

P200 Event-related potential

Introduction

The P200 wave is an event-related brain potential (ERP) measured using electroencephalography (EEG). P200 refers to a spike in activity approximately 150 to 250ms following presentation of a target stimulus that is most commonly auditory. The P200's latency and amplitude vary with aspects of selective attention or stimulus encoding. Latency is considered a measure of stimulus classification speed, and amplitude is proportional to the amount of attentional resources devoted to the task and the degree of information processing required. Amplitude and latency may be measured using tasks using 'standard' and 'oddball' stimuli, where the subject is asked to react only to 'oddball' target stimuli that are hidden as rare occurrences amongst a series of more common, 'standard' stimuli.

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 2000 that report results separately for people with a diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder or first episode schizophrenia. Reviews were identified by searching the databases MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO and the Cochrane library. Hand searching reference lists of identified reviews was also conducted. Reviews with pooled data are prioritised 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-analysis¹). Reviews rated as having less than 50% of items checked have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no

flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. 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 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, there is a dose dependent response or if results are reasonably 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 criteria³.

- Moderate to high quality evidence finds a small reduction in P200 amplitude and latency at the Cz midline electrode during standard stimuli conditions, and a small to medium-sized increase in amplitude and latency at the Fz, Cz and Pz electrodes during oddball stimuli conditions in patients compared to controls.

Ferreira-Santos F, Silveira C, Almeida PR, Palha A, Barbosa F, Marques-Teixeira J

The auditory P200 is both increased and reduced in schizophrenia? A meta-analytic dissociation of the effect for standard and target stimuli in the oddball task

Clinical Neurophysiology 2012; 123: 1300-1308

[View review abstract online](#)

Comparison	Comparison of P200 ERP amplitude and latency in people with schizophrenia vs. healthy controls.
Summary of evidence	Moderate to high quality evidence (large samples, mostly inconsistent, mostly precise, direct) suggests a small reduction in P200 amplitude and latency at the Cz midline electrode during standard stimuli conditions, and a small to medium increase in amplitude and latency at the Fz, Cz and Pz electrodes during oddball stimuli conditions.

P200 activity

Standard stimuli

Small effect size suggests significantly reduced amplitude at Cz in people with schizophrenia;

Fz: N = 502, 5 studies, $d = -0.09$, 95%CI -0.26 to 0.08, $p > 0.05$, (Q = 0.03, $p = 0.008$)

Cz: N = 1238, 15 studies, $d = -0.36$, 95%CI -0.52 to -0.20, $p < 0.05$, (Q = 0.09, $p < 0.001$)

Pz: N = 502, 5 studies, $d = -0.22$, 95%CI -0.43 to 0.00, $p = 0.05$, (Q = 0.05, $p < 0.001$)

Small effect size suggests significantly reduced latency at Cz in people with schizophrenia;

Fz: N = 282, 3 studies, $d = 0.05$, 95%CI -0.43 to 0.54, $p > 0.05$, (Q = 0.17, $p < 0.001$)

Cz: N = 998, 13 studies, $d = -0.32$, 95%CI -0.54 to -0.10, $p < 0.05$, (Q = 0.14, $p < 0.001$)

Pz: N = 282, 3 studies, $d = -0.16$, 95%CI -0.80 to 0.47, $p > 0.05$, (Q = 0.30, $p < 0.001$)

Oddball stimuli

Small to medium-sized effect suggests significantly increased amplitude at Fz, Cz and PZ in people with schizophrenia;

Fz: N = 465, 5 studies, $d = 0.34$, 95%CI 0.06 to 0.62, $p < 0.05$, (Q = 0.09, $p < 0.001$)

Cz: N = 653, 9 studies, $d = 0.48$, 95%CI 0.16 to 0.81, $p < 0.05$, (Q = 0.23, $p < 0.001$)

Pz: N = 465, 5 studies, $d = 0.46$, 95%CI 0.13 to 0.79, $p < 0.05$, (Q = 0.13, $p < 0.001$)

Small to medium-sized effect suggests significantly increased latency at Fz, Cz and PZ in people with schizophrenia;

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Fz: N = 385, 4 studies, $d = 0.27$, 95%CI 0.11 to 0.42, $p < 0.05$, ($Q = 0.02$, $p = 0.070$)

Cz: N = 516, 7 studies, $d = 0.42$, 95%CI 0.23 to 0.62, $p < 0.05$, ($Q = 0.05$, $p < 0.001$)

Pz: N = 385, 4 studies, $d = 0.45$, 95%CI 0.35 to 0.55, $p < 0.05$, ($Q = 0.00$, $p = 0.394$)

Meta-regression identified that the greater the male percentage in studies, the larger the effect size for target amplitude ($r = 0.674$, $p = 0.047$). Increased chlorpromazine equivalent dosage was related to a decrease in effect size for standard latency ($r = -0.765$, $p = 0.027$).

Authors also indicate evidence of publication bias for Fz and Pz latency comparisons; Egger test $p < 0.01$.

Consistency in results[†]	Inconsistent for all except latency at Fz and Pz with oddball stimuli.
Precision in results[§]	Precise for all except latency at Pz with standard stimuli.
Directness of results	Direct

Explanation of acronyms

CI = Confidence Interval, CZ = central electrode, d = Cohen's d and g = Hedges' g = standardized mean differences (see below for interpretation of effect sizes), EEG = electroencephalogram, ERP = event-related potential, FZ = frontal lobe electrode, N = number of participants, p = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), PZ = parietal lobe electrode, Q = Q statistic (chi-square) for the test of heterogeneity in results across studies, Q_b = between group heterogeneity, Q_w = within group heterogeneity, SE = standard error, T3/ TCP1= Left temporal lobe electrodes, T4/TCP2 = Right temporal lobe electrodes, 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 small⁴.

† Different effect measures are reported by different reviews.

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) which 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. 0.2 represents a small

effect, 0.5 a medium effect, and 0.8 and over represents a large treatment effect⁴.

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).

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, an 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. An 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. InOR stands for logarithmic OR where a InOR 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 between variables. They are an indication of prediction, but do not confirm causality due to possible and often unforeseen 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 dependent variable, statistically controlling for the other

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independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

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.

‡ Inconsistency refers to differing estimates of treatment 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 substantial heterogeneity and 75% to 100%: considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula;

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

§ 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, this criteria should be relaxed⁶.

|| 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, which 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 so is 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.

References

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