distractors in parietal, but not in frontal and central regions of people with PTSD compared to healthy controls.

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Johnson JD, Allana TN, Medlin MD, Harris EW, Karl A

Meta-analytic review of P3 components in posttraumatic stress disorder and their clinical utility

Clinical EEG and Neuroscience 2013; 44: 112-34

View review abstract online

Comparison	**P3 amplitude and latency in people with PTSD vs. controls (healthy, medicated with PTSD, or non-PTSD trauma exposed) to neutral, novel, emotional, and trauma-related distractors.**
Summary of evidence	**Moderate quality evidence (large samples for P3b only, mostly inconsistent, precise, direct) found large increases in P3a (involuntary attention) amplitude with trauma-related distractors in people with PTSD compared to people without PTSD but with trauma exposure. Medium-sized effects showed P3b (voluntary attention) amplitude was also increased with trauma-related distractors in frontal and central regions, but not in parietal regions, in people with PTSD compared to people without PTSD but with trauma exposure.** **There were medium-sized reductions in P3b amplitude with neutral distractors in people with PTSD compared to healthy controls, and there were small reductions in P3wm (working memory) amplitude with neutral distractors in parietal, but not in frontal and central regions of people with PTSD compared to healthy controls.**

P3a: involuntary attention

Large effects showed P3a amplitude was significantly increased with trauma-related distractors in people with PTSD compared to people without PTSD but with trauma exposure;

Frontal: 3 studies, N = 100, $r = 0.499$, 95%CI 0.330 to 0.637, $p < 0.001$, $I^2 = 0\%$

Central: 4 studies, N = 140, $r = 0.476$, 95%CI 0.228 to 0.666, $p < 0.001$, $I^2 = 62\%$

Parietal: 4 studies, N = 140, $r = 0.433$, 95%CI 0.142 to 0.655, $p < 0.001$, $I^2 = 70\%$

There were no significant differences between people with PTSD and people without PTSD but with trauma exposure in P3a amplitude to neutral or novel distractors.

There were no significant differences between people with PTSD and people without PTSD but with trauma exposure in P3a latency to neutral stimuli or trauma distractors (novel distractors were not assessed).

There were no significant differences between medicated and non-medicated PTSD patients.

P3b: voluntary attention

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Medium-sized effects showed P3b amplitude was significantly reduced with neutral distractors in people with PTSD compared to healthy controls; Frontal: 8 studies, N = 627, *r* = -0.244, 95%CI -0.394 to -0.080, *p* = 0.004, I^2 = 72% Central: 7 studies, N = 573, *r* = -0.397, 95%CI -0.635 to -0.090, *p* = 0.013, I^2 = 93% Parietal: 9 studies, N = 817, *r* = -0.213, 95%CI -0.213 to -0.323, *p* = 0.0003, I^2 = 62% There were no significant differences between people with PTSD and healthy controls in P3b latency to neutral stimuli (other distractors were not assessed). *Medium-sized effects showed P3b amplitude was significantly increased with trauma-related distractors in frontal and central regions, but not in parietal regions, in people with PTSD compared to people without PTSD but with trauma exposure;* Frontal: 3 studies, N = 100, *r* = 0.322, 95%CI 0.101 to 0.513, *p* = 0.005, I^2 = 20% Central: 4 studies, N = 140, *r* = 0.171, 95%CI 0.000 to 0.333, *p* = 0.51, I^2 = 0% Parietal: 4 studies, N = 140, *r* = 0.031, 95%CI -0.141 to 0.201, *p* = 0.726, I^2 = 0% There were no significant differences between people with PTSD and people without PTSD but with trauma exposure in P3b amplitude to neutral, novel, or emotional distractors. There were no significant differences between people with PTSD and people without PTSD but with trauma exposure in P3b latency to neutral, emotional, or trauma distractors (novel distractors were not assessed). There were no significant differences between medicated and non-medicated PTSD patients.
P3wm: working memory
Small effects showed P3wm amplitude was significantly reduced with neutral distractors in parietal, but not in frontal and central regions, of people with PTSD compared to healthy controls; Frontal: 3 studies, N = 238, *r* = -0.150, 95%CI -0.565 to 0.324, *p* = 0.542, I^2 = 89% Central: 3 studies, N = 238, *r* = -0.147, 95%CI -0.516 to 0.267, *p* = 0.491, I^2 = 85% Parietal: 4 studies, N = 408, *r* = -0.238, 95%CI -0.328 to -0.143, *p* < 0.001, I^2 = 0% There were no significant differences between people with PTSD and healthy controls in P3wm latency to neutral stimuli (other distractors were not assessed). There were no significant differences between medicated and non-medicated PTSD patients.

Consistency in results‡	Consistent for P3b trauma exposed controls analyses and working memory parietal region only.
Precision in results§	Precise
Directness of results‖	Direct

Explanation of acronyms

CI = confidence interval, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), N = number of participants, *p* = statistical probability of obtaining that result, *r* = correlation coefficient, vs. = versus

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Explanation of technical terms

* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias – selective reporting of results; publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small[4].

† Different effect measures are reported by different reviews.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. Less than 0.4 represents a small effect, around 0.5 a medium effect, and over 0.8 represents a large effect[4].

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or < 0.2[5]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

Correlation coefficients (eg, r) indicate the strength of association or relationship

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between variables. They can provide an indirect indication of prediction, but do not confirm causality due to possible and often unforseen confounding variables. An r of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised (*b*) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent considerable heterogeneity and over this is considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula[4];

$$I^2 = \left(\frac{Q - df}{Q}\right) \times 100\%$$

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, these criteria should be relaxed[6].

‖ Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and/or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available and is therefore inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.

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