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ERP Indices of Performance Monitoring and Feedback Processing in Psychosis: A Meta-Analysis

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Abstract

Background: Although individuals with, or at risk for, psychotic disorders often show difficulties with performance monitoring and feedback processing, findings from studies using event-related potentials (ERPs) to index these processes are not consistent. This meta-analytic review focused on studies of two different indexes of performance monitoring, the early error-related negativity (ERN; n = 25) and the later error positivity (Pe; n = 17), and one index of feedback processing, the feedback negativity (FN; n = 6).

Methods: We evaluated whether individuals (1) with psychotic disorders, or (2) at heightened risk for these disorders differ from healthy controls in available studies of the ERN, Pe, and FN.

Results: There was a significant, large ERN reduction in those with psychosis ($g = -.96$) compared to controls, and a significant, moderate ERN reduction in those at-risk ($g = -.48$). In contrast, there were uniformly non-significant, small between-group differences for Pe and FN (gs ≤ l.16l).

Conclusions: The results reveal a differential pattern of impairment in psychosis. Early performance monitoring (ERN) impairments are substantial among those with psychotic disorders in general and may be a useful vulnerability indicator for these disorders. However, later performance monitoring (Pe) and basic feedback processing (FN) appear to be relatively spared in psychosis.

Keywords

ERN; Pe; FN; error-related negativity; error positivity; feedback-related negativity

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1. Introduction

Impairments in daily life functioning, including diminished engagement in productive and pleasurable activities, are hallmarks of psychotic disorders (Barch and Dowd, 2010; Blanchard et al., 2011). These impairments are directly linked to cognitive deficits, which have been extensively documented in psychosis and psychosis-risk. The ability to accurately monitor one's performance, and integrate internal (e.g., self-generated comparisons of whether performed actions match their intended outcomes) and external performance feedback (e.g., externally-generated information indicating favorable vs. unfavorable outcomes), are critical aspects of cognition, reward processing, and learning as they guide adaptive decision-making and productive behavior (Falkenstein et al., 1990; Gehring et al., 1993; Holroyd and Coles, 2002). A number of investigators have used event-related potentials (ERPs) to assess whether distinct aspects of performance monitoring and feedback processing are impacted in those with schizophrenia, with psychotic disorders more broadly, or at heightened risk for developing one of these disorders. Most investigations have focused on two ERP components that measure performance monitoring, the error-related negativity (ERN) and error positivity (Pe), and one that measures feedback processing, the feedback negativity (FN). Study findings have varied considerably across these three components, making it hard to draw conclusions. To date, there has not been an integrative quantitative review of this literature.

The purpose of this meta-analytic review is to determine whether individuals with psychotic disorders (including schizophrenia, schizoaffective disorder, delusional disorder, schizophreniform disorder, schizophrenia spectrum disorders otherwise specified, and mood disorders with psychotic features) or at heightened risk for these psychotic disorders (either genetic risk, clinical high-risk, or psychometric high-risk samples) differ from healthy controls on these three ERP components. Additionally, we will evaluate potential moderators of these components, where applicable. This information can shed light on how performance monitoring and feedback processing is impacted in psychosis-related psychopathology.

1.1. ERPs associated with performance monitoring: ERN and Pe

The ERN (also known as the Ne) is a response-locked ERP that has been associated with performance monitoring of actions and detecting errors (Falkenstein et al., 1990; Gehring et al., 1993; Simons, 2010). It is generally assessed with choice reaction time tasks, such as the flanker or go/no go paradigms. The onset of the ERN occurs shortly before or at the moment of an erroneous response and peaks approximately 100 ms later at midline frontocentral scalp locations (Gehring et al., 2012). Initial evidence from source localization, functional magnetic resonance imaging, and single unit recording studies suggests that the ERN may be generated within the dorsal region of the anterior cingulate cortex (ACC) (e.g., Debener et al., 2005; Holroyd and Coles, 2002), a structure centrally involved in performance monitoring and error detection (Taylor et al., 2007).

In psychosis research, the ERN has received the most attention of the three ERP components considered in this review. Across 22 separate studies of individuals with schizophrenia, the vast majority have reported reduced ERN compared to healthy controls. The overall magnitude of the reduction is unclear and the potential impact of methodological differences

across studies (e.g., sample characteristics, type of paradigm) has not been evaluated. A smaller number of studies have examined the ERN in individuals with more broadly defined psychotic disorders (n = 4) or at-risk groups (n = 7). Although ERN reductions are also typically reported in these samples, the overall magnitude of the reductions has not been evaluated.

The ERN is typically followed by the Pe component. The Pe peaks in the centroparietal region between 200 and 400 ms after an erroneous response. Despite some debate (Gehring et al., 2012; e.g., Van Veen and Carter, 2002), the Pe is typically thought to index error awareness or the ability to detect errors (Endrass et al., 2007; Nieuwenhuis et al., 2001), and it has been reported that the Pe may be generated by the rostral ACC (Endrass et al., 2007).

Compared to the ERN, fewer studies have examined the Pe in those with schizophrenia (n = 13), those with broadly defined psychotic disorders (n = 3), or at-risk groups (n = 7). In contrast to the consistent reports of reduced ERN, studies of the Pe have been decidedly mixed, finding either relatively small reductions or no differences between these groups and healthy controls. It is unclear whether differences in methodologies or clinical characteristics may account for inconsistencies across studies.

1.2. ERP associated with external feedback processing: FN

The FN is typically assessed using simple gambling or feedback-based learning paradigms (Simons, 2010) and, in contrast to the ERN and Pe, is elicited by externally provided feedback about positive versus negative outcomes. The feedback stimulus-locked FN peaks between 250 and 300 ms after feedback onset and is maximal over the frontocentral region. In addition, it is relatively more negative-going after unfavorable versus favorable feedback (e.g., a monetary loss compared to a monetary gain). The FN has historically been viewed as tracking the occurrence of unfavorable outcomes (negative reward prediction errors). Some, however, have argued that the FN tracks the occurrence of favorable outcomes (positive reward prediction error), resulting in a reward-related positivity (i.e., “Reward Positivity”) that is absent or suppressed following an unfavorable outcome (for a review, see Proudfit, 2015). This is supported by tentative evidence that the FN originates from the striatum (e.g., Carlson et al., 2011; Foti et al., 2011). Others propose the FN reflects an unsigned salience/surprise signal or that multiple processes (e.g., positive reward prediction error and unsigned salience signal) may contribute to the FN (Hauser et al., 2014; Cavanaugh & Frank, 2014; Sambrook & Goslin, 2016). For the sake of consistency with previous research in this area, the current review will refer to this component as the "FN".

Compared to the ERN and Pe, relatively few studies investigated the FN in those with schizophrenia (n = 4), broadly defined psychosis (n = 1) or at risk for psychotic disorders (n = 1). Almost all reported intact FN in schizophrenia across these groups. However, the sample sizes were relatively small, and it is unclear whether reliable differences between these groups and healthy controls are detectable.

1.3. The current study

Overall, findings from the ERP literature regarding performance monitoring and feedback processing in psychotic disorders and at-risk populations are mixed. To clarify these

findings, we employed meta-analysis, a powerful statistical technique that can identify trends across relatively small studies. For the ERN and Pe, the goals of the review were to: (1) determine whether individuals with psychotic disorders or at-risk groups show reliable impairments compared to non-psychiatric controls and to quantify the corresponding effect sizes, and (2) evaluate potential methodological (type of paradigm, ERP quantification methods) and patient characteristic (diagnosis, patient status, phase of illness) moderators of these components. Given the smaller database for the FN, we focused on determining whether individuals with psychosis show a reliable impairment compared to healthy controls and quantifying the effect size.

2. Materials and method

2.1. Eligibility Criteria for Meta-Analysis

The current meta-analysis followed PRISMA guidelines (Moher et al., 2009) for transparent and replicable methods and findings. Please see the Supplementary Table 1 for the PRISMA checklist.

Inclusion criteria for the current analyses were as follows: 1) the study included a sample of either 1A) all patients meeting DSM-III-R (APA, 1987) or DSM-IV (APA, 2000) criteria for schizophrenia or schizoaffective disorder, 1B) patients with any DSM disorder also reporting psychotic symptoms (e.g., schizophrenia, major depressive disorder with psychotic features) or 1C) individuals "at risk" for schizophrenia-spectrum disorders identified by either a structured clinical interview (clinical risk), a family history of a 1st degree family member with schizophrenia/schizoaffective disorder (genetic risk), or standardized questionnaire measures (psychometrically-defined risk); 2) a nonpsychiatric control sample (i.e., sample with no history of psychopathology determined by study-specific methods/criteria); 3) the study task required overt participant responses and is generally recognized as a reliable elicitor of ERN, Pe, or FN ERPs; 4) amplitude of the ERN, Pe, or FN ERP waveform was reported for patients/at risk and control subjects; 5) statistics were reported that allowed for calculation of effect size (standardized mean difference or Hedges' *g*) of ERN/Pe/FN ERP waveform amplitude; and 6) study findings were reported in an English language, peer-reviewed journal article. Studies were excluded if they did not meet inclusion criteria. There were no other exclusion criteria. The literature search began on February 2, 2017, and ended on March 21, 2017.[1]

There were inconsistencies in the literature regarding nomenclature, measured time windows, specific electrodes included, and quantification of the waveforms. However, of the included studies, the ERN was characterized as a negative-going waveform, recorded at the frontocentral region (e.g., Fz, FCz, Cz; American Encephalographic Society, 1994), and occurring between 0 and 100 msec after an incorrect response. Similarly, the Pe was categorized as a positive-going waveform, recorded at the midline (e.g., Pz; American Encephalographic Society, 1994), and occurring approximately 200-500 msec after an

[1]We used the Risk of Bias Assessment Tool for Nonrandomized Studies (RoBANS; Kim et al., 2013). Two raters (M. Moore and A. McCleery) completed independent ratings of each study with good inter-rater agreement (91% agreement, Cohen's kappa=0.80). Scoring discrepancies were resolved by consensus ratings. For the majority of studies, risk of potential bias was low. A summary of the RoBANS data can be found in Supplementary Table 2.

incorrect response. Finally, the FN was categorized as a negative-going waveform, recorded at the frontocentral region, and occurring between 250-350 msec after a response performance feedback was given.

2.2. Information Sources, Search Terms, and Study Selection

We identified relevant studies using PubMed and PsycINFO online databases using the following search terms: (schizophrenia OR schizoaffective OR psychotic* OR psychosis) AND (EEG OR ERP) AND (ERN OR Pe OR FN or FRN or error* or feedback*). For all of the relevant papers that were identified by the computer searches, we examined the references to see if other relevant articles would be identified. Additionally, we conducted a cited reference search of each included article. For every article identified in the computer search, the authors on the current article reviewed the title and abstract to ensure that it was appropriate to be included in the meta-analysis. Multiple studies from the same research group were flagged for further review to ensure that the samples were nonoverlapping. When the study results were ambiguous or insufficient for meta-analysis (e.g., information required to calculate effect size was not reported), the corresponding author of that particular study was contacted for further information.

A PRISMA diagram outlining the systematic review and selection of studies is presented in Figure 1 (Moher et al., 2009). Combined searches of PubMed and PsycINFO yielded 189 unique records. After screening the titles and abstracts, 33 records were identified as possibly fulfilling inclusion criteria and were subject to further review. Six articles were subsequently excluded for the following reasons: 3 studies did not include sufficient information to calculate Hedges' g and requests for information from the first and corresponding authors were unsuccessful (Alain et al., 2002; Charles et al., 2017; Kopp and Rist, 1999); 2 studies did not include a nonpsychiatric control group (Foti et al., 2016; Schneider et al., 2013); and 1 study had an overlapping sample that was already included (Foti et al., 2013). Thus, 27 full-text articles were included in the current analyses: 5 reporting ERN only, 2 reporting FN only, 16 reporting both ERN and Pe, 2 reporting ERN and FN, and 2 reporting all three components. No articles reported the Pe only or both Pe and FN only. Subsequent searches (i.e., reference lists and cited reference searches of included articles) yielded no additional records. Two coders (E. Martin and M. Moore) recorded relevant data from each article and confirmed the accuracy through consensus meetings of the information coded. For access to the review protocol, including coding book, please contact the corresponding author (E. Martin).

2.3. Moderators Examined

For ERN and Pe, each identified article was coded for several potential moderators related to study methodology and sample characteristics. From the information available, we examined moderators when the effect size distributions were heterogeneous. One moderator was type of activation task employed (i.e., non-verbal vs. verbal task). A "non-verbal" task was one that involved simple visual stimuli and a speeded motor response to stimuli (Go/No Go, Flanker) whereas a "verbal" task (Stroop, picture-word matching task) was one that involved word reading followed by a response. Another moderator examined was method of ERP component calculation (difference score between error and correct trials vs. baseline

comparison). A third moderator was diagnosis of psychosis patient samples (schizophrenia/schizoaffective disorder only vs. broadly-defined psychotic disorders). A fourth moderator examined was clinical status of the patient samples (inpatients vs. outpatients). Finally, we examined whether phase of illness of the patient samples (early vs. chronic phase) moderated any effects. Patients were characterized as being in the early phase of illness if their onset of psychosis was 5 years or less before testing, and were characterized as being in the chronic phase if the onset was greater than 5 years prior to testing.

2.4. Data Analysis Plan

The primary variables of interest were the amplitudes of the ERN, Pe, and FN ERP waveforms for the patient and at-risk samples compared to healthy control subjects. For the ERN and Pe, we used or calculated delta scores for ERN (error – correct trials) and Pe (error - correct trials) whenever possible. This was not possible for 10 ERN and 8 Pe studies, and we instead used the response to error trials for ERN and Pe. For all FN studies, a delta score (non-reward – reward) trials was calculated. For each study, Hedges' g and SE, 95% confidence interval (CI), inverse variance weight, and weighted effect size (ES) of ERN, Pe, and/or FN waveform amplitude were calculated. For studies with multiple psychosis groups, i.e., a schizophrenia/schizoaffective group and a broadly-defined psychosis group (Foti et al., 2012; Minzenberg et al., 2014), the overall difference between cases and controls in ERP response was used for calculation of Hedges' g in the primary analysis. Similarly, for studies with multiple conditions (e.g., Morris et al., 2006), the overall difference between groups in ERP response across conditions was used for calculation of Hedges' g.

Across studies, the overall weighted mean effect size and SE and 95% CI were calculated for the ERN, Pe, and FN waveforms, and z tests were performed to determine if they were significantly different from zero. Estimates were derived from fixed effect models. Random effects models were not employed due to an increased risk for Type I error when the number of studies is small (Guolo and Varin, 2017). Homogeneity of the effect size distributions was assessed using the Q and I^2 statistic. For analyses with fifteen or more studies, potential publication bias was assessed using funnel plots, which graph the effect size against the total sample size of each study, and Egger's regression test of funnel plot asymmetry. For the funnel plot, a symmetrical, inverted cone-shaped distribution of effect sizes centered about the overall weighted mean effect size suggests absence of publication bias. Impact of potential moderators was assessed using the partitioned Q statistic.

3. Results

3.1. Characteristics of included studies and samples

Information about the study paradigms, including type of activation task and ERP component(s) examined, are presented in Table 1. The total sample size of the studies (N = 27) ranged from 18 to 267 (median = 36). For studies that examined the ERN or Pe, 17 used a nonverbal task (e.g., flanker task) and 9 used a verbal behavioral task (e.g., Stroop task). Regarding method of ERP component calculation, 10 reported peak amplitude and 17 reported mean amplitude; of these 27 studies, 17 reported delta amplitudes (i.e., error-correct amplitudes).

Table 2 presents descriptive data for studies of patient and at-risk samples. For the psychosis studies, the grand mean age was 37.6 years (SD = 9.3), and the grand mean for level of education was 13.6 years (SD = 0.8). For the at-risk samples, the grand mean age was 19.57 years (SD = 4.66), and the grand mean for level of education was 14.41 years (SD = 0.41).

Across all studies, eight reported medication dosing information and 22 reported symptom ratings. Exclusion criteria for patients included history of neurological conditions (14 studies) or head injury (12 studies), current substance abuse (18 studies), intellectual disability (5 studies), or previous electroconvulsive therapy (2 studies). Regarding inclusion criteria for nonpsychiatric control samples, 18 studies screened participants for DSM-IV Axis I psychotic conditions using a structured or semi-structured clinical interview, 5 screened for DSM-IV Axis II conditions, 19 excluded for recent history of substance abuse, and 13 studies excluded participants with a history of psychotic disorder in a first-degree relative. Seventeen studies excluded control participants with a history of neurological disorder, and 12 studies excluded controls with a history of head injury.

3.2. ERN results

The ERN results for the two groups are summarized in Table 3, and corresponding forest plots of the effect size and 95% CI for each study is presented in Figure 2.

3.2.1. Psychosis group—For the psychosis group, the weighted mean effect size of the 20 studies was large in magnitude [ES=−0.84]. However, the distribution of effect sizes was significantly heterogeneous [$Q_{total}(19)=48.73$, $p<0.001$; $I^2=63.06\%$]. Subsequent analysis indicated that a single study (Perez et al., 2012) made an unusually large contribution to the heterogeneity statistic Q due to its relatively small effect size (accounting for 34.72% of Q_{total}). The data were re-analyzed with the outlying study removed. The weighted mean effect size of the remaining 19 studies was large in magnitude [ES=−0.96, SE=0.07, 95% CI: −1.09, −0.82], with the ERN amplitude of the psychosis group being smaller than that of the control group. The effect size was significantly different from zero [$z=-13.87$, $p<0.001$]. The distribution of effect sizes remained significantly heterogeneous [$Q_{total}(18)=31.81$, $p=0.02$; $I^2=49.70\%$]. The funnel plot was roughly symmetrical, giving little indication of publication bias (see Figure 3). That is, there was more variability of effect sizes for studies with smaller sample sizes, and the effect sizes of the larger studies more closely approximate the overall weighted mean effect size. Egger's regression test of funnel plot asymmetry was not statistically significant [intercept=−0.95, SE=0.96, $p=0.34$, 95% CI: −2.97, 1.07].

We conducted follow-up analyses to examine the impact of possible moderators on study effect size. Regarding task characteristics, the type of activation task significantly contributed to the heterogeneity of effect sizes. Twelve studies used non-verbal tasks (e.g., Flanker task, Go/No-Go) and seven studies used verbal tasks (e.g., Stroop). The weighted mean effect size from studies that employed non-verbal tasks was larger than the weighted mean effect size from studies that used verbal tasks [$Q_{between}(1)=5.82$, $p=0.02$; $ES_{non\text{-}verbal}=-1.10$, SE=0.09; $ES_{verbal}=-0.76$, SE=0.11] However, the method of ERN calculation (difference waves [13 studies] vs. ERPs to error trials [6 studies]) did not significantly

contribute to heterogeneity of effect sizes [$Q_{between}(1)=0.001$, $p=0.97$; $ES_{ERN}=-0.96$, SE=0.14; $ES_{\Delta ERN}=-0.96$, SE=0.08].

Regarding sample characteristics, diagnosis of the patient participant sample, i.e., schizophrenia/schizoaffective disorder [16 studies] vs. broadly-defined psychotic disorders [3 studies], did not account for a significant proportion of the heterogeneity of effect sizes [$Q_{between}(1)=0.01$, $p=0.92$; $ES_{schizophrenia}=-0.95$, SE=0.08; $ES_{psychotic}=-0.96$, SE=0.13]. Clinical status (10 outpatient studies, 5 inpatient or mixed studies, 4 not reported) did not significantly contribute to heterogeneity of effect sizes [$Q_{between}(1)=2.37$, $p=0.12$; $ES_{outpatient}=-0.85$, SE=0.08; $ES_{inpatient/mixed\ sample}=-1.16$, SE=0.18], nor did phase of illness (2 recent-onset studies, 17 chronic or mixed sample studies) [$Q_{between}(1)=0.86$, $p=0.35$; $ES_{recent\text{-}onset}=-0.84$, SE=0.14; $ES_{chronic}=-0.99$, SE=0.08]. Moreover, mean age of the patient sample was not significantly correlated with study effect size [$r=0.23$, $p=0.34$].

3.2.2. At-risk group—For the at-risk group, the weighted mean effect size of the seven studies was medium in magnitude [ES=−0.48, SE=0.11, 95% CI: −0.69, −0.28], with the ERN amplitude of the high-risk group being smaller than that of the control group. The weighted mean effect size significantly differed from zero [$z=-4.60$, $p<0.001$], and the distribution of the effect sizes was not significantly heterogeneous [$Q_{total}(6)=10.58$, $p=0.10$; $I^2=43.3\%$].

3.3. Pe results

The Pe results are summarized in Table 4, and a forest plot of the effect size and 95% CI of each study is presented in Figure 4.

3.3.1. Psychosis group—For the psychosis group, the weighted mean effect size of the 12 studies was small in magnitude [ES=−0.24], with the Pe amplitude of the psychosis group being smaller than that of the control group. However, the distribution of effect sizes was significantly heterogeneous [$Q_{total}(11)=39.63$, $p<0.001$; $I^2=74.8\%$]. Subsequent analysis indicated that a single study (Perez et al., 2012) made an unusually large contribution to the heterogeneity statistic Q_{total} due to its relatively large effect size (accounting for 43.2% of Q_{total}). The data were then re-analyzed with the outlying study removed. The weighted mean effect size of the remaining 11 studies was small in magnitude [ES=−0.09, SE=0.08, 95% CI: −0.24, 0.07], with the Pe amplitude of the psychosis group being slightly smaller than that of the control group. The effect size was not significantly different from zero [$z=-1.10$, $p=0.27$]. The distribution of effect sizes was significantly heterogeneous [$Q_{total}(10)=22.50$, $p=0.01$; $I^2=55.6\%$].

Follow-up analyses were conducted to investigate potential sources of heterogeneity of the effect sizes. Regarding task characteristics, the method of Pe calculation (difference waves [7 studies] vs. ERPs to error trials [4 studies]) did not account for a statistically significant proportion of the heterogeneity of the effect sizes [$Q_{between}(1)=0.90$, p=0,34; $ES_{pe}=-0.22$, SE=0.16, 95% CI: −0.54, 0.10; $ES_{\Delta Pe}=-0.05$, SE=0.09, 95%CI: −0.22, 0.13]. Similarly, the type of activation task (7 non-verbal, 4 verbal) did not significantly contribute [$Q_{between}(1)=113$, p=0.29; $ES_{non\text{-}verbal}=-0.15$, SE=0.10; $ES_{verbal}=0.02$, SE=0.13].

Regarding patient characteristics, diagnosis of the patient participant sample, i.e., schizophrenia/schizoaffective disorder [8 studies] vs. broadly-defined psychotic disorders [3 studies], did not account for a significant proportion of the heterogeneity of effect sizes [$Q_{between}(1)=0.03$, $p=0.86$; $ES_{schizophrenia}=-0.08$, SE=0.10; $ES_{psychotic}=-0.10$, SE=0.12]. Similarly, the clinical status of the patient sample (7 outpatient studies, 2 inpatient studies) did not account for a significant proportion of the heterogeneity [$Q_{between}(1)=0.28$, $p=0.59$; $ES_{outpatient}=-0.10$, SE=0.09; $ES_{inpatient/mixed\ sample}=0.05$, SE=0.27]. Likewise, phase of illness of the patient sample (2 recent-onset studies, 9 chronic phase studies) did not significantly contribute [$Q_{between}(1)=0.33$, $p=0.56$; $ES_{recent\text{-}onset}=-0.02$, SE=0.14; $ES_{chronic}=-0.11$, SE=0.10], and mean age of the patient sample was not significantly correlated with study effect size [$r=-0.15$, $p=0.66$].

Given that we were unable to identify the source(s) of heterogeneity, we re-analyzed the data to identify a subset of homogeneous studies. One study (Kansal et al., 2014) made a large contribution to heterogeneity (accounting for 37.12% of Q_{total}). Removing this study from the analysis yielded a homogeneous subset of 10 studies with a weighted mean effect size that was small in magnitude [ES=−0.03, SE=0.08, 95%CI: −0.19, 0.13, $Q_{total}(9)= 14.15$, $p=0.12$, $I^2=36.4\%$], with the Pe amplitude of the psychosis group being slightly smaller than that of the control group. The effect size was not significantly different from zero [$z=-0.42$, $p=0.68$].

3.3.2. At-risk group—For the at-risk group, the weighted mean effect size of the seven studies was very small in magnitude [ES=−0.06, SE=0.10, 95% CI: −0.26, 0.15], with the Pe amplitude of the high-risk group being smaller than that of the control group. The weighted mean effect size did not significantly differ from zero [$z=-0.53$, $p=0.60$]. The distribution of the effect sizes was moderately heterogeneous [$Q_{total}(6)= 13.29$, $p=0.04$; $I^2=54.9\%$].

Follow-up analyses indicated that method of Pe calculation (difference waves [3 studies] vs. ERPs to error trials [4 studies]) accounted for a statistically significant proportion of the heterogeneity of the effect sizes [$Q_{between}(1)=7.10$, $p=0.008$], with the two calculation methods yielding weighted small to moderate mean effect sizes in opposing directions [$ES_{Pe}=-0.24$, SE=0.12, 95% CI: −0.48, 0.01, $z=-1.91$, $p=0.06$; $ES_{\Delta Pe}=0.37$, SE=0.19, 95%CI:−0.01, 0.74, $z=1.93$, $p=0.05$]. Note, however, that the confidence intervals both overlap with zero. The type of activation task (5 non-verbal studies, 2 verbal studies) did not significantly contribute to heterogeneity of effect sizes [$Q_{between}(1)=0.49$, p=0.48; $ES_{non\text{-}verbal}=-0.12$, SE=0.14; $ES_{verbal}=0.03$, SE=0.16].[2]

3.4. FN results

3.4.1. Psychosis group—For the psychosis group, FN results are presented in Table 5, and a forest plot of the effect size and 95% CI of each study is presented in Figure 3. The weighted mean effect size of the five studies was small in magnitude [ES=−0.15, SE=0.11,

[2]Delta scores (i.e., ERP response to error trials minus response to correct trials) were calculated from available data for six ERN studies and four Pe studies. Weighted mean effect sizes for ERN and Pe in both the psychosis and high-risk groups, calculated using the originally reported metric for these studies (i.e., ERN or Pe to error trials only), were similar to those reported above calculated using delta scores.

95% CI: −0.37, 0.06], with smaller FN amplitude in the psychosis group compared to the control group. The weighted mean effect size did not significantly differ from zero [z=−1.39, p=0.08], and the distribution of effect sizes was homogeneous [$Q_{total}(4)$=0.32, p=0.99; I^2=0%].

3.4.2. At-risk group—FN has been examined in only one at-risk group study (Karcher et al., 2016). Karcher and colleagues examined FN in separate non-clinical samples with elevated psychotic experiences (PE group) or social anhedonia (SocAnh group), and these two groups were compared to healthy controls. The effect size was moderate in magnitude for the PE group [g=−0.49, SE=0.32, 95% CI: −1.11, 0.13], with the FN amplitude of the PE group being smaller than that of the control group. For the SocAnh group, the effect was very small in size [g=0.05, SE=0.31, 95% CI: −0.54, 0.65], with the FN amplitude being slightly larger in the SocAnh group than the control group. The confidence intervals for both comparisons overlap with zero.

3.5. Association between behavioral performance accuracy and Pe amplitude

Last, we examined the relationship between performance accuracy on the activation task and ERP amplitude. Only six studies reported correlations between performance accuracy and ERN amplitude, four studies with Pe amplitude, and one with FN amplitude. The results were mixed, with some studies reporting a significant positive association between performance accuracy and ERP amplitude in at-risk or psychosis samples (ERN: Bates et al., 2002, Kim et al., 2015, Perez et al., 2012; Pe: Chan et al., 2015b; FN: Morris et al., 2008) and others reporting no significant association (ERN: Chan et al., 2015b; Minzenberg et al., 2014; Morris et al., 2008; Pe: Kim et al., 2015; Minzenberg et al., 2014; Perez et al., 2012). Next, we examined whether effect size for performance accuracy on the activation task was associated with effect size for the ERP components across studies. Based on data provided in the papers, we were able to calculate the effect size for performance accuracy for 23 studies of ERN and 16 studies of Pe. Given that only one study measuring FN also reported performance accuracy data, we could not conduct the same analysis for that component. Across studies, there were no statistically significant correlations between performance accuracy effect size and ERN or Pe effect size ($ps \geq 0.14$).

4. Discussion

The results of this meta-analysis indicate that not all aspects of performance monitoring and feedback processing are disrupted in psychosis. A large number of studies indicate that early performance monitoring (ERN) impairments are substantial among those with psychotic disorders in general and are also detectable among those at risk for developing these disorders. In contrast, the smaller literatures on later performance monitoring (Pe) and feedback processing (FN) indicate that these processes appear relatively spared. These findings shed light on the nature of how performance monitoring and feedback processing is impacted in psychosis-related disorders and provide guidance for further research.

4.1. ERN: Substantial impairment in psychotic disorders and disorder risk in general

The results provide clear and consistent evidence of a large ERN reduction in those with psychosis, accompanied by a moderate ERN reduction in those at risk for these disorders. For the psychosis studies, there was no strong evidence for presence of publication bias, though there were too few studies to evaluate this in the at-risk group. There was significant heterogeneity in effect sizes for the psychosis group and this was partly accounted for by the type of activation task. The magnitude of impairment was significantly larger for non-verbal tasks, such as the flanker task (which shows the strongest psychometric properties of all tasks used to elicit the ERN (Weinberg et al., 2015)) than verbal tasks. Notably, a study using a picture-matching task (Perez et al., 2012) yielded unusual findings for both the ERN and Pe, indicating that the task may not be optimized to index the typical ERN/Pe response. Heterogeneity of effect size estimates was not impacted by factors such as method of ERN calculation, clinical diagnosis or status, or phase of illness. Overall, this robust pattern of ERN reduction across those with and at-risk for psychosis suggests that the ERN may be a useful biomarker or endophenotype (Gottesman and Gould, 2003) for psychosis.

One factor that makes the ERN an attractive biomarker is that a fair amount is known about the neural generators of this component. Given the considerable evidence that the ERN is generated by the dorsal ACC (e.g., Debener et al., 2005; Holroyd and Coles, 2002), our results suggest dysfunction of this region is associated with both psychosis and psychosis-risk. This is indeed consistent with substantial evidence of structural and functional ACC abnormalities in those with (Nelson et al., 2015; Salgado-Pineda et al., 2014) and at risk for (e.g., Fornito et al., 2008; Park et al., 2013) psychotic disorders. Furthermore, studies employing simultaneous fMRI and ERP recording have linked error processing abnormalities to ACC dysfunction in those with and at risk for psychosis (Ford et al., 2009). It should be noted, however, that error processing involves coordinated activity in a network of regions and the ERN deficits seen in psychosis may reflect dysfunction within, or in connectivity among, these regions (e.g., anterior PFC, anterior insula, inferior parietal lobe, thalamus, cerebellum; Becerril and Barch, 2013; Ford et al., 2009; Ramyead et al., 2017), rather than dysfunction specific to the ACC.

Several factors support the viability of the ERN as an endophenotype for psychosis. Endophenotypes are defined as biological or psychological phenomena that are associated with genetic contributions to a disorder (e.g., Glahn et al., 2014; Miller and Rockstroh, 2016; Ritsner and Gottesman, 2011). Aside from its consistent association with psychosis, there is evidence that the ERN meets several additional criteria for an endophenotype (Gottesman and Gould, 2003). For example, the ERN is a heritable trait in the general population with heritability estimates ranging from .30-.50 (Anohkin et al., 2008). Along these lines, initial evidence indicates that unaffected relatives of probands with psychotic disorders show significant ERN reductions compared to healthy controls (Simmonite et al., 2012). Further, among those with psychotic disorders, the ERN reduction appears to be largely state-independent and longitudinally stable: the majority of relevant studies reported no significant correlations between ERN and positive, disorganized, or negative symptoms (Chan et al., 2015b, Horan et al., 2012; Kim et al., 2006; Llerena et al., 2016; Minzenberg et al., 2014; but see Foti et al., 2012, Reinhart et al., 2015; Mathalon et al., 2002), and good

longitudinal stability has been found from one month to four years (Foti et al., 2016; Llerena et al., 2016). These converging lines of evidence suggest that performance monitoring abnormalities indexed by the ERN are an endophenotype associated with genetic predisposition for psychosis, perhaps aiding researchers to identify genes associated with the illness.

At this point, however, the ERN reduction does not appear to be uniquely associated with psychosis. Although this reduction does differ from individuals with obsessive-compulsive disorder, depression, and generalized anxiety disorder who show *elevated* ERN, reduced ERN is also seen in ADHD, substance use disorders, and other externalizing disorders (for a review, see Weinberg et al., 2015). It is possible that more fine-grained paradigms could identify certain characteristics of abnormal ERN that are more specifically associated with psychosis. Initial work hints as the possibility that the ERN reduction in psychosis may be less responsive to reward manipulations than other disorders. For example, baseline ERN reductions have been found to significantly improve during a performance-based reward incentive condition in young people with ADHD (i.e., providing monetary rewards for good performance increase the amplitude of the ERN; Groom et al., 2013), whereas similar incentives did not ameliorate the ERN reduction in individuals with schizophrenia (Morris et al., 2006). Further research to more precisely define the scope of ERN reductions in psychotic compared to other types of disorders will be an important next step.

4.2. Pe and FN: Largely spared in psychosis

In contrast to the robust early ERN impairments, later performance monitoring indexed by Pe appears largely normal across the two groups. This result is tempered to some extent by the significant heterogeneity of effect sizes for the Pe for the psychosis and at-risk groups. We were unable to identify significant subgroups or moderators of the heterogeneity for the schizophrenia group. For the at-risk group, only method of Pe calculation accounted for a statistically significant proportion of the heterogeneity, but this is not a robust finding since the confidence intervals associated with both calculation methods overlapped with zero. Our evaluation of potential moderators was necessarily constrained by the information that was reported with sufficient frequency across the studies. Overall, the amplitude of the Pe appears to be very similar in psychosis and psychosis-risk groups compared to healthy individuals. Given the limited number of studies available, further investigation is warranted to determine whether a relatively small Pe impairment is associated with a certain patient subgroup or methodological characteristic.

Feedback processing indexed by the FN also appears largely spared in psychosis. For the FN, the distribution of effect sizes was homogeneous, indicating that methodological and clinical factors do not appear to have an important impact on the findings. These results must be interpreted cautiously since they are based on a small number studies and our power to detect a small effect was limited. However, confidence in the FN results is bolstered by consistent findings of broadly intact hedonic responses in schizophrenia across a range of complementary methods. For example, individuals with schizophrenia subjectively report normal levels of “in the moment” pleasure and show normal psychophysiological responses when they are exposed to pleasant stimuli (Cohen and Minor, 2010). They also show

responses biases towards more rewarding stimuli that are similar to healthy controls on behavioral paradigms (Barch and Sheffield, 2017; Heerey et al., 2008). Furthermore, fMRI studies indicate that striatal responses to monetary reward in both medicated and unmedicated individuals with schizophrenia are similar to healthy individuals (Barch and Dowd, 2010; Gilleen et al., 2015; Nielsen et al., 2012; Schlagenhauf et al., 2009; Simon et al., 2010; Waltz et al., 2010). Thus, several lines of evidence support the current review's finding of normal feedback processing in schizophrenia. As noted above, the precise process(es) that the FN indexes remains an active area of research.

At this point, it is not possible to draw conclusions about the consistency or magnitude of FN disturbances with regard to the at-risk group since only one relevant study was available. Given the evidence pointing toward normal FN in psychosis, one would likely expect similarly normal findings in the at-risk group. However, this is a research gap that remains to be filled.

4.3. Integration: what does the pattern of findings mean for performance monitoring in psychosis?

Despite a substantial ERN deficit, the largely intact Pe indicates relatively preserved error awareness or error detection capacity in those with psychosis and psychosis risk. This pattern converges with experimental findings in healthy samples demonstrating that ERN and Pe are functionally dissociable (e.g., Hughes and Yeung, 2011; Overbeek et al., 2005). The intact Pe also illustrates a means by which individuals with psychosis area able to adjust their performance to task demands. Although the efficiency of their trial and error learning is likely compromised by an early performance monitoring impairment, their error awareness/ detection abilities may at least partly compensate for this limitation, enabling them to make strategic adjustments to improve task performance.

The finding of a relatively intact FN indicates typical external feedback responsivity in psychosis. This area of preserved functioning reflects a relative rarity in psychosis research and an important strength that could, for example, be exploited in novel psychosocial rehabilitation approaches. However, translating normal “in-the-moment” external feedback processing into complex adaptive behavior, such as seeking out potentially rewarding events, depends on involves several other processes that may be impaired in schizophrenia. For example, individuals with schizophrenia have deficits associated with learning, anticipating, or decisionmaking to guide goal-directed behavior (Barch and Dowd, 2010, Morris et al., 2011), which may in turn influence responding to and integrating reward feedback.

Taken together, performance monitoring and feedback processing play essential roles in action selection and goal-directed behavior. Thus, abnormalities in performance monitoring, coupled with intact feedback processing, may reflect impairments in the ability to attribute values linked to different choices (e.g., one response option is associated with a small, immediate reward whereas another option is associated with a larger, future reward; Gold et al., 2008), leading to difficulties in predicting associations between responses and outcomes (Morris et al., 2011). This reduced ability to predict outcomes may impede patients' ability to guide future action selection.

As mentioned above, decreased ERN is not diagnostically specific to psychosis spectrum disorders. It is possible, however, that the pattern across the three ERP components examined in this review has greater specificity. A recent review reported a similar pattern of decreased early performance monitoring (ERN) accompanied by relatively intact Pe and FN in people with autism spectrum disorders (Hupen et al., 2016). These comparable patterns are intriguing to consider in the context of the longstanding interest in the potential overlapping vulnerability to psychosis and autism spectrum disorders (Stone and Iguchi, 2011).

4.4. Limitations and conclusions

Although the database for the ERN meta-analyses was fairly large for psychosis, an important limitation of this review is the smaller number of studies that examined the ERN in at-risk groups, and the generally smaller number of Pe and FN studies. This is particularly true for the FN results, which should be viewed as preliminary. In addition, given the limited number of studies available, we were unable to directly compare effect sizes across components. This review was also limited by the large number of studies that did not report correlations between clinical symptoms or medication dosage and ERP components, which made it impossible to test for moderation by these factors. Finally, because we did not seek out unpublished data for this review, the findings could be biased by studies that found significant, publishable results. Importantly though, the funnel plot for ERN does not suggest the file drawer problem is a major concern. The more limited number of Pe and FN studies precluded assessment of potential publication bias.

Despite these limitations, the current meta-analytic review is the first to quantitatively highlight the similar early performance monitoring abnormalities in psychosis/psychosis-risk and the relatively normal feedback processing ability in psychosis. It also identifies gaps in the literature (e.g., research on FN in psychosis and psychosis-risk) and avenues for future research (e.g., the use of the ERN as an endophenotype for psychosis risk, identification of moderators of Pe). Further investigation of these ERP components will refine our understanding of performance monitoring and feedback processing in psychosis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- There were moderate to large ERN reductions in psychosis and psychosis-risk.
- There were non-significant, small differences from controls for Pe and FN.
- Early responding monitoring is impaired in psychosis/psychosis-risk.
- Later responding monitoring appears relatively intact across groups.
- External feedback processing also appears to be relatively intact.

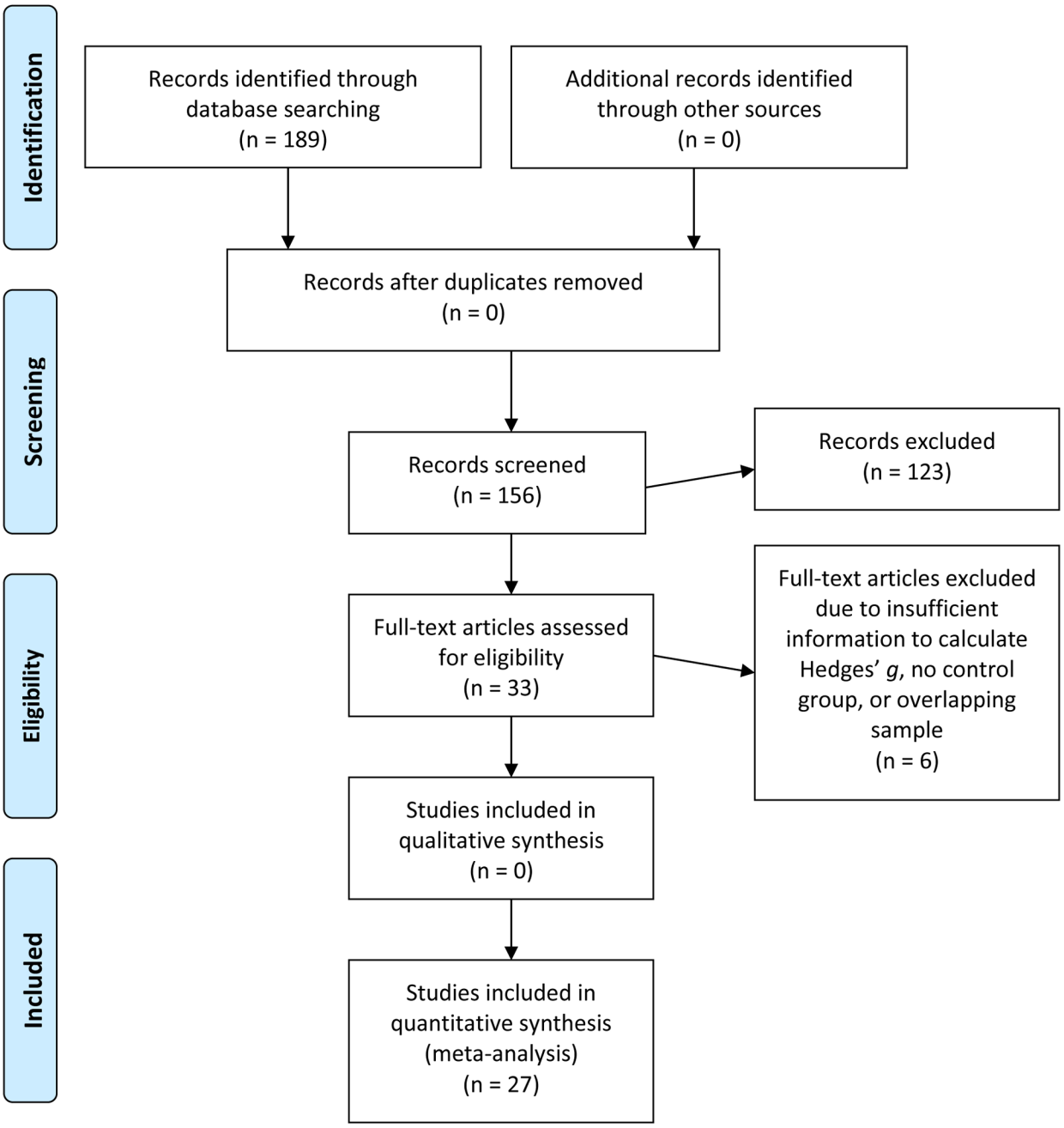

Figure 1.
PRISMA Flow Diagram.

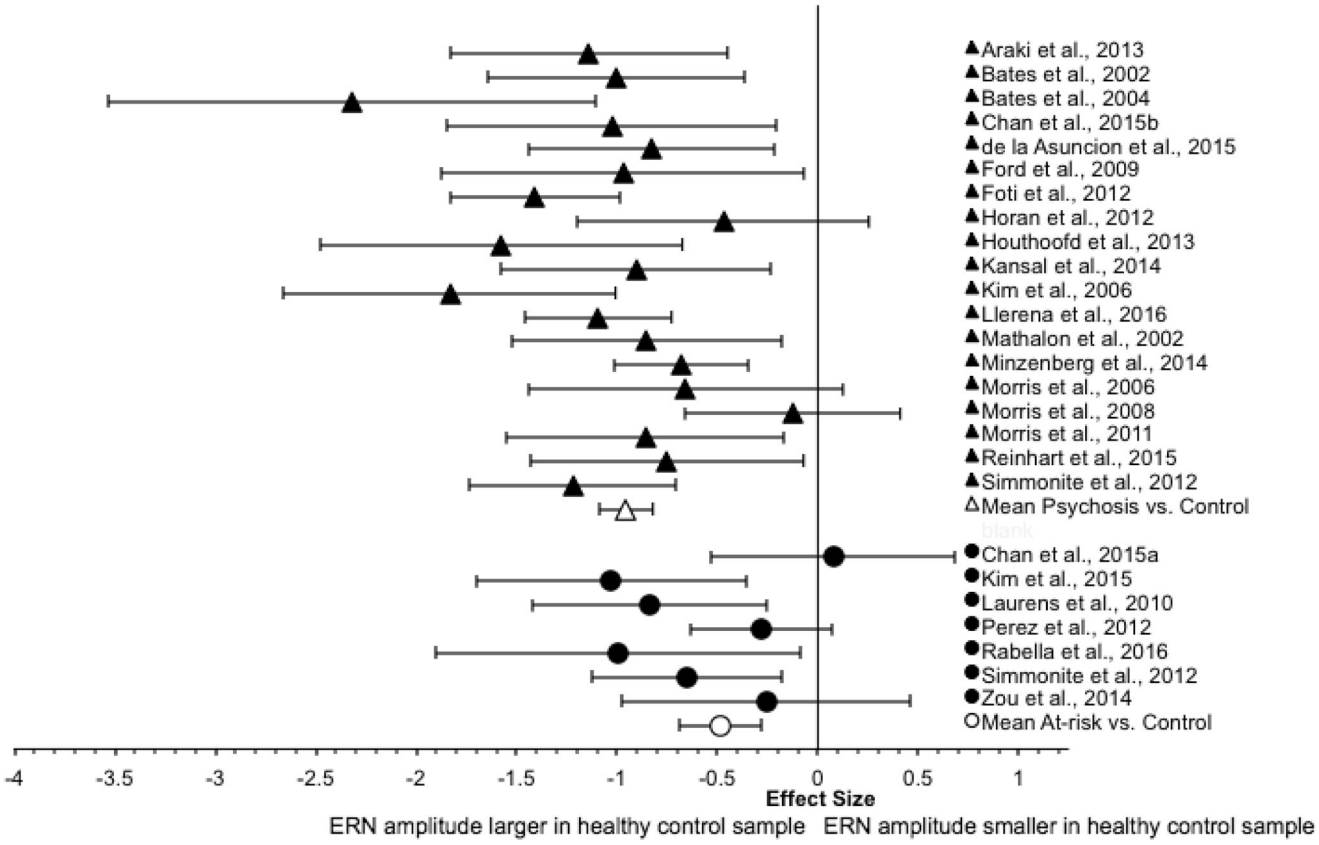

Figure 2.
Forest plot of ERN effect sizes.

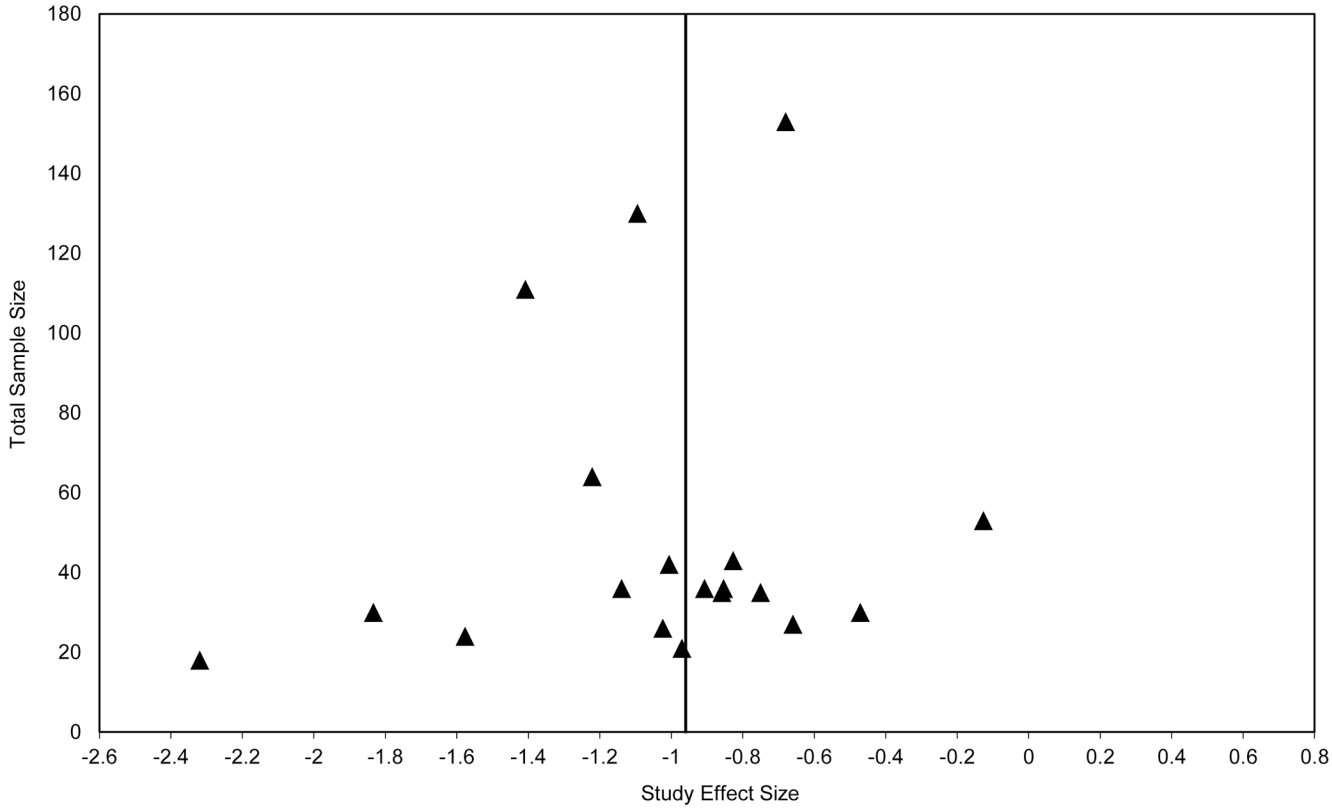

Figure 3.
Funnel plot of ERN effect sizes, Psychosis vs. Control studies

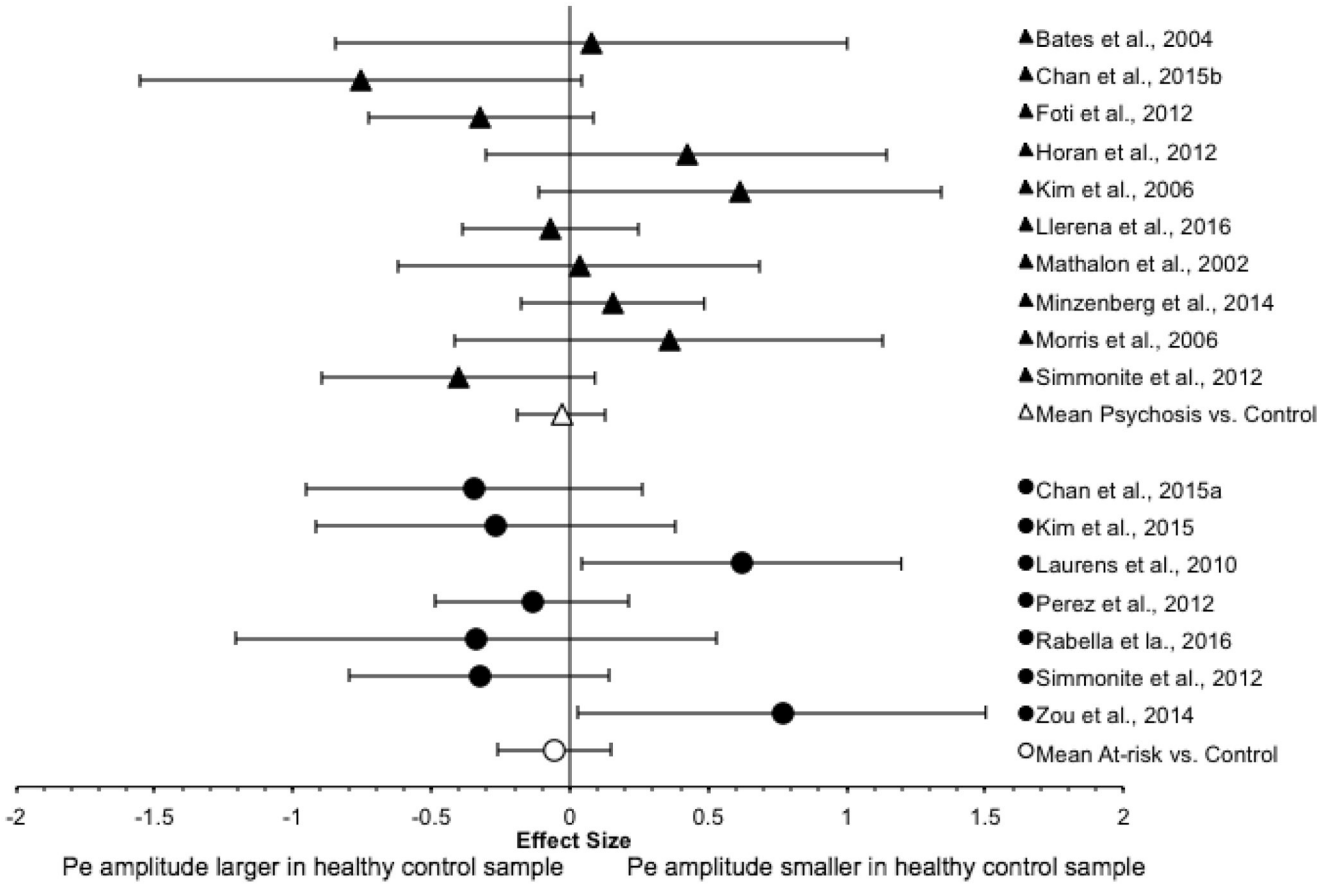

Figure 4.
Forest plot of Pe effect sizes

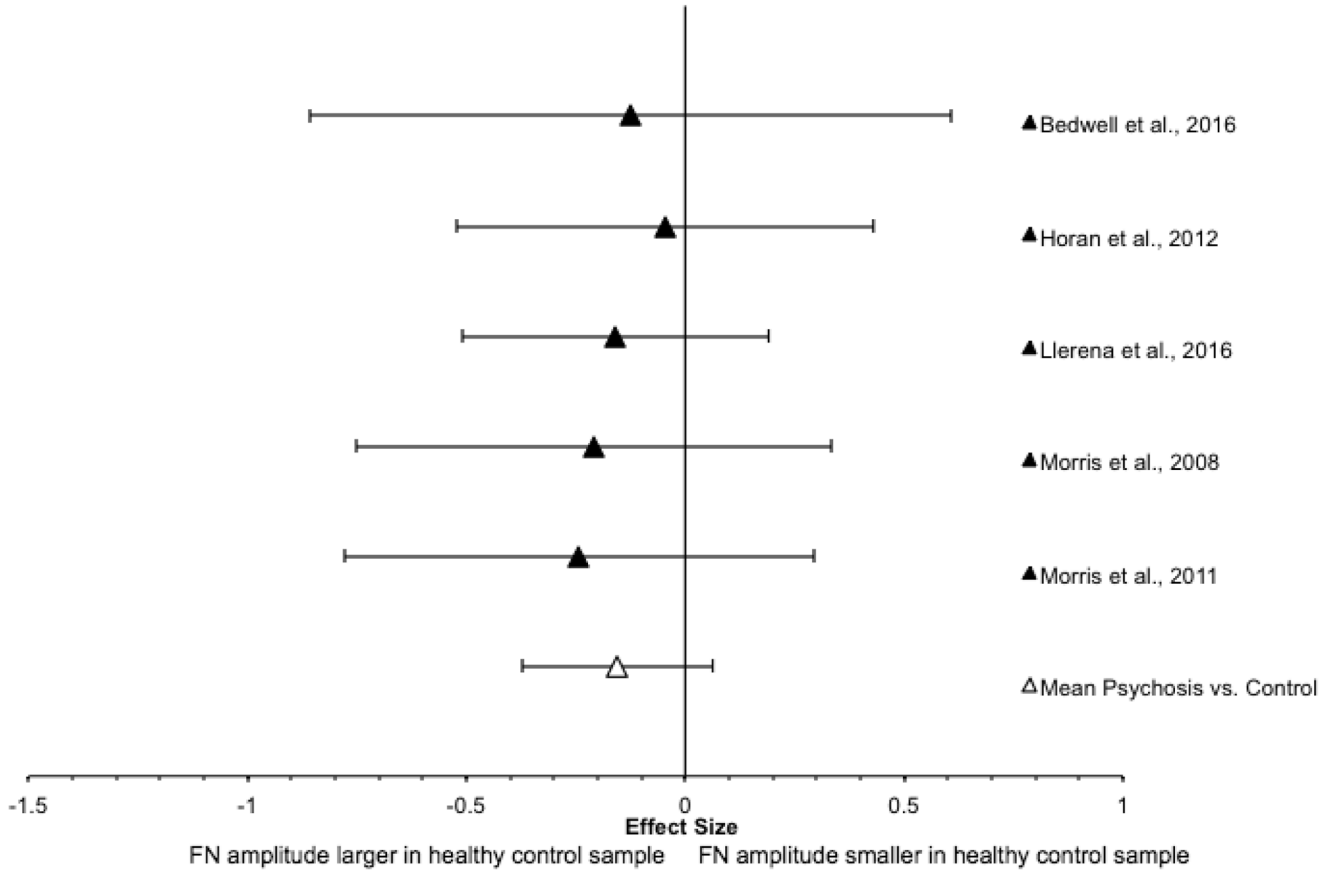

Figure 5.
Forest plot of FN effect sizes.

Table 1:

Study characteristics

Study and Country of Origin	Sample size (Cases: Controls)	Activation Task	ERP assessed
Araki et al. (2013) USA	18:18	Stroop task	Mean amplitude ΔERN
Bates et al. (2002) Canada	21:21	Go/No-Go	Peak amplitude ΔERN
Bates et al. (2004) Canada	9:9	Go/No-Go	Peak amplitude ΔERN, ΔPe
Bedwell et al. (2016) USA	31:13	Pavlovian monetary reward	Mean amplitude ΔFN
Chan et al. (2015a) USA	22:20	Flanker task	Mean amplitude ERN, Pe
Chan et al. (2015b) USA	14:12	Flanker task	Mean amplitude ERN, Pe
de la Asuncion et al. (2015) Belgium	22:21	Simon Task	Peak amplitude ERN
Ford et al. (2009) USA	11:10	Go/No-Go	Peak amplitude ERN
Foti et al. (2012) USA	104:33	Flanker task	Mean amplitude ΔERN, ΔPe
Horan et al. (2012)	16:14	Flanker task	Mean amplitudeΔERN, ΔPe, ΔFN
USA		Monetary gambling task	
Houthoofd et al. (2013) Belgium	12:12	Flanker task	Mean amplitude ΔERN
Kansal et al. (2014) Canada	18:18	Stroop task	Mean amplitude ΔERN, ΔPe
Karcher et al. (2016) USA	42:20	Reversal learning task	Mean amplitude ΔFN
Kim et al. (2006) Korea	15:15	Stroop task	Mean amplitude ΔERN, ΔPe
Kim et al. (2015) Korea	17:20	Simon Task	Peak amplitude ΔERN, ΔPe
Laurens et al. (2010) UK	22:26	Go/No-Go	Peak amplitude ΔERN, ΔPe
Llerena et al. (2016)	82:48	Flanker task	Mean amplitude ΔERN, ΔPe, ΔFN
USA		Time estimation task	
Mathalon et al. (2002) USA	18:18	Picture-word matching task	Mean amplitude ERN, Pe
Minzenberg et al. (2014) USA	73:54	Stroop task	Mean amplitude ΔERN, ΔPe
Morris et al. (2006) USA	16:11	Flanker task	Mean amplitude ERN, Pe
Morris et al. (2008) USA	26:27	Probabilistic learning task	Mean amplitude ΔERN, ΔFN
Morris et al. (2011)	20:15	Flanker task	Peak amplitude ΔERN, ΔFN
USA		Passive gambling task	
Perez et al. (2012) USA	132:135	Picture-word matching task	Mean amplitude ERN, Pe
Rabella et al. (2016) Spain	9:12	Flanker task	Peak amplitude ERN, Pe

Study and Country of Origin	Sample size (Cases: Controls)	Activation Task	ERP assessed
Reinhart et al. (2015) USA	17:18	Feedback learning task	Mean amplitude ΔERN
Simmonite et al. (2012) UK	29:35	Go/No-Go	Peak amplitude ERN, Pe
Zou et al. (2014) China	15:15	Go/No-Go	Peak amplitude ΔERN, ΔPe

Table 2.

Sample characteristics, a) psychosis studies (*k*=23) and b) at-risk studies (*k*=8).

Study	Mean age years (s.d.)		Gender Female: Male		Mean education years (s.d.)		Mean duration of illness years (s.d.)	Mean symptom ratings (s.d.)	Clinical status and diagnostic group
	Case	Ctrl	Case	Ctrl	Case	Ctrl			
a. Psychosis studies									
Araki et al. (2013)	44.0 (10.3)	36.9 (12.0)	0:18	0:18	13.3 (1.4)	15.3 (1.3)	NR	PANSS Total= 80.4 (23.6)	NR Schizophrenia
Bedwell et al. (2016)	NR	NR	NR	NR	NR	NR	NR	PANSS Positive= 12.3 (5.5) PANSS Negative=12.6 (5.6)	Outpatients Psychotic d/o
Bates et al. (2002)	35.0 (8.7)	34.0 (8.1)	4:17	4:17	NR	NR	NR	NR	Inpatients Schizophrenia
Bates et al. (2004)	35.8 (7.2)	32.8 (6.6)	0:9	0:9	NR	NR	NR	NR	Inpatients Schizophrenia
Chan et al. (2015b)	36.9 (7.8)	37.2 (8.8)	9:05	8:4	14.5 (3.2)	14.5 (1.9)	NR	PANSS Positive= 16.1 (6.0) PANSS Negative= 15.9 (6.6) PANSS General= 28.3 (7.8)	Outpatients Psychotic d/o
de La Asuncionet al. (2015)	33.0 (9.7)	28.1 (8.5)	4:18	2:19	NR	NR	9.0 (8.0)	SAPS Total=12.8 (11.6) SANS Total=33.3 (18.8)	NR Schizophrenia
Ford et al. (2009)	37.9 (12.7)	37.7 (10.3)	3:8	3:7	12.8 (3.4)	18.9 (2.5)	NR	BPRS Total=39.0 (9.6)	Inpatients and outpatients Schizophrenia
Foti et al. (2012)	43.7 (9.2)	43.8 (12.8)	25:53	11:22	NR	NR	NR	SAPS Psychotic= 2.5 (5.5) SAPS Disorganized= 2.2 (3.7) SANS Total= 12.5 (10.9)	Outpatients Psychotic d/o
Horan et al. (2012)	46.9 (7.6)	43.5 (9.3)	9:26	8:25	13.1 (1.5)	14.6 (1.6)	23.5 (8.6)	BPRS Positive=2.1 (0.8) BPRS Negative=1.7 (0.9) BPRS Total=41.6 (10.5)	Outpatients Schizophrenia
Houthoofd et al. (2013)	31.1 (11.3)	28.0 (8.8)	1:11	4:7	NR	NR	NR	PANSS Positive= 22.2 (7.3) PANSS Negative=	Inpatients Schizophrenia

Study	Mean age years (s.d.)		Gender Female: Male		Mean education years (s.d.)		Mean duration of illness years (s.d.)	Mean symptom ratings (s.d.)	Clinical status and diagnostic group
	Case	Ctrl	Case	Ctrl	Case	Ctrl			
								21.9 (8.0) PANSS General= 40.4 (9.6)	
Kansal et al. (2014)	43.2 (7.8)	41.1 (9.8)	7:11	10:8	NR	NR	NR	SAPS Total= 4.2 (4.3) SANS Total= 8.9 (4.0)	Outpatients Schizophrenia
Kim et al. (2006)	27.9 (5.4)	26.1 (4.3)	6:9	6:9	15.1 (3.0)	16.0 (1.3)	5.5 (4.4)	PANSS Positive= 16.2 (7.4) PANSS Negative= 16.0 (7.1) PANSS General= 29.5 (9.8)	NR Schizophrenia
Llerena et al. (2016)	59.5 (10.7)	47.5 (8.8)	23:70	23:40	13.1 (1.8)	14.6 (1.9)	NR	PANSS Positive= 18.0 (7.2) PANSS Negative= 14.8 (6.3)	Outpatients Schizophrenia
Mathalon et al. (2002)	40.0 (8.0)	43.0 (10.0)	1:17	1:17	14.2 (2.0)	16.9 (2.0)	NR	BPRS Total= 42.6 (7.8)	Inpatients and outpatients Schizophrenia
Minzenberg et**al. (2014)**	21.1 (3.4)	20.1 (2.4)	24:75	26:28	12.6 (2.1)	13.6 (2.0)	<1	SAPS Total= 8.6 (11.5) SANS Total= 10.7 (9.0)	Outpatients Psychotic d/o (early phase)
Morris et al. (2006)	31.4 (7.4)	31.6 (6.1)	5:11	4:7	14.1 (1.6)	15.2 (1.2)	7.38 (6.5)	SANS Total= 6.4 (3.8) BPRS Total= 27.9 (5.4)	Outpatients Schizophrenia
Morris et al. (2008)	45.0 (6.3)	43.4 (11.3)	8:18	11:16	12.9 (2.9)	15.2 (3.0)	NR	SANS Total= 33.1 (17.6) BPRS Total= 37.0 (10.5)	Outpatients Schizophrenia
Morris et al. (2011)	47.1 (6.7)	46.7 (11.0)	6:26	5:18	14.5 (2.3)	13.0 (1.7)	NR	SANS Total=32.2 (16.2) BPRS Total= 36.1 (11.3)	Outpatients Schizophrenia
Perez et al. (2012)	29.6 (11.6)	27.9 (9.8)	20:64	42:68	NR	NR	NR	PANSS Total= 66.4 (16.4)	Outpatients Schizophrenia (early phase and chronic phase)
Reinhart et al. (2015)	43.1 (7.8)	38.2 (10.8)	8:11	8:10	12.6 (1.98)	NR	22.6(7.86)	SAPS Total=16.8 (15.4) SANS Total= 31.7 (16.9)	Outpatients Schizophrenia
Simmonite et al. (2012)	19.5 (1.7)	17.9 (2.2)	10:19 20:15 NR	NR	<5	NR	NR Schizophrenia (early phase)		

Study	Mean age years (s.d.)		Gender Female: Male		Mean education years (s.d.)		Mean duration of illness years (s.d.)	Mean symptom ratings (s.d.)	Clinical status and diagnostic group
	Case	Ctrl	Case	Ctrl	Case	Ctrl			
b. At-risk studies									
Chan et al. (2015a)	19.2 (1.7)	19.9 (2.2)	11:11	11:9	NR	NR	n/a	SPQ-BR Total= 73.7 (16.1)	College students, not seeking treatment, psychometric schizotypy
Karcher et al. (2016)	PE= 18.5 (0.6) SocAnh= 18.7 (0.8)	18.4 (0.8)	15:17	10:11	NR	NR	n/a	NR	College students, not seeking treatment, psychometric schizotypy
Kim et al. (2015)	21.0 (1.5)	21.4 (2.0)	9:8	10:10	14.82 (.81)	14.55 (.95)	n/a	SPQ Total= 41.7(5.5)	College students, not seeking treatment, psychometric schizotypy
Laurens et al. (2010)	11.2 (0.9)	11.3 (0.8)	8:14	14:12	NR	NR	n/a	NR	School-age children, psychometrically defined putative antecedents of Sz
Perez et al. (2012)	18.9 (4.1)	20.0 (4.3)	19:29	41:47	NR	NR	n/a	SOPS Total= 32.3 (13.7)	Clinical high-risk
Rabella et al. (2016)	30.4 (5.8)	28.2 (6.8)	7:2	5:7	NR	NR	n/a	SPQ Total = 44.7(6.8) O-LIFE Total= 61.7(9.4)	not seeking treatment, Schizotypal personality disorder
Simmonite et al. (2012)	17.9 (2.2)	17.9 (2.2)	21:15	20:15	NR	NR	n/a	NR	not seeking treatment, Unaffected siblings of Sz probands
Zou et al. (2014)	20.3 (1.8)	20.8 (1.5)	8:7	9:6	14.00 (1.34)	14.87 (1.73)	n/a	SPQ Total= 42.0 (6.6)	College sample, not seeking treatment, psychometric schizotypy

Note: BPRS, Brief Psychiatric Symptom Scale; Ctrl, healthy control group; NR, not reported; O-LIFE, Oxford-Liverpool Inventory of Feelings and Experiences; PANSS, Positive and Negative Syndrome Scale; PE, psychotic experiences group; Psychotic d/o; broadly-defined psychotic disorders; SANS, Scale for the Assessment of Negative Symptoms; SAPS, Scale for the Assessment of Positive Symptoms; SocAnh, social anhedonia group; SOPS, Scale of Prodromal Symptoms; SPQ, Schizotypal Personality Questionnaire; SPQ-BR, SPQ-Brief version; Schizophrenia, schizophrenia/schizoaffective/ schizophreniform disorder.

Table 3.

ERN effect sizes.

	Study Name	*n* Case: *n* Ctrl	*g* (SE)	95% CI	Weighted ES
Psychosis vs. Ctrl	Araki et al., 2013	18: 18	−1.14 (0.35)	−1.83, −0.45	−9.23
	Bates et al., 2002	21: 21	−1.01 (0.33)	−1.65, −0.36	−9.37
	Bates et al., 2004	9: 9	−2.32 (0.62)	−3.54, −1.10	−6.02
	Chan et al., 2015b	14: 12	−1.02 (0.42)	−1.84, −0.20	−5.85
	de la Asuncion et al., 2015	22: 21	−0.83 (0.31)	−1.44, −0.21	−8.44
	Ford et al., 2009	11: 10	−0.97 (0.46)	−1.87, −0.07	−4.60
	Foti et al., 2012	78: 33	−1.41 (0.22)	−1.83, −0.98	−30.01
	Horan et al., 2012	16: 14	−0.47 (0.37)	−1.20, 0.25	−3.45
	Houthoofd et al., 2013	12: 12	−1.58 (0.46)	−2.48, −0.67	−7.45
	Kansal et al., 2014	18: 18	−0.91 (0.34)	−1.58, −0.23	−7.63
	Kim et al., 2006	15: 15	−1.83 (0.42)	−2.66, −1.01	−10.34
	Llerena et al., 2016	82: 48	−1.09 (0.19)	−1.46, −0.73	−31.51
	Mathalon et al., 2002	18: 18	−0.85 (0.34)	−1.53, −0.18	−7.23
	Minzenberg et al., 2014	99: 54	−0.68 (0.17)	−1.01, −0.35	−23.34
	Morris et al., 2006	16: 11	−0.66 (0.40)	−1.44, 0.12	−4.12
	Morris et al., 2008	26: 27	−0.13 (0.27)	−0.66, 0.41	−1.69
	Morris et al., 2011	20: 15	−0.86 (0.35)	−1.55, −0.17	−6.92
	Reinhart et al., 2015	17: 18	−0.75 (0.35)	−1.43, −0.07	−6.26
	Simmonite et al., 2012	29: 35	−1.22 (0.26)	−1.74, −0.71	−17.69
	Total	541:409	−0.96(0.07)	−1.09, −0.82	
At-risk vs. Ctrl	Chan et al., 2015a	22: 20	0.08 (0.31)	−0.53, 0.68	0.80
	Kim et al., 2015	17: 20	−1.03 (0.34)	−1.70, −0.35	−8.67
	Laurens et al., 2010	22: 26	−0.84 (0.30)	−1.42, −0.25	−9.49
	Perez et al., 2012	48: 88	−0.28 (0.18)	−0.63, 0.07	−8.61
	Rabella et al., 2016	9: 12	−1.00 (0.46)	−1.91, −0.09	−4.62
	Simmonite et al., 2012	36: 35	−0.65 (0.24)	−1.12, −0.18	−11.26
	Zou et al., 2014	15: 15	−0.26 (0.37)	−0.98, 0.46	−1.92
	Total	169: 216	−0.48 (0.11)	−0.69, −.28	

Note: CI, confidence interval; Ctrl, healthy control subject sample; ES, effect size; SE, standard error.

Table 4.

Pe effect sizes

	Study Name	*n* Case: *n* Ctrl	*g* (SE)	95% CI	Weighted ES
Psychosis vs. Ctrl†	Bates et al., 2004	9: 9	0.08 (0.47)	−0.85, 1.00	0.37
	Chan et al., 2015b	14: 12	−0.75 (0.41)	−1.55, 0.04	−4.55
	Foti et al., 2012	78: 33	−0.32 (0.21)	−0.73, 0.09	−7.43
	Horan et al., 2012	16: 14	0.42 (0.37)	−0.30, 1.14	3.10
	Kim et al., 2006	15: 15	0.62 (0.37)	−0.11, 1.34	4.46
	Llerena et al., 2016	93: 63	−0.07 (0.47)	−0.39, 0.32	−2.67
	Mathalon et al., 2002	18: 18	0.03 (0.33)	−0.62, 0.69	0.30
	Minzenberg et al., 2014	99: 54	0.15 (0.17)	−0.18, 0.49	5.36
	Morris et al., 2006	16: 11	0.36 (0.39)	−0.41, 1.13	2.31
	Simmonite et al., 2012	29: 35	−0.40 (0.25)	−0.89, 0.09	−6.37
	Total	387: 264	−0.03 (0.08)	−0.19, 0.13	
At-risk vs. Ctrl	Chan et al., 2015a	22: 20	−0.34 (0.31)	−0.95, 0.26	−3.57
	Kim et al., 2015	17: 20	−0.27 (0.33)	−0.92, 0.38	−2.45
	Laurens et al., 2010	22: 26	0.62 (0.29)	0.05, 1.20	7.20
	Perez et al., 2012	48: 88	−0.14 (0.18)	−0.49, 0.22	−4.24
	Rabella et al., 2016	9: 12	−0.34 (0.44)	−1.21, 0.53	−1.72
	Simmonite et al., 2012	36: 35	−0.33 (0.24)	−0.79, 0.14	−5.76
	Zou et al., 2014	15: 15	0.77 (0.37)	0.03, 1.50	5.45
	Total	169: 216	−0.06 (0.10)	−0.26, 0.15	

Note: CI, confidence interval; Ctrl, healthy control subject sample; ES, effect size; SE, standard error.

Table 5.

FN effect sizes

	Study Name	*n* Case: *n* Ctrl	*g* (SE)	95% CI	Weighted ES
Psychosis vs. Ctrl	Bedwell et al., 2016	16: 13	−0.12 (0.37)	−0.86, 0.61	−0.89
	Horan et al., 2012	35: 33	−0.05 (0.24)	−0.52, 0.43	−0.78
	Llerena et al., 2016	74: 55	−0.16 (0.18)	−0.51, 0.19	−5.00
	Morris et al., 2008	26: 26	−0.21 (0.28)	−0.75, 0.33	−2.76
	Morris et al., 2011	32: 23	−0.24 (0.27)	−0.78, 0.29	−3.23
	Total	183:150	−0.16 (0.12)	−0.38, 0.07	

Note: CI, confidence interval; Ctrl, healthy control subject sample; ES, effect size; SE, standard error.