Anticipatory Pleasure for Future Experiences in Schizophrenia-Spectrum Disorders and
Major Depression: A Systematic Review and Meta-Analysis

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Abstract

Objectives: Deficits in anticipating pleasure may be an important dimension of anhedonia and functioning in psychiatric disorders, particularly schizophrenia and depression, however, inconsistent findings have limited the conclusions that can be drawn. We conducted the first systemic review and meta-analysis of the extant literature for research comparing psychiatric groups to healthy control groups on anticipatory pleasure.

Methods: Academic Search Complete, Science Direct and CINAHL databases were systematically searched up to June 9th 2018 for relevant peer-reviewed articles, book chapters, and dissertations. Reference lists were also hand searched. A total of 36 studies were included in the review.

Results: A moderate-sized deficit was observed in schizophrenia-spectrum disorders ($k = 32$, 1851 patients and 1449 controls, $g = -0.42$ [95%CI = -0.53 - 0.31], $p < .001$), and a large deficit in major depression ($k = 415$ patients and 506 controls, $g = -0.87$ [95%CI = -1.23 - 0.51], $p < .001$), with this effect being significantly larger for depression ($p < .05$). Meta-regression showed that heterogeneity was partially explained in schizophrenia-spectrum by longer duration of illness and lower cognitive functioning predicting larger deficits. In depression, some evidence was found that ruling out a history of psychiatric illness in controls may be related to larger effects. There was evidence for small study bias inflating estimates in schizophrenia-spectrum disorders.

Conclusions: Deficits in anticipatory pleasure are manifest in these disorders, and significantly more so in major depression. These findings indicate a possible therapeutic target to link cognitive, affective, and behavioural factors that precipitate and maintain disorder.

Keywords: anticipatory pleasure; anhedonia; schizophrenia; major depression; meta-analysis

Anhedonia refers to a lack of ability to feel pleasure and enjoyment in response to experiences that might otherwise elicit a pleasurable, hedonic response. Anhedonia is diagnostically-characteristic of two psychiatric disorders. In the case of schizophrenia, anhedonia might be considered as part of a cluster of negative symptoms including apathy, avolition, and social withdrawal. In major depression, anhedonia is a core diagnostic criterion referred to directly in terms of loss of interest and pleasure from experiences that were previously enjoyed (American Psychiatric Association, 2013).

Hedonic responses can relate to pleasure from in-the-moment experience, pleasure from recalling a previous positive experience, or pleasure derived from anticipating a positive future experience. These different dimensions have previously been considered in the context of psychopathology (Klein, 1984), however, research has only more recently been focused on this future-oriented hedonic response for further study (Gard et al., 2006; Gard et al., 2007). The ability to mentally-simulate future experiences and anticipate enjoyment is one of the significantly adaptive functions of the “*prospective brain*” (Schacter et al., 2007), and neurologically distinct from reward consumption (Berridge & Robinson, 2003), also referred to as consummatory pleasure. Anticipatory pleasure is implicated in motivation to engage in rewarding and goal-directed behaviour (Engel et al., 2013; Sherdell et al., 2012). Indeed, lower levels of anticipatory pleasure are predictive of lower motivation for reward (Foussias & Remington, 2008; Treadway & Zald, 2011), lower responsiveness to reward (Foussias & Remington, 2008), and poorer functional outcomes (Foussias et al., 2011).

It is noted that anticipation of pleasure can refer to the prediction of pleasure from a future experience *and* an affective response to thinking about it. Although conceptually distinct, the anticipation of an event being positive is a prerequisite to experiencing a

rewarding affective response when thinking about it, and likely to give rise to such a response. This dependency is demonstrated through empirical findings, where questions distinguishing these two concepts are very highly correlated (Barsics, Van Der Linden, & D'Argembeau, 2016; *removed for blinding*). For parsimony, we refer to both here as anticipatory pleasure. We focus here on anticipatory pleasure as it has only recently been parsed from the notion of anhedonia as an absence of pleasure during the consumption of reward (Berridge & Robinson, 2003). Further, any deficits that are observed in this cognitive-affective process are proximal to decision-making (Mellers, Schwartz & Ritov, 1999) and subsequent behavioural and psychosocial outcomes, and would represent a specific therapeutic target requiring particular interventions to alter.

It has previously been implied that the capacity to experience emotions is diminished in schizophrenia-spectrum disorders (Meehl, 1962). While emotional expression appears to be low in general (Trémeau, 2006), research to date on self-reported emotional experience is less clear. Laboratory studies show that subjectively reported pleasure in response to stimuli (Cohen & Minor, 2008), and self-reported arousal (Llerena et al., 2006), do not differ from healthy controls. Further, findings on self-reported consummatory pleasure using trait-style checklists and diary studies have been inconsistent, with most studies showing no difference between patients and healthy controls, but some showing significant differences (Frost & Strauss, 2016). Despite this, those with schizophrenia do appear to engage in less pleasant events (Oorschot et al., 2011), which suggests that it may be a lower anticipation of pleasure which affects the tendency to engage in rewarding activities. A number of narrative and systematic reviews have appeared in the literature that discuss deficits in this cognitive-affective process that might maintain psychopathology (Cohen et al., 2011; Edwards et al., 2015; Frost & Strauss, 2016). As Frost and Strauss (2016) note, significant inconsistencies in

findings are observed between studies examining anticipatory pleasure in schizophrenia-spectrum disorders relative to control groups. As with consummatory pleasure, it is unclear why these inconsistencies occur. It may be due to small sample sizes and a related lack of statistical power to detect small effects. Alternatively, heterogeneity in sample characteristics might be the cause of inconsistencies, such as duration of illness, type of psychotic disorder, symptom severity, presence of co-morbid psychiatric disorders that affect anticipatory pleasure, or deficits in cognitive processing required to mentally represent future events. Meta-analytic approaches to studying the available data may help resolve this.

In major depression, a body of research indicates that self-reported consummatory pleasure is typically blunted (e.g., Barge-Schaapveld, Nicolson, Berkhof, & deVries, 1999; Bylsma, Morris, & Rottenberg, 2008; Fawcett, Clark, Schefter, & Gibbons, 1983; Wu et al., 2017; Yang et al. 2014, 2017). However, research into anhedonia in major depression has not typically differentiated between anticipatory and consummatory pleasure (Treadway & Zald, 2011), with the former being in earlier stages of research. To date, findings are mixed on anticipatory pleasure, with some studies showing that depressed individuals report reduced anticipatory hedonic responses (Wu et al., 2017), while others indicate mixed findings (Bjärehed et al., 2014). These have yet to be meta-analyzed to estimate an overall effect. Given that depressed individuals also appear to engage in less numbers of pleasant activities (Bylsma et al., 2011; Lewinsohn & Graf, 1973), estimating the size and robustness of effects on anticipatory pleasure in this population may help to clarify whether this is a possible maintaining factor in impaired functioning. Finally, there may be deficits in an anticipatory pleasure in other disorders, although the extant literature has not been formally assessed. Resolving inconsistencies in findings to date will help to clarify if anticipatory pleasure is indeed a deficit in psychopathology.

The aim of this study was to systematically review and meta-analyse data from studies comparing groups of individuals with psychiatric disorders with control groups to provide the best current estimate of any differences in self-reported anticipatory pleasure. It was hypothesised that there would be significant deficits in schizophrenia-spectrum and major depressive disorders, relative to healthy controls. We also sought to examine moderators of any effects that were observed, with some specific hypotheses, and the remaining being exploratory in nature. Based on the notion that deficits in anticipatory pleasure are linked with psychopathological processes, it was hypothesised that symptom severity and duration of illness would predict larger deficits. Group differences in cognitive functioning were also predicted to explain variance in anticipatory pleasure, given that deficits that are found in some mental health disorders (Heinrichs & Zakzanis, 1998) may impair the ability to mentally-represent future events, and therefore either negate or blunt the experience of associated anticipatory pleasure. It was also expected that a higher proportion of patients on first-generation antipsychotics would be associated with greater differences in anticipatory pleasure, given that they are a dopamine antagonist, and that reductions in dopamine are linked to problems with appetitive, wanting behaviour (Berridge, 2016). Lastly, it was hypothesised that ruling out a history of any psychiatric disorder in the control group, not just the disorder being examined, would be related to larger group differences, given that anticipatory pleasure may be affected by a number of disorders.

Method

The review was conducted in accordance with the evidence-based guidelines for systematic reviews described in the PRISMA statement (Liberati et al., 2009). The review was preregistered with PROSPERO (Registration number: CRD42018099843).

Data Sources and Search Strategy

On June 9nd 2018 Academic Search Complete, Science Direct and CINAHL databases were searched on EBSCO for all peer-reviewed articles, book chapters, and dissertations published in English up to this date. All searches were conducted by the authors who are doctoral-level researchers with experience in systematic reviews. The following terms were search for in full text: “Anticipatory emotion” OR “anticipated emotion” OR “anticipatory pleasure” OR “anticipated pleasure” OR “affective forecasting” OR “expected emo*” OR “future reward” OR “future pleasure” OR “future emotion” AND “psychi*” OR “disorder” OR “diagnos*” OR “mental*” OR “DSM*” OR “ICD*” OR “symptom*” OR “patient*” OR “psychopatho*”. Reference lists from the identified articles were also hand searched.

Study Selection

Inclusion criteria were:

- written in English:
- compared a group diagnosed with a psychiatric disorder, as assessed using standardized criteria by mental health professionals or structured diagnostic interviews, with a control group;
- Assessed anticipatory pleasure in relation to future events, as noted, this included studies referring to anticipatory and anticipated pleasure;
- presented sufficient information so that the methodology and results could be extracted for meta-analysis, or this could be obtained from the authors; and,
- presented original empirical data.

Exclusion criteria were:

- patient groups characterised by neurological disorders, pervasive developmental disorders, or brain injuries;

Data Extraction

The following information was extracted, or authors were contacted for the information: year of publication, characteristics of the sample used in analyses (sample size, age, percentage female, diagnosis of interest, duration of illness, standardised scores of estimates of IQ or cognitive functioning, symptom severity, proportion of patients taking psychotropic medications, the assessment method for diagnosis and anticipatory pleasure, and the criteria for the control group. To assess study quality, information on methodology was extracted to complete items on the Newcastle-Ottawa-Scale (NOS; Wells et al., 2018). On the NOS, various criterion relating to quality in case-control studies are assessed using a star system, and these are then summed to provide an ordinal rating of quality. Items relating to blinded ascertainment of psychiatric diagnosis and response proportions were not scored, given the noted limitations of using these items in case-control studies (Stang, 2010). This left a possible score range from 0 to 7, with higher scores indicating higher study quality. The first author and another researcher not otherwise associated with the review rated 50% of the studies. Inter-rater reliability was found to be good (intraclass correlation coefficient = .96, $p < .001$), and the remaining studies were coded by the first author. Data required to calculate the size of effect for measures of anticipatory pleasure were also extracted. This consisted of means and standard deviations, t statistics, and p values.

Statistical Analyses

Meta-analytic calculations were performed using Review Manager 5.3.5. We used random effects models, anticipating heterogeneity between the effect sizes of the individual

studies. We used information extracted from the studies to calculate effect sizes using the standardized mean difference. Hedge's g was used as the metric for effect size, as this provides a corrected estimate to reduce the upward bias that can occur in small sample sizes. The magnitude of the effect sizes was interpreted approximately as small = 0.2, medium = 0.5, and large = .08 (Egger et al., 2001). Heterogeneity between the effect sizes was assessed using the Q statistic and the I^2 statistic, where the former indicates the probability of differences between effect sizes being by chance (with corresponding p -value), and the latter is an estimate of the amount of heterogeneity, whereby 50% and higher indicates notable variance (Higgins & Thompson, 2002).

File drawer statistics were used to account for the possibility of an overrepresentation of positive findings. We computed classic fail-safe N 's (Rosenthal, 1979) which showed the number of additional studies that would be required to make the effect size non-significant at the $p < .05$ level. We also computed Orwin's fail-safe N 's (Orwin, 1983), which indicated how many studies would need to show no effect to reduce any observed group differences to a trivial level (defined here as a standard mean difference of 0.10). Funnel plots were generated to assess for publication bias (Duval & Tweedie, 2000), and show how studies are distributed around the point estimate using the effect size (standardized mean difference) and precision (standardized error). Asymmetry indicates publication bias, where smaller samples are associated with larger effect sizes, and was statistically tested for using Egger's regression test for asymmetry (Egger et al., 1997). For sensitivity analysis, we used the trim and fill procedure (Duval & Tweedie, 2000) to first estimate the number of studies that might be missing due to asymmetry, and then re-impute them to generate an adjusted effect size. We note that this method is based on the possibility of suppression of studies with small effect

sizes which, although a useful analysis, is not synonymous with publication bias relating to studies with non-significant effects (Simonsohn, Nelson, & Simmons, 2014).

Results

Figure 1 presents a flowchart of the study selection process. The initial search returned 3,148 articles. The search engine removed 69 duplicates, leaving 3,079 articles. After scanning the abstracts, 2950 were removed, and 129 were identified as potentially meeting criteria. Both authors independently examined the full text of a random subsample of 30 of these articles for eligibility. Inter-rater reliability was found to be good (Cohen's $\kappa = .87$, $p < .001$), and discrepancies were resolved through discussion. The first author assessed the remaining articles, and 34 met criteria for inclusion. Two more studies were found through cross-referencing, totalling 36. Only one study examined bipolar disorder (Tso et al., 2014) and one examined opioid dependence (Garfield et al., 2017). Therefore these were not meta-analysed, although the former study also examined Major Depression and these data were included. Three authors were contacted for further information needed to assess effect sizes, and all three responded and supplied this.

For meta-analyses, the 35 eligible articles yielded 40 independent effect sizes, as some articles reported multiple studies and samples (Gard et al., 2007; Li et al., 2015a; Liu et al., 2015; Schlosser et al., 2014). Both authors independently extracted means and standard deviation data from a random subsample of 30% the studies, demonstrating excellent inter-rater reliability (Cohen's $\kappa = 1.0$, $p < .001$). One study reported multiple effects using the same measure that varied on the temporal distance of the anticipated event (Li et al., 2015b), and others reported multiple subscales or items from the same scale (Bjärehed et al., 2014; Gur et al., 2015; Li et al., 2015a; Liu et al., 2011; Schlosser et al., 2014). In these cases, data

were collapsed to produce one overall effect for the study. In one study (Wu et al., 2017) there were effects on two different measures reported. We opted to include the Temporal Experience of Pleasure Scale (TEPS; Gard et al., 2006) as it has been previously validated. One study (Barch et al., 2014) reported a majority of the same participants as another study (Mann et al., 2013). The former study was used as this contained a larger sample of psychiatric patients.

Study Characteristics

The details of the 36 articles included in review are presented in Table 1. All articles were from peer-reviewed journals, and the majority were published in the last 10 years ($n = 34$; 94%). The majority of the articles examined schizophrenia-spectrum disorders ($n = 28$; 77%), with less examining major depression ($n = 8$; 22%), and one bipolar disorder ($n = 1$; 3%) and opioid dependence ($n = 1$; 3%; Note: this equals over 100% as two studies examined two disorders (Li et al., 2015b; Tso et al., 2014)). In all studies, except for one (Schlosser et al., 2014), case and control samples were reasonably matched on age and gender proportion.

For schizophrenia-spectrum, there were a total of 1851 patients and 1449 controls. The mean age of patients was 28.7 years, and on average 30.5% of the sample were female. Half the samples included only those with a diagnosis of schizophrenia ($n = 18$; 56%), and the remainder schizophrenia and schizoaffective disorder ($n = 14$; 44%). In the majority of the samples, the TEPS was used to assess anticipatory pleasure ($n = 27$; 84%), and structured interviews to assess for diagnoses ($n = 27$; 84%). There were several different measures of symptom severity used across samples, however, the most frequently used was the Positive and Negative Syndrome Scale (PANSS; $n = 14$; 43.7%; Kay, Fiszbein, & Opler, 1987). The positive, negative, and general symptom scales from the PANSS were used in moderator

analyses. The frequency of antipsychotic use was reported for most samples ($n = 22$; 68.7%), and standardised estimates of IQ or cognitive functioning for patient and control groups were provided for 11 samples (34.3%) which were used in moderator analysis.

For studies on major depression, 415 patients and 506 controls were included. The mean age of the psychiatric samples was 35.2 years of age, and on average 55.5% of the sample were female. In the majority of the studies, the TEPS was used to assess anticipatory pleasure ($n = 6$; 75%), and structured interviews were used to assess for diagnoses in just over half ($n = 5$; 62%). Five studies (62.5%) reported the proportion of patients on antidepressants. Only two studies (25%) reported estimates of IQ for patient and control groups, too few to be included in analyses.

Effect size analysis

For schizophrenia-spectrum disorder, a small-to-moderate sized effect was found of $g = -0.42$ (95%CI = -0.53-0.31, $p < .001$). The heterogeneity statistics indicated there was a moderate amount of between-study variance, $Q = 75.1$, $I^2 = 59\%$, $p < .001$.

For major depression, a large-sized effect was found of $g = -0.87$ (95%CI = -1.23-0.51, $p < .001$). The heterogeneity statistics indicated there was a large amount of between-study variance, $Q = 37.5$, $I^2 = 81$, $p < .001$.

A statistically significant difference was found between the effect sizes in the two psychiatric groups, $Q = 5.5$, $p = .020$, indicating that individuals with major depressive disorder showed larger deficits in anticipatory pleasure relative to those with schizophrenia-spectrum disorders. Figure 2 shows a forest plot of study effects from both psychiatric groups.

The one study on bipolar disorder (with no current mood episode) reported a non-significant effect of $g = -0.13$ (95%CI = -0.65-0.38, $p = .603$), while the study examining opioid dependence reported a large, significant effect of $g = -0.96$ (95%CI = -1.36-0.56, $p < .001$).

➔ *Insert Figure 2 about here.*

Assessment of Bias

For schizophrenia-spectrum disorder, the classic fail-safe N was 1,015 and Orwin's fail-safe N was 82, indicating a large number of studies were needed before the average effect became non-significant, or trivial in size, respectively. Egger's regression test was significant, intercept = -2.00, $SE = 0.686$, $t(30) = 2.92$, $p = .006$, indicating the possibility of small study bias. Inspection of the funnel plot indicated some asymmetry (see Figure 3), and the trim and fill procedure estimated 10 studies may be missing to the right side of the mean. After imputing these studies, the adjusted effect size was smaller, -0.26 (95%CI = -0.38-0.14), and only slightly overlapping with the unadjusted effect. Given this, we can surmise that there was some evidence for small study bias and that adjusting for this reduces the overall effect size.

For major depression, the classic fail-safe N was 224 and Orwin's fail-safe N was 48, indicating a large number of studies were needed before the average effect became non-significant, or trivial in size, respectively. Egger's test was not significant, intercept = -2.79, $SE = 1.72$, $t(6) = 1.61$, $p = .157$, however, we note that the statistical power of this test is low given the small number of studies. Inspection of the funnel plot indicated some asymmetry (see Figure 4), and the trim and fill procedure estimated that two studies were missing to the

left side of the mean. After imputing these studies, the adjusted effect size was larger, $g = -1.04$ (95%CI = -1.45-0.63), but overlapped substantially with the unadjusted effect.

Moderation Analyses

Meta-regression using random effects models were conducted in Comprehensive Meta-Analysis (Version 3.3.070) to assess for variables that might account for any observed heterogeneity in effect sizes. Enough data were extracted to analyse the mean age of the sample, proportion of females, structured interviews versus patient records for diagnosis, duration of illness, whether a strict control of a history of any psychiatric disorder was used, whether the sample included only schizophrenia or schizoaffective and schizophrenia disorder, symptom severity, proportions for psychotropic medicine use, and IQ and cognitive functioning scores for the schizophrenia-spectrum samples. The type of measure of anticipatory pleasure constituted another possible moderating variable, with studies categorised as using the TEPS or another measure of anticipatory pleasure. Notably, the TEPS refers to experiencing pleasure now from thinking about an upcoming event, and all other measures referred to experiencing pleasure in the future. Therefore, the influence of this distinction on effect sizes could be assessed for.

The results of meta-regression in schizophrenia-spectrum disorders showed two predictors: Longer duration of illness was predictive of larger deficits in anticipatory pleasure, unstandardized regression coefficient = -0.020 ($k = 18$, 95%CI = -0.035-0.004), $SE = 0.007$, $z = 2.56$, $p = .010$, and accounted for 39% of variance in the effect sizes (see scatterplot in Figure 5). Lower IQ in the patient sample also predicted larger deficits in anticipatory pleasure, unstandardized regression coefficient = 0.031 ($k = 11$, 95%CI = 0.009-0.053), $SE = 0.011$, $z = 2.85$, $p = .004$, and accounted for 50% of variance in the effect sizes

(see scatterplot in Figure 6). The remaining predictors were not statistically significant (see Supplemental File 1). A multivariate meta-regression was conducted using the two significant predictors, showing a significant overall effect for the model, $Q = 11.85$, $df = 2$, $p = .002$, and predicting 86% of variance in group differences in anticipatory pleasure. In this model, duration of illness was found to be a significant predictor at the trend level (unstandardized regression coefficient = -0.026 (95% CI = -0.055 - 0.002), $SE = 0.014$, $z = -1.77$, $p = .076$), and group difference in IQ score was a significant predictor (unstandardized regression coefficient = 0.067 ($k = 11$, 95% CI = 0.020 - 0.114), $SE = 0.024$, $z = 2.82$, $p = .004$). It is noted that this multivariate analysis only included seven studies from the complete sample, and therefore must be interpreted with caution.

For major depression, ruling out a history of any psychiatric disorder amongst control participants was associated with larger deficits in anticipatory pleasure, unstandardized regression coefficient = -0.625 ($k = 8$, 95% CI = -1.260 - 0.010), $SE = 0.324$, $z = -1.93$, $p = .053$, albeit not quite reaching the threshold of $p < .05$ for statistical significance, and accounted for 36% of variance between the effect sizes (see scatterplot in Figure 7). The remaining predictors were not statistically significant (see Supplemental File 1 for full results of meta-regression). It is cautioned here that the small number of studies means statistical power to detect effects was low, increasing the chance of a type II error. These results should therefore be interpreted as a preliminary estimation of possible effect sizes and associated confidence intervals.

Discussion

The results indicated that anticipatory pleasure was significantly lower in individuals with schizophrenia-spectrum disorders relative to controls. A small-to-moderate effect was

found, however, taking bias assessment into account, there was evidence that these effects were closer to small in magnitude. This suggests that a lack of significant group differences in some studies might be accounted for by small sample size and related lack of statistical power.

There was a moderate amount of heterogeneity between the study effects for schizophrenia-spectrum disorders. Meta-regression provided evidence that this might be accounted for a longer duration of illness and larger deficits in cognitive functioning in the patient samples being predictive of larger effects. In regards to duration of illness, this indicates that hedonic responses to thoughts of positive future events may diminish across the course of the illness. This is significant, given that anticipatory pleasure is linked with functional outcomes in schizophrenia (Foussias et al., 2011). This explains, in part, some of the occupational and social withdrawal observed in schizophrenia-spectrum disorders, however, on this latter domain other processes such as conceptualisations of social reward and punishment contingencies may also account for this (Fulford & Campellone, 2018). These findings provide some evidence that deficits in cognitive functioning might account, in part, for deficits in anticipatory pleasure in schizophrenia-spectrum disorders, possibly through difficulties in mentally-constructing and simulating possible future experiences. Future studies on anticipatory pleasure should report measures of cognitive functioning, and particularly executive functioning which seems linked to the higher-order task of episodic simulation (Addis, Hach, & Tippett, 2016). Interestingly, the severity of symptoms, and in particular negative symptoms, did not account for heterogeneity. This was despite there typically being significant variation in phenotypes of schizophrenia-spectrum disorders (Marneros et al., 1991). This suggests that deficits in anticipatory pleasure may be distinct from negative symptoms, and especially some such as alogia or affective flattening which

reflect lower emotional expression (Trémeau, 2006) and not necessarily internal emotional processes (Cohen & Minor, 2008; Llerena et al., 2006). The proportion of patients on first or second-generation antipsychotics did not significantly predict any variance in group differences in a subset of studies. The effects were in the direction that might be expected though if first-generation antipsychotics dampened reward prediction through reduced dopamine activity, and second-generation antipsychotics improved the capacity for anticipatory pleasure (Juckett et al., 2006). Any significant effects are likely to be small in nature though if more samples are included in future to increase statistical power.

Large effects were found for major depression, although heterogeneity was high. Collectively, these studies provide evidence that anhedonia in major depression, as a cardinal diagnostic criteria, relates to significant deficits in the ability to anticipate pleasure from future events. This builds upon previous research examining depressed patients' ability to generate positive future events (MacLeod & Byrne, 1996; MacLeod & Salaminiou, 2001), by indicating there are deficits in affective-motivational components as part of future thinking also. Some evidence was found that larger study effects were predicted by more stringent exclusion criteria for the control group involving a rule out of any historical psychiatric disorder, although this narrowly missed reaching the threshold for statistical significance. Evidence indicates that deficits in anticipatory pleasure are observed in subsyndromal/prodromal depression (Yang et al., 2014), and following the remission of depression (Thompson et al., 2017; Yang et al., 2014). This suggests that reduced anticipatory pleasure may be a cognitive-affective marker that is present before onset and following remission of depression, and therefore potentially a predictor of the course of the illness. Ruling out previous depressive episodes and subclinical depression in control groups in future studies of anticipatory pleasure should provide a more stringent test of the effect of

depressive disorders. Future research may also examine whether number of previous episodes predicts stronger deficits.

Activating and maintaining cognitive representations of experience are thought to be crucial for the anticipation of positive affect and reward (Kring & Caponigro, 2010). Schizophrenia-spectrum disorders and major depression are both associated with difficulties mentally-simulating possible future events (Hallford et al., 2018), and retrieving content in memory from which to construct these events (Berna et al., 2015; Liu et al., 2013). This less vivid and specific mental simulation has been linked with affective variables, such as apathy (Raffard et al., 2014), and subsequent motivation to engage in the imagined event or behaviour (Da Silva et al., 2017). Specificity in generating mental simulations of past events has been shown to predict the course of depressive illness (Sumner, Griffiths, & Mineka, 2010), and it may be interesting to examine whether this and difficulty generating specific mental simulations of future events might co-vary with anticipatory pleasure in predicting depressive illness over time. Some of these deficits are likely associated with general impairments in neurocognitive functioning (Heinrichs & Zakzanis, 1998; Rock et al., 2014), which is also supported by the findings here in a subset of samples with schizophrenia-spectrum disorders. However, additional factors may account for the effects, especially in major depression, such as relatively impaired dopamine signalling and reward for in-the-moment experience, which could impact on learning and subsequent anticipatory pleasure and selection of behaviours (Barch et al., 2015). While different mechanisms may underlie the type and cause of anhedonia in schizophrenia-spectrum disorders and major depression, these findings at least suggest common deficits in anticipatory pleasure, albeit of varying magnitude (Barch et al., 2015).

Another important consideration, not addressed in the current study, is how deficits in anticipatory pleasure might relate to consummatory pleasure. The deficits identified here may be reflective of reduced consummatory pleasure, in the sense that when experiences are less pleasurable they may be encoded as such, and then evoke less anticipatory pleasure when later thought about. As above, findings on consummatory pleasure appear more consistent for depression relative to schizophrenia-spectrum disorders, but in both cases this may be one possible explanation of reduced anticipatory pleasure. Another possibility has been identified by recent research indicating that reward learning, rather than simply reward experience, may be impaired in both schizophrenia-spectrum and depression (e.g., Kumar, Waiter, Ahearn, Milders, & Steele; Vrieze et al., 2013; see Whitton, Treadway, & Pizzagalli, 2015 for a review). This suggests that an individual may experience consummatory pleasure, but have a diminished capacity to effectively learn and encode the experience as being pleasurable. This would represent some level of dissociation in the experience of consummatory and subsequent anticipatory pleasure. The findings regarding cognitive functioning moderating effects in schizophrenia-spectrum disorder potentially support this explanation. The present findings are unable to disentangle these causal pathways, but rather indicates that self-reported anticipatory pleasure may be reduced in these disorders. Future studies may therefore examine deficits in self-reported consummatory pleasure, and the strength of association with anticipatory pleasure.

Increasing anticipatory pleasure for positive future events may improve motivation, rewarding behaviour, and psychosocial functioning. Although some clinical studies have specifically targeted positive mental imagery (Blackwell et al., 2015; Murphy et al., 2015), and observed effects on behavioural activation (Renner et al., 2017), these have not been for actual events that individuals might engage in their daily lives. Although conceptions

(Nguyen et al., 2016) and pilot studies (Favrod et al., 2010; Favrod et al., 2015) of such targeted interventions have emerged, applied research is still in early stages. Introducing mental simulations to induce an anticipatory hedonic response might prove to enhance treatments such as behavioural activation, however, this is yet to be investigated. Cognitive interventions that aim to increase specificity and detail in autobiographical memory (Raes et al., 2009), or are adapted for future thinking, might also have effects on anticipated pleasure.

Several limitations are noted. Most meta-regression analyses were conducted in subsets of samples, limiting the statistical power and generalisability to the overall sample. Although the results provide evidence that deficits in anticipatory pleasure do occur in major depression, the small number of studies, and high heterogeneity, limit the accuracy of the effect size estimate. Given the findings in schizophrenia-spectrum disorders, it would have been interesting to assess the role of cognitive functioning in anticipatory pleasure in major depression also, however, there were too few studies that reported this. The lack of studies on younger and older adults was another limitation. Future research might clarify whether deficits are found in these age groups also, and whether this larger range predicts more variance in differences in future meta-analyses. Future studies may parse the dimensions of *experiencing* pleasure from mentally simulating an event and *predicting* pleasure from a mentally simulated event more finely (e.g., see Baumgartner, Pieters, & Bagozzi, 2008). However, we maintain that these experiences mostly overlap phenomenologically, and meta-regression from this study showed no evidence of a difference in effect sizes based on this distinction.

A paucity of studies in other psychiatric groups meant no other meta-analysis could be conducted. More studies are needed in other diagnostic groups to ascertain if deficits are

found, and what role they might play in maintaining psychopathology. In particular, disorders that involve avoidance driven by anticipatory anhedonia for specific events, such as social anxiety disorder or avoidant personality disorder. Our search returned some studies on schizotypy personality traits which showed an association with lower anticipatory pleasure (e.g., Gooding et al., 2014; Yan et al., 2016). While these studies did not fit our criteria of diagnosed psychiatric disorder, their findings were consistent with the notion that these deficits may be observable on a continuum of schizophrenia-spectrum disorders.

Conclusion

The results showed evidence for deficits in anticipatory pleasure in schizophrenia-spectrum and major depressive disorders. For the former, there was a moderate amount of heterogeneity, explained in part by the duration of illness and cognitive functioning, and evidence was found for small study bias and a smaller, adjusted effect size. A small number of studies were found for major depression, and heterogeneity was high, but a large overall effect size was observed that was partially explained by the stringency of ruling out a history of psychiatric disorder in the control group. These findings provide the best current estimate of anticipatory pleasure deficits in schizophrenia-spectrum disorders and major depression, and indicate robust cognitive-affective deficits that are linked with behavioural outcomes, and represent a target for therapeutic intervention.

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Figure 1. Search Flowchart

Figure 2. Forest plot showing study and group-level effects, and sample sizes for all studies in the meta-analysis.

Figure 3. Funnel plot of studies in the schizophrenia-spectrum disorder sample plotted by standard difference in means and standard error. White dots indicated observed studies, and black dots indicate re-imputed studies that were estimated to be missing following the trim and fill procedure.

Figure 4. Funnel plot of studies in the major depressive disorder sample plotted by standard difference in means and standard error. White dots indicated observed studies studies, and black dots indicate re-imputed studies that were estimated to be missing following the trim and fill procedure.

Figure 5. Scatterplot of meta-regression indicating longer duration of illness in schizophrenia-spectrum disorders is associated with larger deficits in anticipatory pleasure.

Figure 6. Scatterplot of meta-regression indicating group differences in IQ is associated with larger deficits in anticipatory pleasure. Note: negative scores indicate lower scores in IQ the patient sample relative to the control sample.

Figure 7. Scatterplot of meta-regression indicating that ruling out a history of psychiatric disorder in the control group was associated with larger deficits in anticipatory pleasure in Major Depressive Disorder.

Table 1.

Details of Studies That Met Eligibility Criteria for the Systematic Review

Author (Year)	Clinical Group (N)	Mean Age (%) Female (N)	Control Group (N)	Age (%) Female (N)	Average Duration of Illness in Years	Diagnosis of Interest	Assessment of Diagnosis Used	Assessment of Anticipatory/Anticipated Pleasure	Criteria for Control Group	NOS Score
Barch et al., 2014	59	39 (42)	39	37 (51)	N/A	Schizophrenia (78%) or Schizoaffective disorder (22%)	Diagnostic interview DSM-IV-TR		Ruled out history of psychosis and bipolar disorder, did not rule out history of other psychiatric disorder	3
Bjärehed et al., 2010	20	39 (65)	20	39 (65)	N/A	MDD	Diagnostic interview DSM-IV-TR	TEPS-A Anticipated pleasure for possible positive future events generated using the Future Thinking Task (MacLeod et al., 1993). Single likert scale for each event - -3 to +3	Did not rule out history of any psychiatric disorder	2
Cassidy et al., 2012	91	25 (25)	91	25 (31)	3.4	Affective or non-affective psychosis	N/A	TEPS-A	Ruled out history of psychosis, did not rule out history of other psychiatric disorder	5

Da Silva et al., 2017	84	35 (41)	81	34 (44)	11.8	Schizophrenia (82%) or Schizoaffective disorder (18%)	Diagnostic interview DSM-IV-TR	TEPS-A	Ruled out history of psychosis, did not rule out history of other psychiatric disorder	4
Edwards et al., 2015	53	40 (37)	52	43 (26)	N/A	Schizophrenia	Diagnostic interview DSM-IV-TR	TEPS-A	Ruled out history of any psychiatric disorder	4
Engel et al., 2016	20	36 (50)	20	26 (47)	N/A	Schizophrenia (77.5%) or Schizoaffective disorder (17.5%)	Diagnostic interview DSM-IV-TR	11-point unipolar scale relating to positive emotions that might be felt in relation to a positive social event	Ruled out history of any psychiatric disorder	3
Fortunati et al., 2015	53	40 (40)	46	38 (50)		Schizophrenia	Diagnostic interview DSM-IV-TR	TEPS-A	Ruled out history of any psychiatric disorder	3
Gard et al., 2007 (Study 1)	15	42 (33)	12	36 (58)	N/A	Schizophrenia (67%) or Schizoaffective disorder (33%)	Diagnostic interview DSM-IV-TR	Likert scale to rate expected pleasure from events they were looking forward to	Ruled out history of any psychiatric disorder	3
Gard et al., 2007 (Study 2)	51	48 (29)	50	47 (50)	N/A	Schizophrenia (67%) or Schizoaffective disorder (33%)	Diagnostic interview DSM-IV-TR	TEPS-A	Ruled out history of psychosis and bipolar disorder, did not rule out history of other psychiatric disorder	4

Gard et al., 2014	47	39 (26)	41	37 (37)	N/A	Schizophrenia (70%) or Schizoaffective disorder (30%)	Diagnostic interview DSM-IV-TR	Likert scale to rate expected pleasure in relation to prompts through the day for upcoming goals	No evidence of ruling out history of any psychiatric disorderN	4
Garfield et al., 2017	12	36 (28)	33	36 (76)	N/A	Opioid dependence	Diagnostic interview DSM-IV-TR	TEPS-A (state version)	Did not rule out history of any psychiatric disorder	4
Gur et al., 2015	31	23 (32)	32	20 (59)	N/A	Schizophrenia	Diagnostic interview DSM-IV-TR	Items from the CAINS assessing expected pleasure for social, school, work, and recreation	Did not rule out history of any psychiatric disorder	6
Lee et al., 2012	14	30 (36)	16	30 (56)	7.9	Schizophrenia	Diagnostic interview DSM-IV-TR	TEPS-A	Did not rule out history of any psychiatric disorder	3
Li et al., 2015 (Study 1)	16	27 (46)	114	29 (46)	5.7	Schizophrenia	N/A	TEPS-A	Did not rule out history of any psychiatric disorder	2
Li et al., 2015 (Study 2)	75	24 (51)	78	25 (46)	3	Schizophrenia	N/A	TEPS-A	Did not rule out history of any psychiatric disorder	2
Li et al., 2015 (Study 3)	45	35 (44)	45	36 (33)	9.46	Schizophrenia	N/A	TEPS-A	Did not rule out history of any psychiatric disorder	2
Li, Mou et al., 2015	17	35 (45)	268	34 (49)	5.7	MDD	DSM-IV-TR diagnosis	TEPS-A	Did not rule out history of any	0

(Sample 1)							from hospital records		psychiatric disorder	
Li, Mou et al., 2015(Sa mple 2)	34 6	33 (48)	268	34 (49)	8.1	Schizophrenia	DSM-IV-TR diagnosis from hospital records	TEPS-A	Did not rule out history of any psychiatric disorder	0
Li, Yan et al., 2017	26	23 (42)	26	24 (42)	3.8	Schizophrenia	Diagnostic interview DSM-IV-TR	TEPS-A	Ruled out history of any psychiatric disorder	6
Lui et al., 2011	43	28 (56)	44	27 (52)	2.3	MDD	DSM-IV-TR diagnosis from hospital records	TEPS-A	Ruled out history of any psychiatric disorder	1
Lui et al., 2014	27	30 (59)	27	34 (55)	1.8	MDD	DSM-IV-TR diagnosis from hospital records	TEPS-A	Ruled out history of any psychiatric disorder	5
Lui et al., 2015	27	23 (54)	26	21 (30)	1.33	Schizophrenia	Diagnostic interview DSM-IV-TR	TEPS-A	Ruled out history of any psychiatric disorder	5
MacLeod & Salamini ou, 2001	22	59 (45)	22	55 (45)	N/A	MDD	ICD-10 diagnosis from hospital records	Anticipated pleasure for possible positive future events generated using the Future Thinking Task (MacLeod et al., 1993). Single likert scale for each event	Did not rule out history of any psychiatric disorder	0

Makowski et al., 2016	15	33 (26)	15	35 (40)	N/A	Schizophrenia	Diagnostic interview DSM-IV-TR	TEPS-A	Case control (no current or historical SCZ, BPAD, or MDD).	3
Mote et al., 2014	88	21 (23)	66	22 (43)	0-1 year	Schizophrenia, Schizoaffective, and Schizophreniform disorder	Diagnostic interview DSM-IV-TR	TEPS-A	Case control (no current mental illness or prior psychosis)	2
Mucci et al., 2015	28	33 (36)	22	32 (54)	N/A	Schizophrenia	Diagnostic interview DSM-IV-TR	TEPS-A	Case control (no current or historical mental illness)	6
Painter & Kring, 2016	32	48 (47)	39	47 (45)	N/A	Schizophrenia (62%) and Schizoaffective disorder, not current mood disorder (38%)	Diagnostic interview DSM-IV-TR	Predict emotional experience for simulated possible positive future events rated on a single likert scale for how positive it would be to experience	Case control (no current mental illness or prior psychosis)	4
Schlosser et al., 2014 (Sample 1)	67	21 (30)	29	17 (52)	1.8	Schizophrenia, Schizoaffective, and Schizophreniform disorder in last five years	Diagnostic interview DSM-IV-TR	TEPS-A	Case control (no current mental illness or prior psychosis)	5
Schlosser et al., 2014	78	43 (30)	29	17 (52)	22.3	Schizophrenia, Schizoaffective, and Schizophreniform	Diagnostic interview DSM-IV-TR	TEPS-A	Case control (no current mental	5

(Sample 2)						disorder over last five years			illness or prior psychosis)	
Simon et al., 2018	51	28 (45)	59	33 (69)	N/A	Schizophrenia (70%) or Schizoaffective disorder (30%)	Diagnostic interview DSM-IV-TR	TEPS-A	Case control (no current mental illness or prior psychosis)	4
Strauss et al., 2011	86	42 (34)	59	44 (44)	N/A	Schizophrenia (92%) or Schizoaffective disorder (8%)	Diagnostic interview DSM-IV-TR	TEPS-A	Case control (no current mental illness or prior psychosis)	4
Strauss et al., 2015	28	45 (32)	25	43 (36)	N/A	Schizophrenia	Diagnostic interview DSM-IV-TR	TEPS-A	Case control (no current mental illness or prior psychosis)	4
Subrama niam et al., 2015	37	45 (32)	20	44 (30)	25.4	Schizophrenia	Diagnostic interview DSM-IV-TR	TEPS-A	Case control (rules out not stated)	4
Tso et al., 2014 (Sample 1)	39	41 (41)	36	40 (36)	21.9	Schizophrenia (77%) or Schizoaffective disorder (23%)	Diagnostic interview DSM-IV-TR	TEPS-A	Case control (no current or historical mental illness)	4
Tso et al., 2014 (Sample 2)	24	41 (46)	36	40 (36)	24	BPAD (no current mood episode)	Diagnostic interview DSM-IV-TR	TEPS-A	Case control (no current or historical mental illness)	4

Vignapiano et al., 2016	30	34 (36)	23	32 (56)		Schizophrenia	Diagnostic interview DSM-IV-TR	TEPS-A	Case control (no current or historical mental illness)	6
Wang et al., 2015	40	34 (67)	29	32 (31)	11.1	Schizophrenia	Hospital records of diagnosis based on DSM-IV-TR	TEPS-A	Case control (no current or historical mental illness)	5
Wu et al., 2017	41	35 (78)	39	32 (82)	N/A	MDD	Diagnostic interview DSM-IV-TR	TEPS-A	Case control (no current or historical mental illness)	4
Wynn et al., 2010	34	44 (21)	36	38 (33)	24.3	Schizophrenia	Diagnostic interview DSM-IV-TR	TEPS-A	Case control (no current or historical mental illness)	4
Yang et al., 2014	46	27 (43)	50	26 (46)	N/A	MDD	Diagnostic interview DSM-IV-TR	TEPS-A	Case control (no current mental illness)	3
Yang et al., 2017	40	29 (53)	36	29 (47)	6.1	MDD	Diagnostic interview DSM-IV-TR	TEPS-A	Case control (no current or historical mental illness)	6
Zou et al. 2017	14 6	36 (44)	73	36 (51)	2.5	Schizophrenia	Diagnostic interview DSM-IV-TR	TEPS-A	Case control (no current or historical mental illness)	5

Note: BPAD = Bipolar Affective Disorder, CAINS = The Clinical Assessment Interview for Negative Symptoms (Kring et al., 2013), ICD-10 = International Classification of Diseases – 10th Edition, MDD = Major Depressive Disorder, NOS = Newcastle-Ottawa Scale (Wells et al., 2019), TEP-A = Anticipated pleasure subscale of the Temporal Experience of Pleasure Scale (Gard et al., 2006)

Supplemental File 1

Additional Results of Meta-Regressions for Schizophrenia-Spectrum Disorders

Moderator	<i>k</i>	<i>b</i>	<i>SE</i>	95%CI Lower	95%CI Upper	<i>z</i>	<i>p</i>
Mean age of sample	32	-0.007	0.007	-0.219	0.006	-1.04	.296
Number of females	32	0.005	0.005	-0.004	0.016	1.07	.283
Included schizoaffective and schizophrenia disorder	32	0.023	0.117	-0.205	0.253	0.20	.839
Diagnosis by structured interview versus patient records	32	-0.252	0.138	-0.522	0.018	-1.83	.067
TEPS or other measure used	32	-0.068	0.171	-0.403	0.267	-0.40	.690
Ruled out history of any psychiatric disorder in control group	32	-0.135	0.117	-0.366	0.095	-1.15	.249
PANSS Negative Symptoms	14	-0.014	0.017	-0.048	0.019	-0.83	.409
PANSS Positive Symptoms	14	0.015	0.023	-0.031	0.062	0.65	.516
PANSS General Symptoms	9	-0.001	0.004	-0.011	0.008	-0.27	.785
Total % taking antipsychotic	22	0.000	0.003	-0.005	0.007	0.20	.838
% taking first-generation antipsychotics	20	0.004	0.002	-0.000	0.008	1.67	.095
% taking second-generation antipsychotics	20	-0.003	0.002	-0.008	0.001	-1.30	.191
Chlorpromazine dose equivalency (mg/daily)	12	-0.003	0.000	-0.001	0.000	-0.46	.644

NOS Study Quality Score	32	-0.048	0.039	-0.125	0.028	-1.23	.218
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NOS = Newcastle-Ottawa-Scale, PANSS = Positive and Negative Syndrome Scale, TEPS = Temporal

Experience of Pleasure Scale