

A systematic review of cognition–brain morphology relationships on the schizophrenia–bipolar disorder spectrum

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Abstract

The nature of the relationship between cognition and brain morphology in schizophrenia-spectrum disorders (SSD) and bipolar disorder (BD) is uncertain. This review aimed to address this, by providing a comprehensive systematic investigation of links between several cognitive domains and brain volume, cortical thickness, and cortical surface area in SSD and BD patients across early and established illness stages. An initial search of PubMed and Scopus databases resulted in 1486 articles, of which 124 met inclusion criteria and were reviewed in detail. The majority of studies focused on SSD, whilst those of BD were scarce. Replicated evidence for specific regions associated with indices of cognition was minimal, however for several cognitive domains the frontal and temporal regions were broadly implicated across both recent-onset and established SSD, and to a lesser extent BD. Collectively, the findings of this review emphasize the significance of both frontal and temporal regions for some domains of cognition in SSD, whilst highlighting the need for future BD-related studies on this topic.

Keywords: neuroimaging, cognition, volume, cortical thickness, cortical surface area

1. Introduction

Schizophrenia-spectrum disorders (SSD), including schizophrenia (SZ) and schizoaffective disorder (SZA), overlap considerably with bipolar disorder (BD) despite nosological distinctions¹⁻⁶. Similar patterns of cognitive deficits⁷⁻¹¹ emphasize the proximity of these disorders on the psychosis-mood spectrum^{9,12-15}. Brain volume, thickness and surface area reductions are also common to both SSD^{16,17} and BD^{18,19}, with large scale ENIGMA mega-analyses indicating the largest effects in frontal and temporal regions^{20,21}. Nonetheless, it is unclear whether these morphological deficits are associated with poor cognitive performance, and if these associations are similar between SSD and BD.

Deviations from healthy brain morphology are likely to have a role in the cognitive impairments that are associated with these disorders¹². Empirical assessment of the relationship between cognition and brain morphology in each disorder has produced examples of inconsistent findings across numerous cognitive domains and brain regions²²⁻²⁷. Without a holistic perspective on the literature, it is unclear whether the discrepancies observed between findings are limited, or pervasive amongst the field. To better understand the extent to which brain morphology is associated with cognition in SSD and BD, there is a need for a *thorough* synthesis of the literature, and an explicit communication of replicated evidence regarding the nature of the relationship.

Existing reviews on the relationship between brain morphology and cognition in BD or SSD are either outdated^{28,29} or limited in *the number of* cognitive domains they examine³⁰⁻³². Generally these reviews suggest that poor cognitive performance is associated with *reductions* in brain morphology. However, this finding is not unanimous amongst studies, with some finding either negative associations between cognitive performance and brain

* The cognitive domains in these studies were limited to verbal memory (Antoniades et al., 2018), memory, attention, and executive function (Dusi et al., 2018), and working memory and attention (Ira et al., 2013).

volume or no association^{28-30,32}. Further, none of these reviews have comprehensively described a wide range of studies, cognitive domains, or the nature of cognition-brain morphology relationships in healthy comparison groups and how they compare to that of patients. These reviews have also not commented on the nature of relationships evident in recent-onset individuals versus those with established illness, which, in the absence of an abundance of longitudinal cognitive studies, is important to understanding the dynamics of brain-cognition relationships across the illness course.

To progress understanding of this area of research, we aimed to summarize the literature concerning cognition-brain morphology relationships in SSD and BD. We focussed on these disorders explicitly, due to strong evidence of their close proximity on the psychosis-mood spectrum⁸; and because this focus allowed for a more detailed investigation of the topic in these disorders than would have been the case if the scope of the review was broader. Specifically, this review aimed to: i) identify the brain volume, cortical thickness and cortical surface area characteristics associated with cognitive performance, and determine how consistent the evidence for these associations is in these disorders; ii) determine whether cognition-brain morphology relationships are consistent across illness stages by comparing studies of patients with recent-onset SSD or BD with those of established or chronic SSD and BD; and iii) examine cognition-brain morphology relationships in the healthy control samples accompanying the clinical samples, to identify whether the nature of these relationships differs between healthy and clinical populations.

2. Method

2.1 Search Strategy

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement³³. We searched the literature

published in the online databases of PubMed and Scopus after January 1st 1990 and before 1st of June 2020. The search syntax we employed was optimized for each database and based on three concepts: diagnosis, cognition, and brain morphology. Record type was limited to full-length, published empirical articles (see Supplementary Material).

2.2 Eligibility Criteria

Study eligibility was assessed at two stages of screening (Figure 1). At stage one, titles, abstracts, and keywords were screened by a single author and included if they met the following criteria: i) written in English and empirical in format; ii) included participants with recent-onset or established SSD (schizophrenia, schizoaffective disorder, schizophreniform disorder) and/or BD; and iii) examined both brain morphology and cognition. Recent-onset was defined by illness onset in the five years prior to assessment, whereas established or chronic was defined by illness onset greater than five years prior to assessment. Brain morphology was inclusive of regional *grey matter* only, or global estimates across the indices of volume, cortical thickness, and cortical surface area, with images recorded by structural imaging.

At stage two, two of the co-authors independently screened full-text articles. A record was eligible if: i) the patient sample's cognitive performance was examined in relation to brain morphology; ii) it included participant samples with a mean age under 65 years of age; iii) it contained independent samples of recent-onset or established BD or SSD; iv) 'cold' cognition (i.e. not social cognition or emotionally-relevant 'hot' cognition) was examined using objective measures (i.e. not subjective self-report measures); v) brain morphology included either grey matter volume, cortical thickness, cortical surface area, or wholistic assessments of brain volume such as total brain volume or intracranial volume; vi) the patient sample was not separated into cognitive subgroups and a univariate statistical approach to

associating cognition and brain morphology was used e.g., univariate correlations or regression. Additionally, in the instance that a sample had been analysed more than once, the article was only included if it involved a different brain measure. If a sample was published with overlapping methodologies and brain measures across papers, only the most comprehensive analysis was included in the review, if eligible. Further detail regarding the inclusion criteria rationale is provided in the supplementary material.

2.3 Evaluation of Study Quality

Information about the evaluation of study quality is presented in the supplementary material under ‘*Study Quality Evaluation*’ and in Table S1.

2.4 Data Extraction

The following information was extracted from all papers: participant demographics including age and sex, positive and negative symptom severity, cognitive domain(s) investigated, morphology index and brain regions, neuroimaging scanner type, covariates used in the analyses, and if there were significant differences in premorbid IQ, age, and sex between patients and healthy controls (Table 1).

To enable a clear synthesis of findings, the cognitive measures within each study were re-categorized by domain to reflect the consensus by the authors of all the studies included in this review (see Supplementary Table S2 for cognitive domain re-categorization). In other words, if a single study employed a measure to assess *attention*, but the majority of studies in this review employed that measure as an assessment of *speed of processing*, the results of that assessment were included under the latter domain. We reasoned that reclassification of cognitive assessments would reduce misinterpretation by the reader as a result of authors using the same cognitive measure to assess different cognitive domains, and thus this method

of recategorization allows for cognition-brain morphology relationships to be better compared across studies. For transparency, the complete cognitive assessments used by each study are summarized in Supplementary Table S3. It should be noted that the domain of *general memory* described below comprises different components of memory that could not be clearly categorized into either verbal or visual memory/learning, such as total scores from combined verbal and visual memory/learning performance.

3. Results

In the following sections we summarize *replicated* findings—those evident across two or more independent studies—of cognition-brain morphology relationships arranged by cognitive domain. Results presented in text are also organised by illness stage (recent onset, established). A rationale for the stratification of results is presented in the supplementary material. A complete and comprehensive review of *all* studies of brain morphology associated with each cognitive domain can be found in Table 1; cognition-morphology relationships identified in the current literature are also summarized and organized alphabetically by diagnosis and cognitive domain in Table 2.

It should be noted that the terms *positive* and *negative* associations are used frequently throughout the sections below to describe the relationship between cognition and brain morphology. In this review a positive association suggests that as cognitive performance increases, brain volume (or thickness or surface area) increases. In turn, a negative association suggests that as cognitive performance decreases, brain morphology increases (e.g. worse performance is associated with thicker cortices). It should be noted that the direction of the relationship reported here may be different to that stated in the original manuscript for some studies. In these instances, we have reversed the direction for ease of interpretation and comparability across measures, since better cognitive performance is

represented by low scores on some cognitive tests and high scores on others. Lastly, within the results section we emphasise and refer to studies as *large* if they comprised at least 100 participants within each independent group of the study (i.e. not studies with 100 participants made up of SSD *and* controls, but rather those with, for example, 100 SSD patients and/or 100 controls).

3.1 General descriptives

One hundred and twenty-four studies met criteria for inclusion in this review. Twenty-seven studies examined the relationship between cognition and brain morphology in recent-onset SSD (RO-SSD), of which 23 were cross-sectional studies, and four longitudinal in design. In contrast, 80 studies investigated these relationships in established SSD, where 77 of these were cross-sectional and three were longitudinal. Five studies investigated the relationship between cognition and brain morphology in recent-onset BD (RO-BD); of which four were cross-sectional and one longitudinal. In contrast, 18 studies examined these relationships in established-BD; all of which were cross-sectional. Across all diagnoses, 111 studies examined volume, 23 examined cortical thickness, and 11 examined cortical surface area. A visual summary of the number of studies examining each index of morphology for each cognitive domain and diagnosis can be found in Figure 2.

3.2 Evidence for consistent cognition-morphology relationships across domains in SSD and BD compared to controls.

A summary of the brain measures implicated in each cognitive domain, as indicated by their replication in at least two independent studies, is presented in Table 3. To be considered a replicated finding, an association between a cognitive domain and a brain measure needed to occur at a specific regional level (i.e. subregions of each lobe), but not

necessarily in the same direction, within the same illness stage and diagnostic group in two or more independent studies. Overall, the replicated findings detailed below were predominantly related to volume, and to a lesser extent, cortical thickness. In contrast, there were no replicated findings concerning cortical surface area. Below, comments about *general/broad* regions (i.e. at the level of the lobe) are only included to provide context and a broad overview of the regions involved, thus, references are only included for the association between cognitive domains and *specific* brain regions (i.e. in subregions of each lobe). For more detail and references pertaining to general regions and uncorroborated findings, please refer to Supplementary Material Section 1 and Table 2.

3.2.1 Attention

In seven independent RO-SSD studies, there was general evidence of positive associations with volume of the frontal region, and mixed positive and negative associations in parietal and subcortical regions. Only the postcentral gyrus *specifically*, was replicated between studies in RO-SSD ^{34,35}; however, the findings were mixed in directionality (positive *and* negative). Two of the three longitudinal RO-SSD studies reported that other cognition-morphology relationships emerged over time, where associations between attention and either parietal or subcortical regions were absent at baseline and present at follow ups between 1–4 years later ^{34,36}. In 14 independent established SSD samples, the frontal, temporal, and parietal lobes were repeatedly implicated across studies, although no specific sub-regional association was reported more than once. In turn, only a single study in either RO-BD and established BD cohorts examined the relationship between attention and morphology, and thus replicated evidence remains to be found. In the control samples included in recent-onset and established SSD and BD studies, there was a general absence of significant relationships.

3.2.2 *Executive Function*

Twelve RO-SSD studies reported a mix of positive and negative associations between executive function and temporal, frontal, subcortical, cerebellum, and basal ganglia regions, broadly; no specific regions were associated in more than one study. In 33 established SSD samples, the findings were far more consistent, generally indicative of positive relationships between executive function and morphology of frontal and temporal lobes, and parietal and subcortical regions, the cerebellum, and total brain volume, albeit not total grey matter volume. Specific regions positively associated with executive function include inferior frontal gyrus volume and thickness³⁷⁻³⁹, volume of the left anterior hippocampus^{40,41}, left and right hippocampus^{41,42}, left inferior frontal gyrus^{39,43}, left middle frontal gyrus^{44,45}, prefrontal cortex^{27,46}, and right middle frontal volume and thickness^{37,47}, and a mixed association with left posterior hippocampus^{41,48}—of the studies reporting these associations, only one was considered a large study by the standards stated in section 3 (Results)⁴⁰. Of the three studies including a RO-BD cohort, regions of the parietal lobe were positively implicated in two studies, unlike in the eight established BD samples, in which broad associations were predominantly identified between executive function and frontal-temporal regions. However, no specific regions were replicated in either recent-onset or established BD cohorts.

In control samples accompanying both recent-onset and established cohorts, there was *no evidence* for a relationship between executive function and brain morphology either broadly or in specific regions. Multiple studies indicated an *absence of associations* with frontal, temporal and subcortical regions, and with both total brain volume and total grey matter volume.

3.2.3 *General memory*

Seven of the nine studies examining morphology-cognition relationships that fit under the domain of general memory were in established SSD cohorts, to which right hippocampus volume was positively associated with general memory performance in three studies ⁴⁹⁻⁵¹. One study examined general memory in a recent-onset SSD sample, albeit findings were not comparable between the remaining two BD studies. Generally, there was an absence of associations between general memory and brain morphology in control comparisons samples; replicated findings across three studies suggested *no association* specifically with the right hippocampus ⁴⁹⁻⁵¹.

3.2.4 *Intelligence/global cognition*

The frontal and temporal lobes were both implicated in intelligence/global cognition in three of the nine studies of RO-SSD, with no region specificity evident in more than one study. Of the 26 established SSD samples, two studies indicated an absence of association with intelligence/global cognition and the cingulate cortex broadly, and the remaining studies reported mixed (positive and no association) relationships in frontal, temporal, cerebellum, and insula regions. Despite these mixed findings, positive associations were identified with the hippocampus in two studies ^{52,53}, of which one was considered to be large ⁵⁶. Total grey matter volume correlated positively with various indices of intelligence/global cognition across four SSD studies ⁵³⁻⁵⁶; of which one was large in size ⁵⁵. In RO-BD, only a single study examined this domain, and in established BD the only consistent findings amongst the seven studies suggested *no association* between current intelligence/global cognition and volume of any region in the brain ^{57,58}.

In control samples accompanying the recent-onset studies, the only replicated finding was that there was *no association* between intelligence/global cognition and total grey matter volume or broadly in the frontal region ^{24,25}. In the healthy cohorts accompanying established

samples, there was a mix of positive, negative, and absent associations in the temporal lobe; furthermore, 15 independent studies reported *no association* between intelligence and brain morphology, across regions such as the frontal region, cerebellum, cingulate cortex, or with total grey matter volume or any region in several whole brain analyses.

3.2.5 *Speed of processing*

In six RO-SSD cohorts, there were no brain regions broadly or specifically implicated in speed of processing in two or more studies. The only replicated finding in RO-SSD patients was that there was *no* relationship between cerebellum volume and speed of processing performance^{59,60}. In contrast, in established SSD the majority of relationships of the 16 studies were positive in direction and most commonly reported in temporal regions, and with regions of the frontal lobe, cerebellum, and total grey matter volume. Nonetheless, specific positive relationships with speed of processing were reported with morphology surrounding the middle frontal region^{45,61} and cerebellum volume^{62,63}—of the studies reporting these relationships, only one was considered to be large⁶³. Only single studies examined speed of processing performance in RO-BD and established BD cohort, and thus replicated evidence remains to be found. Few control comparison samples were included in studies of recent-onset patients—whilst there were no specific replicated findings, several studies found a general positive association with the frontal region and no association with the cerebellum, temporal region, and with total grey matter volume.

3.2.6 *Verbal Fluency*

Two studies examined verbal fluency and both were in established SSD cohorts; there was mixed evidence of associations in frontal regions in both patients and controls. Given the

limited evidence available, the nature of the relationship between this domain and brain morphology is particularly unclear.

3.2.7 *Verbal memory/learning*

In seven RO-SSD studies, there was preliminary evidence to suggest that the temporal region may be positively associated with verbal memory/learning, however, some studies employing whole brain analyses reported no association^{64,65 64,65}. From 29 established SSD cohorts, there was replicated evidence implicating total grey matter volume and the temporal, frontal, subcortical and parietal lobes broadly. Evidence for the specific involvement of the hippocampus was strong and consistent, as several studies reported positive relationships with left^{49,66,67}, right^{41,42,67,68}, and total hippocampus volume^{53,69,70}—these studies were all large in size. Both left amygdala^{42,71} and left prefrontal cortex^{27,46} were also implicated across two studies each, although the findings relating to the amygdala were mixed in direction. Some studies implicated the temporal lobe in verbal memory/learning in both RO-BD and established BD cohorts^{68,72-75}—of which one was considered to be large⁷⁸. Contrary to the SSD cohorts, there was no replication of specific brain regions in either two recent-onset or six established BD cohorts. In the control samples accompanying both recent-onset and established SSD and BD cohorts, there was a general absence of associations across 24 independent studies between verbal memory/learning and the brain morphology measures assessed, with no association with total grey matter volume or regions of the temporal and frontal lobes.

3.2.8 *Visual memory/learning*

From five RO-SSD studies, the only finding replicated was that there was *no association* between visual memory/learning and volume of any region of the brain in their

global analyses^{64,76} (note that one of these studies was large in size)⁷⁹. In established SSD, findings regarding the temporal regions were mixed (eight positive associations, two negative, and eight reported no association). Additionally, the frontal region was also broadly and positively implicated, whilst there appeared to be *no association* between visual memory/learning and the cerebellum. At the regional level, mixed (positive *and* absent) relationships with amygdala^{42,71} and hippocampus volume^{69,70} were reported in more than one study— of which one was considered to be large⁶⁹. There was also evidence to suggest an absence of association with left hippocampal volume^{42,68}, as well as a positive relationship with total prefrontal cortex^{46,77}. In contrast, there were no studies examining brain morphology in relation to visual memory/learning in RO-BD, while in established BD the only replicated evidence from four studies suggested *no association* with the temporal region, broadly. In the accompanying control cohorts, a positive relationship with total prefrontal cortex was also consistently evident^{46,77}. Furthermore, there was an *absence of associations* with total grey matter volume and regions of the temporal lobe broadly, as well as the left hippocampus^{42,68,78}, right hippocampus^{42,68}, and right amygdala^{42,71} specifically.

3.2.9 Working memory

In seven independent studies of RO-SSD, within the frontal lobe, only associations in the superior frontal region were evident across more than one study^{79,80}. A similar pattern was amongst the 23 established SSD studies, with frontal regions implicated but the direction of associations mixed and no specific frontal region implicated in more than one study. Mixed associations were found with several temporal regions, but the right anterior hippocampus was the only specific region repeatedly associated with working memory in multiple studies, albeit, in both positive⁴¹ and negative directions⁴⁸. Further replicated evidence included a positive association with cingulate cortex broadly, and no association

with total grey matter volume^{53,81} or volume of the thalamus^{82,83}. Of these studies, one was considered to be large in size⁵⁶. There was insufficient evidence across four studies to suggest a relationship between working memory performance and brain morphology in established BD patients, and no studies investigated working memory in RO-BD. In the control samples accompanying both recent-onset and established cohorts, there were no consistent findings to suggest a relationship between working memory and brain morphology. Rather, the findings predominantly indicated that there was no association with any measure at all, with the exception of a negative relationship with the left middle frontal gyrus^{84,85}.

4. Discussion

The aim of this review was to synthesize the available literature regarding the relationship between cognition and brain morphology in studies of recent-onset and established SSD and BD to address three key questions: 1) what are the brain morphological characteristics associated with the cognitive domains known to be impaired in SSD and BD, and how consistent is the evidence? 2) how consistent is the relationship between cognition and morphology between recent-onset and established patients, and between BD and SSD patients? and 3) how do cognition-morphology findings in patients compare to controls?

The most consistent finding from existing studies was the involvement of either frontal or temporal regions across all cognitive domains in SSD. While positive associations with the hippocampal region were commonly reported across cognitive domains concerning memory, executive function, and intelligence, the most consistent evidence for a relationship between cognition and brain morphology was found between hippocampal volume and verbal memory/learning in SSD. This aligns with earlier reviews on this topic^{29,30}. In contrast, there was limited replicated evidence in both recent-onset and established BD, as demonstrated

previously³¹. In controls, the replicated evidence generally indicated an absence of a relationship with brain morphology across all cognitive domains. In both SSD and BD, the replicated evidence was predominantly positive in direction and related to volume, and to a lesser extent, cortical thickness; although this may be a product of the vast majority of the studies examining volume. Relevantly, no replicated evidence was identified in relation to cortical surface area.

In the RO-SSD and SSD studies that reported symptom severity, 83% indicated either mild positive or negative symptoms, while 86% of BD studies considered patients to have mild mood symptoms or be affectively stable/euthymic. The vast majority (93%) of MRI scanners used in studies included in our review were also either 1.5T or 3T in strength, suggesting a high degree of comparability in findings in terms of the quality of images produced. Further, the majority (61%) of studies included age as a covariate, and our results were also classified by ‘recent-onset’ and ‘established’ illness duration. Notably, only a small number of studies reported significant differences in age (21%) or sex (12%) between patients and controls. Thus, at a general level, it is unlikely that the aforementioned patient characteristics or MRI scanner strength are confounding factors in our interpretation of the results.

4.1. Dynamics of cognition-morphology relationships in SSD and BD

The limited research available on cognition-brain morphology relationships in recent-onset and established BD samples meant that conclusions regarding the dynamic nature of these relationships in BD could not be drawn. In contrast, the comparatively larger literature in RO-SSD and established SSD patients suggest that the involvement of the frontal lobe in the domain of attention remains stable across the illness course. While inferences regarding the dynamics of brain morphology-cognition relationships could not be made for visual

memory/learning or verbal fluency due to the paucity of studies in RO-SSD patients, evidence suggests there may be dynamic changes in links between brain structure and cognition across several other domains. These include **i) *speed of processing***, where there were no consistent associations in recent-onset patients, but associations with fronto-temporal regions and the cerebellum appeared to develop as the illness became more established; **ii) *verbal memory/learning***, in which temporal region associations were evident early in the illness course and became more focused towards the hippocampus with illness progression; **iii) *intelligence/global cognition***, with both frontal and temporal involvement evident early in the illness course, and temporal associations remaining stable across illness stages but global grey matter volume becoming prominent in established SSD cohorts; and **iv) *working memory***, with frontal involvement evident from onset but extending into temporal regions in established SSD cohorts. A differing pattern was evident for **iv) *executive function***, where temporal involvement was evident early in the illness course but expanded into frontal regions in established SSD cohorts.

The aforementioned findings suggest that the association between cognitive performance and both frontal and temporal lobe morphology becomes more evident as SSD progresses. Such dynamic relationships were most evident in measures of brain volume, and to a lesser extent cortical thickness; however, this may be a product of the disproportionate number of studies on each measure. More research in recent-onset cohorts is needed to enable explicit comparison of effect-sizes in established cohorts to elucidate if this association strengthens or weakens over time. Nonetheless, the apparent lack of association between speed of processing and deficits in brain morphology at an early stage of illness may make it a relevant target of cognitive remediation, as early brain training may protect from brain related deterioration over time. Cognitive remediation has shown reliable improvements in cognition in SSD, and to a lesser extent, BD, with growing evidence of brain changes due to

brain plasticity¹⁰⁷⁻¹⁰⁹. Furthering such research would be important to ensure the findings reported here can be translated to clinical practice.

4.2. *Overlap in cognition-morphology relationships across BD and SSD*

With 70 studies examining volume in SSD across all domains and only 14 in BD (see Figure 2), there was a clear imbalance in research on this topic across the disorders of interest. Nonetheless, the existing evidence suggests similar associations between fronto-temporal regions and executive function, and the temporal lobe and verbal memory. However, the replicated evidence of no association with any morphological brain measure in visual memory/learning and intelligence in established BD, contrasts the repeated associations seen for these domains with fronto-temporal brain regions in SSD.

This discrepancy may be related to differences in the use of medications between disorders, as there is growing evidence to suggest that lithium, a first-line treatment for BD, has neuroprotective properties^{86,87}. Lithium use may have normalized or reduced the presence of brain morphology or cognitive deficits in the BD cohorts, restricting the range of variability. Similarly, the cumulative use of antipsychotic medication in the SSD cohort could have exacerbated brain morphology and cognitive deficits. Medication data was not examined in this review, however, it remains an important point of consideration for future work.

4.3. *Similarity of the cognition-morphology relationship between patients and controls*

Generally, the cognition-brain morphology relationships that were consistent in recent-onset or established SSD and/or BD patients were not evident in the control samples accompanying them (see Table 3). The exceptions to this were the associations seen in *established* SSD patients between visual memory or speed of processing and either the

volume or thickness of frontal cortex, and intelligence/global cognition and the temporal region—associations that were similarly observed in the accompanying control cohorts.

The absence of consistent associations between temporal regions and verbal memory, and frontal regions and executive function in controls is contrary to several examples of general population cohort studies which show these associations⁸⁸⁻⁹². However, there are also several other similar studies in which associations between these measures are not evident⁹³⁻⁹⁵. In combination with the findings of this review, these studies raise questions about the extent to which brain morphology is relevant to certain forms of cognition in healthy individuals.

Potentially, there are underlying processes in healthy individuals that lessen the relevance of brain morphology to cognition compared to those with SSD and BD. There is some evidence that crystallized intelligence—a proxy of cognitive reserve—is associated with both better cognition *and* preservation of brain volume in healthy people⁹⁶⁻⁹⁸. In contrast, cognitive reserve may buffer the impact of age-related brain deterioration on cognition in SSD, such that associations between cognition and brain volume are more prominent in those with low cognitive reserve⁹⁹. If resistance and resilience processes within the brain are different between psychiatric disorders and controls, it may explain why there are divergent results between studies examining cognition and brain structure. Indeed, compared to controls, crystallized intelligence (i.e. cognitive reserve) is often lower in SSD^{100,101} and in a proportion of individuals with BD^{8,9,100,102}. This reduced cognitive reserve (and reduced resilience) may explain why associations between brain morphology and cognition in these psychiatric cohorts are more readily observed. An alternative explanation for the relative absence of associations between brain morphology and cognition in healthy controls may be that there is reduced variance (i.e. restriction of range) in these variables in controls—perhaps related to ceiling effects on cognitive tasks—that renders associations less

observable. In contrast, clinical, cognitive and brain morphology in SSD and BD appear to be highly heterogeneous^{8,103-106}. Future research on this topic would do well to explicitly interrogate these possibilities further.

4.4. Summary, limitations and future directions

This review included 124 studies covering recent-onset and established SSD and BD. The different methods of ascertaining estimates of brain morphology or analysing their association with cognition made for a complex task in synthesizing the literature. Of note was the varied use of different brain atlases and vertex-wise approaches or region of interest approaches across studies, which made it difficult to ascertain the regional specificity of findings or the full extent to which relationships with cognition were present or absent across the brain. Sample size also varied considerably amongst studies. However, a targeted examination of the 17 studies with patient populations greater than 100 did not reveal any associations that were characteristically different from our initial findings—that is, whilst the majority of relationships were positive in direction, negative and no associations were still present. Finally, covariates differed between studies; and approximately one third of the studies did not apply statistical correction or did not make it clear what form of correction (if any) was applied. This brought forth difficulties in comparing findings and raises concerns about the potential for hidden type I errors amongst the literature.

Nevertheless, we identified some consistent findings to suggest that most cognitive domains are associated with frontal and temporal brain regions, and the hippocampus in SSD. With respect to subregions, consistent associations (indexed by replication across at least two independent studies) were most clearly evident between hippocampal regions and verbal memory/learning in SSD, but not the frontal cortex. The comparison of findings in recent-onset and established SSD patients indicated that there may be dynamic brain changes

associated with the domains of speed of processing, verbal and working memory, executive function and intelligence/global cognition—as associated brain regions were circumscribed early in illness course, but more widespread in later stages. Conversely, the link between cognition and morphology was not as clear, and in some cases entirely absent, in BD studies; however, this may be a product of the considerably fewer BD studies. As a result, substantiated conclusions regarding the nature of cognition-brain morphology relationships at early or established stages of BD are difficult to make. Indeed, the only effects that appeared to be somewhat consistent across the limited studies were associations between fronto-temporal brain regions and verbal memory/learning and executive function.

In control samples there was no evidence to suggest that cognition-brain morphology associations manifest uniquely in a particular brain region. Rather, an overlap was evident between controls and patients (both recent-onset and established) regarding frontal and temporal regions and visual memory/learning, speed of processing and intelligence/global cognition. Despite this, generally, the associations of brain morphology and most domains that were evident in patients were not evident in controls. However, not all studies included control subjects. Thus, future studies should include healthy comparison groups as a means of identifying if and how cognition-brain morphology relationships in SSD and/or BD deviate from the norm.

Across the measures of volume, cortical thickness, and cortical surface area, it was clear that volume was the most important and well researched measure to the cognition-brain morphology relationship. Whilst there was a significantly greater proportion of studies that investigated volume relative to both cortical thickness and surface area, generally speaking, it was still evident that the majority of cortical thickness associations were positive in direction, whereas the majority of studies of surface area indicated no association with cognition. As

cortical thickness and surface area are the constituent measures of cortical volume, this may suggest that cortical thickness may be the driving force behind any volume-related findings.

In sum, although the variability in study methodology inhibits a clear understanding of the relationship between cognition and brain morphology in SSD and BD, the literature reviewed here collectively emphasizes the importance of both frontal, temporal, and hippocampal regions with respect to most cognitive domains, particularly in SSD patients. In interpreting the findings of this review however, several points should be considered. First, while white matter was excluded as an aspect of brain morphology to help focus the synthesis, it remains an important constituent of the brain and should be considered in future reviews. Inclusion of this measure in future work will aid our understanding of the cognition-brain morphology relationship, especially in the context of findings where total brain volume, but not total grey matter volume, significantly associate with cognitive performance. Second, we did not stratify the results of the literature search by studies with and without statistical correction or those that included or did not include a control group. However, detail regarding whether statistical correction was applied for each study or whether a control group was included is presented in supplementary Table 1 and included in our evaluation of the quality of each study. Third, while the qualitative synthesis of findings completed here allowed for the inclusion of a diverse range of patient characteristics (e.g., ages, symptom severity, mood states) and methodologies (cognitive measures, neuroimaging techniques, and statistical analyses), this was at the cost of the increased objectivity that comes with quantitative meta-analyses. Hence, while this review identified evidence of consistency in the *presence* of cognition-brain morphology associations, future work should endeavour to ascertain the *magnitude* of effects.

Fourth, although a majority of BD studies included participants with mild mood symptoms or who met criteria for euthymia/remission, there remains a possible confounding

influence of mood state on the outcomes of those studies. We also did not consider other clinical and demographic factors, such as the presence of comorbidities, medication status, or BD psychosis history in our inclusion/exclusion criteria or stratification of results. Whilst this was done in the interests of being comprehensive in our review of the literature, these factors are important considerations that speak to cohort variability. Hence, our findings should be considered as a general representation of the nature of relationships between brain morphology and cognition in SSD and BD broadly. Future reviews on this topic should aim for a more detailed understanding of the impact and nuances of patient variability on relationships between cognition and brain morphology. In relation to this, future research seeking to examine the literature more comprehensively could consider examining more than two databases in the literature search, which some may consider to be a limitation in the methods of this review. To this point, another limitation of our review was the use of only one author conducting title and abstract screening—a logistical issue rather than by design. It is important to consider that screening by a single author does increase the risk of overlooking relevant studies to include in the review.

Finally, this review focused on SSD and BD to limit its scope and because there is strong evidence of an overlap in cognitive and brain morphological abnormalities in these disorders^{9,13,14}. Notably, the term SSD as it is defined in this review, is heterogenous, in that it encompasses schizophrenia, schizoaffective disorder and schizophreniform disorder. The classification of these disorders under the broader umbrella term of SSD was done for practicality purposes, but this does limit our understanding of the nuances associated with each of these separately recognised disorders in the context of relationships between the brain and cognition. Furthermore, there remain other disorders on the mood-psychosis spectrum, including major depressive disorder, that like BD, can also present with cognitive impairments and even psychotic features. Thus, future reviews would do well to examine the

relationships between brain morphology and cognition in other psychosis-mood spectrum disorders as well, to understand similarities and differences with SSD and BD.

Conflict of Interest

The authors declare that there are no conflicts of interest in relation to the subject of this study.

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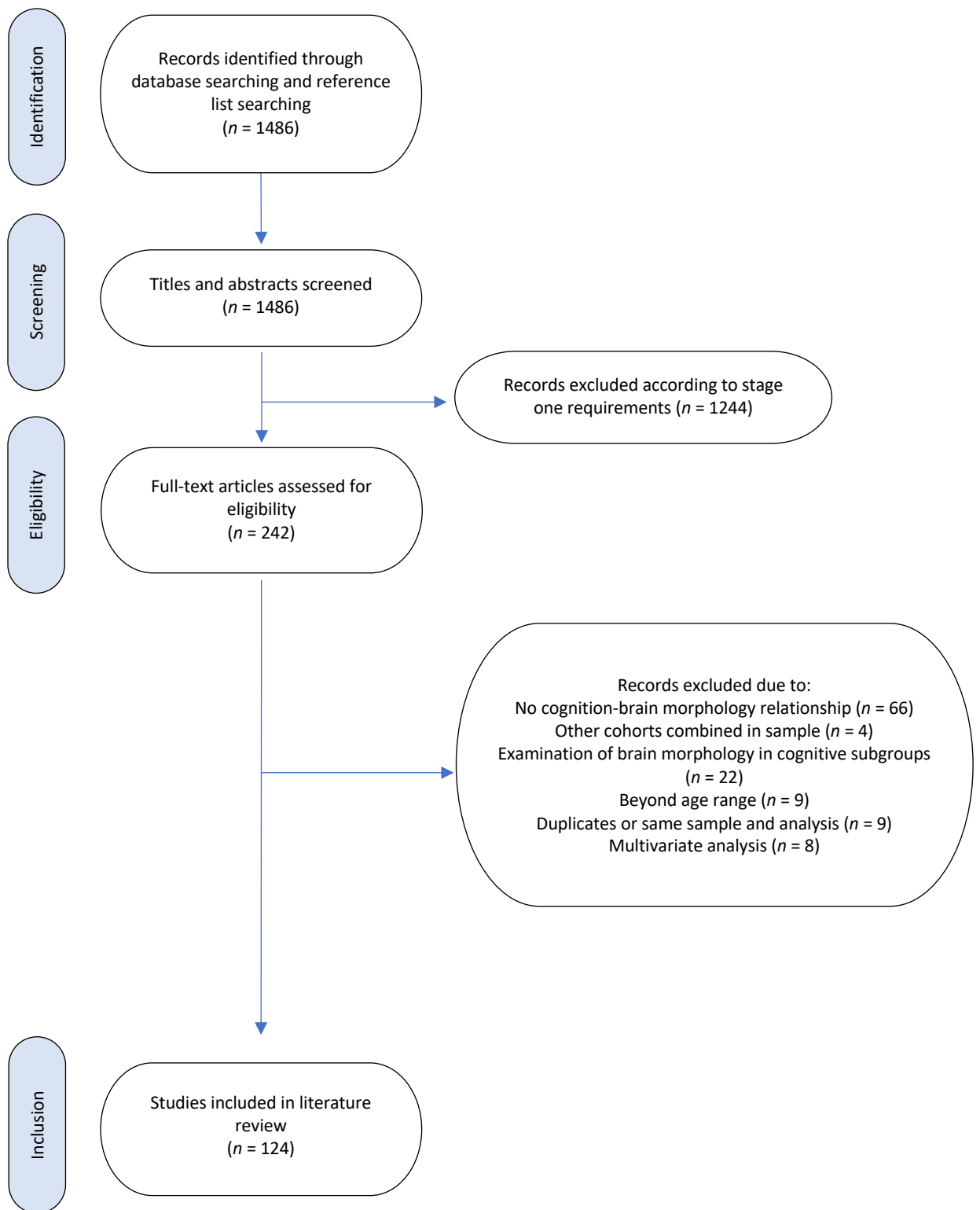


Figure 1. Flowchart of study selection.

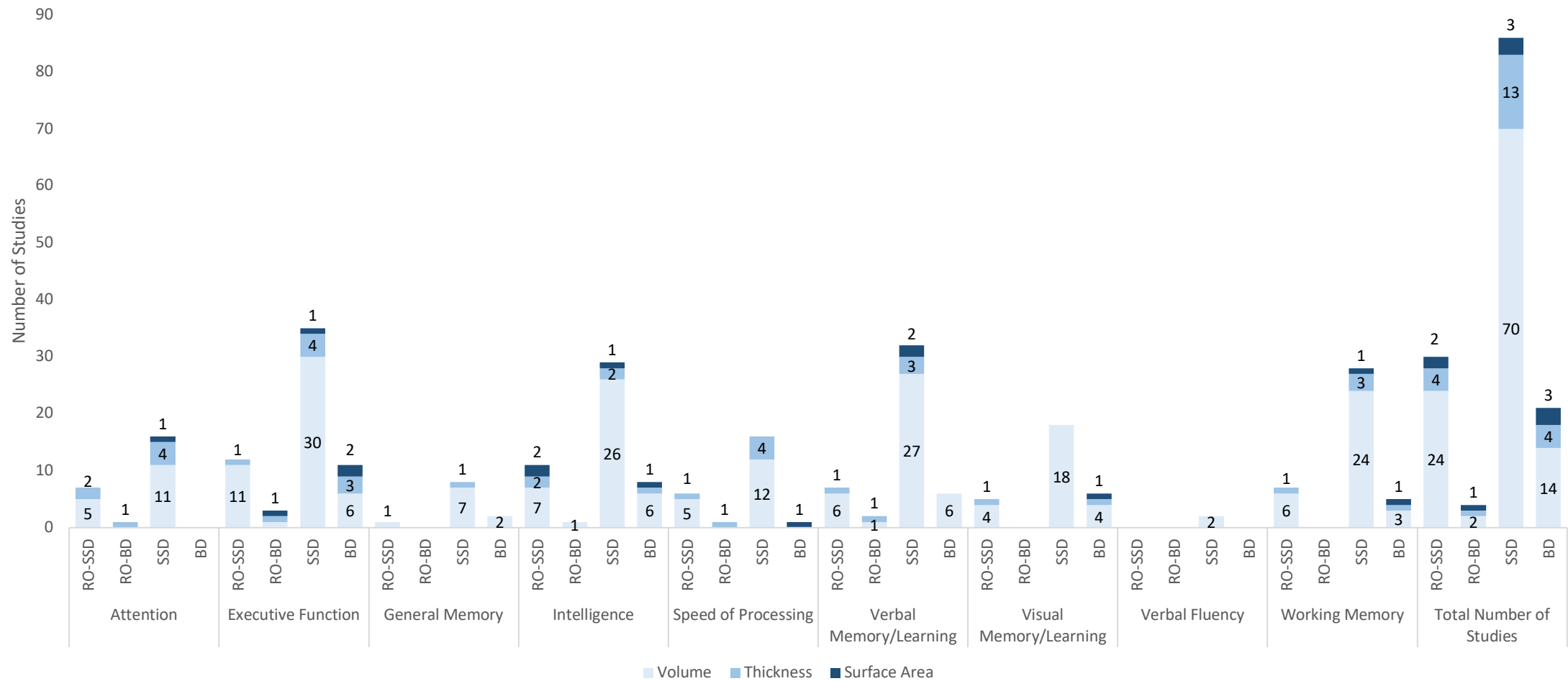


Figure 2: Summary of the number of studies examining each index of brain morphology, per cognitive domain for each disorder.
Note. BD, bipolar disorder; HC, healthy control; RO, recent-onset; SSD, schizophrenia-spectrum disorder.

Table 1: Summary of studies

| Reference | Cohort (#, Dx, Mean age ± SD, M/F) | Symptoms | Cognitive Domain | Neuroimaging | Longitudinal Follow Up | Notes |
|-----------|---|--|---|---|------------------------|---|
| 1 | 49 BD I (39.9 ± 12, 25/24) 28 BD II (38.14 ± 12, 9/19) 83 HC (39 ± 14.8, 40/43) | Manic Symptoms: Mild Depressive Symptoms: Mild | Executive Function | Scanner Strength: 1.5T MRI Morphology: Thickness Brain Region: Whole brain Neuroimaging Analysis: Vertex-wise | NA | Covariates: Sex pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 2 | 202 SSD (24.56 ± 7.14, 184/54) 312 HC (29.69 ± 8.37, 66/59) | Positive Symptoms: NA Negative Symptoms: NA | Verbal Memory/Learning, Attention, Executive Function, Working Memory, Verbal Fluency, Speed of Processing | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI | Follow up: 7.2 years | Covariates: None pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA Large study |
| 3 | 36 SSD (36.4 ± 10.2, 22/14) 28 HC (36.1 ± 10.9, 17/11) | Positive Symptoms: Mild Negative Symptoms: Mild | Verbal Memory/Learning, Visual Memory/Learning, Working Memory | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Thalamus Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 4 | 45 SSD (40.49 ± 11.67, 27/18) 45 HC (33.72 ± 12.37, 25/18) | Positive Symptoms: Moderate Negative Symptoms: Moderate | Premorbid IQ, Current IQ, Verbal Memory/Learning, Visual Memory/Learning, Memory (other), Working Memory, Executive Function, Attention, Verbal Fluency | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: VBM | NA | Covariates: Age, Sex pIQ diff HC: Yes Age diff HC: Yes Sex diff HC: No |
| 5 | 14 SSD (28.5 ± 5.7, 14/0) 14 HC (26.9 ± 5.9, 14/0) | Positive Symptoms: Mild Negative Symptoms: Mild | Verbal Memory/Learning, Visual Memory/Learning, Executive Function, Intelligence | Scanner Strength: 0.5T MRI Morphology: Volume Brain Region: Frontal lobe Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 6 | 29 SSD (25.2 ± 5.7, 18/11) | Positive Symptoms: NA Negative Symptoms: NA | Visual Memory/Learning, Visual Memory/Learning, Speed of Processing, Executive Function, Memory, Attention, Intelligence, Global Cognition | Scanner Strength: 1.0T MRI Morphology: Volume Brain Region: Mesiotemporal lobe Neuroimaging Analysis: ROI | NA | Covariates: Temporal lobe pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |
| 7 | 14 SSD (40.0 ± 7.0, 11/3) 13 HC (35.0 ± 8.0, 11/2) | Positive Symptoms: NA Negative Symptoms: NA | Executive Function, Speed of Processing, Verbal Fluency | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Prefrontal Cortex Neuroimaging Analysis: ROI and VBM | NA | Covariates: Age pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 8 | 54 RO-SSD (23.9 ± 6.2, 35/19) 41 HC (24.8 ± 6.35, 25/16) | Positive Symptoms: Mild Negative Symptoms: Mild | General Memory | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Hippocampus Neuroimaging Analysis: ROI | NA | Covariates: Age, Sex, ICV, Smoking pIQ diff HC: NA Age diff HC: No Sex diff HC: No |

| Reference | Cohort (#, Dx, Mean age ± SD, M/F) | Symptoms | Cognitive Domain | Neuroimaging | Longitudinal Follow Up | Notes |
|-----------|---|---|---|--|------------------------|--|
| 9 | 25 BD I (37.4 ± NA, 10/15) 11 BD II (42.8 ± NA, 3/8) | Manic Symptoms: NA Depressive Symptoms: Mild | Premorbid IQ, Current IQ, Verbal Memory/Learning, Visual Memory/Learning, Executive Function, Working Memory | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: VBM | NA | Covariates: Age, Sex pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |
| 10 | 133 SSD (29.98 ± 5.79, 106/27) 113 HC (29.76 ± 8.01, 54/59) | Positive Symptoms: Mild Negative Symptoms: Mild | Current IQ, Memory | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Insula Neuroimaging Analysis: ROI | NA | Covariates: Age, Sex, ICV, Substance Abuse pIQ diff HC: NA Age diff HC: No Sex diff HC: Yes Large study |
| 11 | 65 SSD (47.6 ± 5.1, 32/33) 53 Concordant Twins (47.7 ± 4.6, 29/24) 118 HC (48.6 ± 6.9, 58/60) | Positive Symptoms: Mild Negative Symptoms: Mild | Working Memory, Attention, Speed of Processing, Verbal Fluency, Verbal Memory/Learning, Visual Memory/Learning | Scanner Strength: 1.0T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI | NA | Covariates: Age, Sex, SES, Substance Abuse pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 12 | 48 BD I (41.02 ± 16.65, 16/32) 33 MDD (39.17 ± 12.42, 10/23) 60 HC (40.57 ± 12.95, 21/39) | Manic Symptoms: Mild Depressive Symptoms: Mild | Current IQ, Premorbid IQ, Verbal Memory/Learning | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Hippocampus Neuroimaging Analysis: ROI | NA | Covariates: Age, Sex pIQ diff HC: No Age diff HC: No Sex diff HC: No |
| 13 | 34 RO-SSD (15.2 ± 1.7, 24/10) 15 RO-BD (16.5 ± 0.7, 9/6) 10 RO-NOS (15.3 ± 1.9, 6/4) 70 HC (15.3 ± 1.5, 48/22) | Baseline: Positive Symptoms: Moderate Negative Symptoms: Mild Follow Up: Positive Symptoms: Mild Negative Symptoms: Mild | Current IQ, Working Memory, Verbal Memory/Learning, Executive Function, Attention | Scanner Strength: NA Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: VBM | Follow up: 2 years | Covariates: Age, Sex, ICV, Site pIQ diff HC: NA Age diff HC: Yes Sex diff HC: No |
| 14 | 31 RO-BD (22.6 ± 4.6, 19/12) 30 HC (23 ± 4.8, 14/16) | Manic Symptoms: Remission Depressive Symptoms: Remission | Verbal Memory/Learning | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Hippocampus, Frontal lobe Neuroimaging Analysis: ROI | NA | Covariates: ICV pIQ diff HC: No Age diff HC: No Sex diff HC: No |
| 15 | 69 SSD (41.08 ± 12.75, 57/12) 35 Unaffected Relatives (45.33 ± 13.24, 14/21) 70 HC (39.4 ± 11.67, 51/19) | Positive Symptoms: Mild Negative Symptoms: Mild | Attention | Scanner Strength: 3T MRI Morphology: Thickness Brain Region: Whole brain Neuroimaging Analysis: ROI | NA | Covariates: Age, Sex pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 16 | 26 BD (38.9 ± 11.5, 8/18) 24 HC (37.4 ± 10.0, 8/16) | Manic Symptoms: Remission Depressive Symptoms: Remission | Working Memory, Premorbid IQ | Scanner Strength: 3T MRI Morphology: Volume, thickness, & surface area Brain Region: Frontal lobe, Parietal lobe Neuroimaging Analysis: ROI | NA | Covariates: ICV pIQ diff HC: No Age diff HC: No Sex diff HC: No |

| Reference | Cohort (#, Dx, Mean age ± SD, M/F) | Symptoms | Cognitive Domain | Neuroimaging | Longitudinal Follow Up | Notes |
|-----------|--|---|--|--|------------------------|--|
| 17 | 17 BD I (31.3 ± 7, 7/10) | Manic Symptoms: Remission Depressive Symptoms: Remission | Executive Function | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI | NA | Covariates: Age, Sex pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |
| 18 | 20 SSD (31.9 ± 11.1, 10/10) 20 HC (30.4 ± 12.8, 11/9) | Positive Symptoms: NA Negative Symptoms: NA | Current IQ, Working Memory, Memory (other), Executive Function | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Frontal lobe, Temporal lobe Neuroimaging Analysis: ROI | Follow up: 2 years | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 19 | 21 RO-SSD (21.6 ± 3.2, 16/5) 41 HC (22.5 ± 6.7, 32/9) | Positive Symptoms: Moderate Negative Symptoms: Moderate | Working Memory | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: VBM | NA | Covariates: Premorbid IQ pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 20 | 142 SSD (29.73 ± 8.7, 88/54) 83 HC (27.57 ± 7.57, 52/31) | Positive Symptoms: Mild Negative Symptoms: Mild | Executive Function, Working Memory, Speed of Processing, Attention, Visual Memory/Learning, Premorbid IQ | Scanner Strength: 1.5T MRI Morphology: Thickness & surface area Brain Region: Whole brain Neuroimaging Analysis: Vertex-wise | NA | Covariates: Age, Sex, Education, Substance Abuse pIQ diff HC: NA Age diff HC: No Sex diff HC: No Large study |
| 21 | 28 RO-SSD + Cannabis (24.1 ± 6.5, 21/7) 78 RO-SSD - Cannabis (29.3 ± 8.6, 31/47) 80 HC (30.4 ± 8.3, 41/39) | Positive Symptoms: NA Negative Symptoms: NA | Attention, Working Memory, Verbal Fluency, Executive Function | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Frontal lobe, Insula, Hippocampus, Parahippocampus Neuroimaging Analysis: ROI and VBM | NA | Covariates: Age, Sex pIQ diff HC: NA Age diff HC: Yes (RO-SSD + C) Sex diff HC: Yes (RO-SSD + C) |
| 22 | 48 SSD (35.12 ± 12.05, 33/15) 60 HC (36.4 ± 12.96, 36/24) | Positive Symptoms: NA Negative Symptoms: NA | Verbal Memory/Learning | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI | NA | Covariates: ICV pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 23 | 20 RO-SSD (27.3 ± 8, 15/5) 5 HC (28.2 ± 6, 3/2) | Positive Symptoms: NA Negative Symptoms: NA | Intelligence, Executive Function, Speed of Processing, Attention, Memory | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain, Subcortical, Superior Temporal Neuroimaging Analysis: ROI | Follow up: 4 years | Covariates: None pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |
| 24 | 16 RO-SSD (24.08 ± 7.21, 13/3) | Positive Symptoms: Mild Negative Symptoms: Mild | Executive Function | Scanner Strength: MRS Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: VBM | Follow up: 6.6 years | Covariates: None pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |

| Reference | Cohort (#, Dx, Mean age ± SD, M/F) | Symptoms | Cognitive Domain | Neuroimaging | Longitudinal Follow Up | Notes |
|-----------|---|--|--|---|------------------------|--|
| 25 | 25 SSD (NA ± NA, 13/12) 17 HC (NA ± NA, 10/7) | Positive Symptoms: Moderate Negative Symptoms: NA | General Cognition | Scanner Strength: 0.5T MRI Morphology: Volume Brain Region: Temporal lobe Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 26 | 51 SSD (44.12 ± 10.35, 38/13) 50 HC (44.12 ± 10.35, 32/18) | Positive Symptoms: NA Negative Symptoms: NA | Current IQ, Attention | Scanner Strength: 1.5T MRI Morphology: Thickness Brain Region: Prefrontal Cortex, Superior Temporal Gyrus Neuroimaging Analysis: Vertex-wise | NA | Covariates: Age pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |
| 27 | 31 RO-SSD (27.3 ± 6.02, 22/9) 59 ARMS (25 ± 6.01, 47/12) | Positive Symptoms: Mild Negative Symptoms: NA | Verbal Memory/Learning | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Total Brain Volume, Subcortical Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 28 | 131 SSD (33 ± 11, 99/32) 138 HC (31.8 ± 11.5, 90/48) | Positive Symptoms: Mild Negative Symptoms: Mild | Working Memory, Verbal Memory/Learning, Visual Memory/Learning, Verbal Fluency, Premorbid IQ, Executive Function, Intelligence | Scanner Strength: 1.5T MRI Morphology: Thickness Brain Region: Whole brain Neuroimaging Analysis: Vertex-wise | NA | Covariates: Age, Sex, Site pIQ diff HC: Yes Age diff HC: No Sex diff HC: No Large study |
| 29 | 15 RO-SSD (29 ± 9, 10/5) 15 HC (28 ± 8, 10/5) | Positive Symptoms: Mild Negative Symptoms: Mild | Full Scale IQ, Visual Memory/Learning, Speed of Processing, Working Memory, Executive Function | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Cerebellum Neuroimaging Analysis: ROI | NA | Covariates: Total Brain Volume pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 30 | 14 SSD (males) (31 ± 11, NA) 7 SSD (females) (32 ± 10, NA) 8 HC (females) (32 ± 9, NA) 13 HC (males) (29 ± 10, NA) | Positive Symptoms: NA Negative Symptoms: NA | Verbal Memory/Learning, Visual Memory/Learning | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Hippocampus Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 31 | 170 RO-SSD (24.56 ± 5.49, 88/82) 88 HC (28.26 ± 6.71, 38/50) | Positive Symptoms: Mild Negative Symptoms: Mild | Speed of Processing, Attention, Working Memory, Verbal Memory/Learning, Visual Memory/Learning, Executive Function | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Subcortical, Total Cortical Grey Matter, ICV Neuroimaging Analysis: ROI | NA | Covariates: Age, Education, Site, Sex pIQ diff HC: NA Age diff HC: Yes Sex diff HC: No Large study |
| 32 | 56 RO-SSD (29.57 ± 8.14, 36/20) 56 HC (29.11 ± 8.22, 36/20) | Positive Symptoms: Mild Negative Symptoms: Mild | Verbal Memory/Learning, Visual Memory/Learning, Executive Function, Working Memory, Speed of Processing, Attention, Premorbid IQ, Verbal Memory/Learning, Visual Memory/Learning, Executive Function, Working Memory, Speed of Processing, Premorbid IQ, | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Postcentral Neuroimaging Analysis: ROI | Follow up: 1 years | Covariates: Age, ICV pIQ diff HC: Yes Age diff HC: No Sex diff HC: No |

| Reference | Cohort (#, Dx, Mean age \pm SD, M/F) | Symptoms | Cognitive Domain | Neuroimaging | Longitudinal Follow Up | Notes |
|-----------|--|--|---|--|------------------------|--|
| 33 | 50 SSD (males) (30.3 \pm 8.5, 50/0) 22 SSD (females) (30 \pm 8.4, 0/22) 27 HC (females) (31.3 \pm 11.9, 0/27) 32 HC (males) (31.8 \pm 11, 32/0) | Positive Symptoms: Mild Negative Symptoms: Mild | Intelligence | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI | NA | Covariates: Head size pIQ diff HC: NA Age diff HC: No Sex diff HC: NA |
| 34 | 18 SSD (\leq 10 years) (29.2 \pm 8.6, 8/10) 15 SSD (\geq 10 years) (42.7 \pm 7.4, 9/6) 24 HC (30.3 \pm 10.2, 9/15) | Positive Symptoms: Mild Negative Symptoms: Moderate | Executive Function | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: VBM | NA | Covariates: Age, Sex, Education pIQ diff HC: No Age diff HC: Yes Sex diff HC: No |
| 35 | 43 BD (paediatric) (11.3 \pm 2.7, 23/20) 20 HC (11 \pm 2.6, 12/8) | Manic Symptoms: NA Depressive Symptoms: NA | Current IQ | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Subcortical Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 36 | 26 SSD (37.1 \pm 7.6, 13/13) 20 HC (37.8 \pm 7.4, 10/10) | Positive Symptoms: Mild Negative Symptoms: Mild | Current IQ, Visual Memory/Learning | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Anterior Cingulate Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 37 | 29 SSD (38.2 \pm 11.3, 18/11) 26 HC (30.5 \pm 11.3, 13/13) | Positive Symptoms: NA Negative Symptoms: Moderate | Working Memory | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Frontal lobe Neuroimaging Analysis: ROI | NA | Covariates: Age, Parental Education, Negative Symptoms pIQ diff HC: NA Age diff HC: Yes Sex diff HC: No |
| 38 | 17 SSD (43.1 \pm 10.1, 13/4) 15 SSD FDR (48.8 \pm 7.8, 5/10) 18 HC (34.1 \pm 10, 9/9) | Positive Symptoms: Mild Negative Symptoms: Mild | Working Memory | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Frontal lobe Neuroimaging Analysis: ROI | NA | Covariates: Scanner pIQ diff HC: No Age diff HC: Yes Sex diff HC: Yes |
| 39 | 15 SSD MZ Twins (32 \pm NA, 8/7) | Positive Symptoms: NA Negative Symptoms: NA | Verbal Memory/Learning, Visual Memory/Learning, Speed of Processing, Executive Function, Intelligence | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Hippocampus Neuroimaging Analysis: ROI | NA | Covariates: Current IQ pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |
| 40 | 51 SSD (22.5 \pm 4.1, 33/18) 41 HC (22.8 \pm 3.9, 24/14) | Positive Symptoms: Moderate Negative Symptoms: Moderate | Speed of Processing, Working Memory, Verbal Memory/Learning, Visual Memory/Learning, Executive Function | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: VBM | NA | Covariates: Age, Sex, Education, Total symptoms pIQ diff HC: NA Age diff HC: No Sex diff HC: No |

| Reference | Cohort (#, Dx, Mean age ± SD, M/F) | Symptoms | Cognitive Domain | Neuroimaging | Longitudinal Follow Up | Notes |
|-----------|--|--|--|--|------------------------|--|
| 41 | 130 SSD (29.2 ± 7.5, 75/55) 130 HC (27.7 ± 6, 75/55) | Positive Symptoms: Mild Negative Symptoms: Mild | Speed of Processing, Executive Function, Visual Memory/Learning, Verbal Memory/Learning, Attention, Intelligence | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI | NA | Covariates: Age pIQ diff HC: NA Age diff HC: No Sex diff HC: No Large study |
| 42 | 100 SSD (29.2 ± 7.3, 58/42) 110 HC (26.1 ± 6.3, 51/55) | Positive Symptoms: Mild Negative Symptoms: Mild | Speed of Processing, Executive Function, Visual Memory/Learning, Verbal Memory/Learning, Attention, Intelligence | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Hippocampus, Amygdala, Temporal lobe Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: Yes Sex diff HC: No Large study |
| 43 | 25 BD I (37.4 ± 10, 10/15) 11 BD II (42.8 ± 7.1, 3/11) | Manic Symptoms: NA Depressive Symptoms: Mild | Premorbid IQ, Current IQ, Visual Memory/Learning, Executive Function | Scanner Strength: 1.5T MRI Morphology: Volume, thickness, & surface area Brain Region: Frontal lobe, Temporal lobe Neuroimaging Analysis: SBM | NA | Covariates: Age, Sex, Diagnosis, Cognitive Scores, Age, Sex, Diagnosis, Cognition pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |
| 44 | 27 RO-SSD (25.9 ± 6.5, 17/10) 25 HC (26.8 ± 7.1, 14/11) | Positive Symptoms: Mild Negative Symptoms: Mild | Premorbid IQ, Current IQ, Executive Function, Verbal Memory/Learning | Scanner Strength: 1.5T MRI Morphology: Volume, thickness, & surface area Brain Region: Whole brain Neuroimaging Analysis: SBM | Follow up: 2 years | Covariates: Age, Sex, Duration of Follow Up pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 45 | 25 SSD (22.6 ± 3.2, 20/5) 25 SSD FDR (22.3 ± 3.5, 10/15) 40 HC FDR (20 ± 3.5, 11/29) 40 HC (21.2 ± 14.2, 22/18) | Positive Symptoms: NA Negative Symptoms: NA | Attention, Working Memory, Executive Function | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Thalamus Neuroimaging Analysis: ROI | NA | Covariates: Sex pIQ diff HC: NA Age diff HC: Yes Sex diff HC: Yes |
| 46 | 26 SSD (22.7 ± 3, 22/4) 26 SSD FDR (22.3 ± 3.4, 10/16) 40 HC FDR (20.3 ± 3.6, 12/20) 40 HC (21.2 ± 3.6, 23/17) | Positive Symptoms: NA Negative Symptoms: NA | Working Memory, Verbal Memory/Learning, Executive Function, Attention | Scanner Strength: 1.5T MRI Morphology: Volume, thickness, & surface area Brain Region: Prefrontal Cortex Neuroimaging Analysis: ROI | NA | Covariates: ICV pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |
| 47 | 67 SSD (41.9 ± 7.3, 53/14) 69 HC (43.2 ± 8.5, 41/28) | Positive Symptoms: NA Negative Symptoms: NA | Verbal Memory/Learning, Executive Function, Working Memory, Intelligence | Scanner Strength: 1.5T MRI Morphology: Thickness Brain Region: Whole brain Neuroimaging Analysis: ROI and vertex-wise | NA | Covariates: Age, Sex pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 48 | 117 SSD (31.7 ± 7.9, 68/49) 121 BD (34.7 ± 11.4, 49/72) 192 HC (36.1 ± 9.6, 98/94) | Positive Symptoms: Mild (BD & SSD) Negative Symptoms: Mild (BD & SSD) | Premorbid IQ, Verbal Memory/Learning, Speed of Processing, Working Memory, Executive Function, Current IQ | Scanner Strength: 1.5T MRI Morphology: Thickness & surface area Brain Region: Whole brain Neuroimaging Analysis: ROI and vertex-wise | NA | Covariates: Age, Sex pIQ diff HC: No Age diff HC: Yes (SSD) Sex diff HC: Yes (SSD) Large study |

| Reference | Cohort (#, Dx, Mean age ± SD, M/F) | Symptoms | Cognitive Domain | Neuroimaging | Longitudinal Follow Up | Notes |
|-----------|--|--|---|---|------------------------|--|
| 49 | 117 SSD (31.7 ± 7.9, 68/49) 121 BD (34.7 ± 11.4, 49/72) 192 HC (36.1 ± 9.6, 98/94) | Positive Symptoms: Mild (BD & SSD) Negative Symptoms: Mild (BD & SSD) | Premorbid IQ, Verbal Memory/Learning, Speed of Processing, Working Memory, Executive Function, Current IQ | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Subcortical Neuroimaging Analysis: ROI | NA | Covariates: Age, ICV pIQ diff HC: No Age diff HC: Yes (SSD) Sex diff HC: Yes (SSD) Large study |
| 50 | 41 RO-SSD (28.35 ± 7.05, 28/13) 53 HC (39.69 ± 12.37, 21/32) | Positive Symptoms: Moderate Negative Symptoms: Moderate | Verbal Memory/Learning, Verbal Fluency, Executive Function | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Hippocampus Neuroimaging Analysis: ROI | NA | Covariates: Age, Education, Sex pIQ diff HC: Yes Age diff HC: Yes Sex diff HC: Yes |
| 51 | 40 RO-SSD (23.5 ± 3.4, 29/11) 73 RO-BD (21.9 ± 3.6, 21/51) 49 HC (24.2 ± 2.7, 21/28) | Positive Symptoms: Moderate (RO-BD), Mild (RO-SSD) Negative Symptoms: Mild (RO-SSD & RO-BD) | Attention, Executive Function, Memory (other), Verbal Fluency, Verbal Memory/Learning | Scanner Strength: 3T MRI Morphology: Volume & thickness Brain Region: Whole brain Neuroimaging Analysis: ROI and VBM | NA | Covariates: Education, Sex pIQ diff HC: NA Age diff HC: Yes (RO-BD) Sex diff HC: Yes |
| 52 | 210 SSD (32 ± 9.3, 125/85) 192 BD (35.1 ± 11.5, 77/115) 300 HC (35.3 ± 9.9, 158/142) | Positive Symptoms: Mild (BD & SSD) Negative Symptoms: Mild (BD & SSD) | Verbal Memory/Learning, Global Cognition | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Hippocampus Neuroimaging Analysis: ROI | NA | Covariates: Age, ICV, Sex pIQ diff HC: No Age diff HC: Yes Sex diff HC: Yes Large study |
| 53 | 25 SSD (older) (55.92 ± 6.85, 17/8) 23 SSD (younger) (32.78 ± 7, 14/9) 21 HC (53.67 ± 8, 12/9) | Positive Symptoms: Mild Negative Symptoms: Mild | Verbal Memory/Learning, Working Memory, Executive Function, Speed of Processing, Memory (other) | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Hippocampus Neuroimaging Analysis: ROI | NA | Covariates: ICV pIQ diff HC: NA Age diff HC: Yes Sex diff HC: NA |
| 54 | 116 SSD (39.3 ± 11.1, 66/50) 118 HC (40 ± 13.6, 58/60) | Positive Symptoms: Mild Negative Symptoms: Mild | Verbal Memory/Learning, Working Memory, Speed of Processing, Verbal Fluency, Attention, Executive Function, Global Cognition | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: VBM | NA | Covariates: Age, Sex, Medication pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 55 | 113 RO-PS (15.00 ± 2.80, 57/56) 117 RO-BD (16.80 ± 3.50, 56/61) 109 RO-BD+PS* (15.90 ± 3.00, 52/57) 376 HC (15.10 ± 3.70, 194/182) *PS, psychosis-spectrum | Positive Symptoms: NA Negative Symptoms: NA | Complex Cognition (language reasoning, nonverbal reasoning, spatial ability), Executive Control (mental flexibility, attention, working memory) | Scanner Strength: 3T MRI Morphology: Volume, thickness, & surface area Brain Region: Subcortical, Cortical Thickness, Cortical Surface Area Neuroimaging Analysis: ROI | NA | Covariates: ICV pIQ diff HC: NA Age diff HC: RO-BD > HC & RO-PS Sex diff HC: No Large study |
| 56 | 54 RO-SSD (24.69 ± 5.93, 31/23) 56 HC (24.91 ± 5.61, 33/23) | Positive Symptoms: Mild Negative Symptoms: Mild | Current IQ | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: No |

| Reference | Cohort (#, Dx, Mean age ± SD, M/F) | Symptoms | Cognitive Domain | Neuroimaging | Longitudinal Follow Up | Notes |
|-----------|--|--|---|--|------------------------|---|
| 57 | 247 SSD (33.48 ± 11.6, 153/93) 205 HC (36.4 ± 11.7, 87/118) | Positive Symptoms: NA Negative Symptoms: NA | Executive Function, Working Memory, Verbal Memory/Learning, Verbal Fluency, Speed of Processing, Global Cognition | Scanner Strength: NA Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI | NA | Covariates: Age, Sex pIQ diff HC: NA Age diff HC: Yes Sex diff HC: Yes Large study |
| 58 | 24 RO-SSD (16.1 ± 1.9, 12/12) 33 HC (15.8 ± 1.8, 15/17) | Positive Symptoms: Mild Negative Symptoms: Mild | Speed of Processing, Attention, Working Memory, Verbal Memory/Learning, Visual Memory/Learning, Executive Function, Full Scale IQ | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Subcortical Neuroimaging Analysis: ROI | NA | Covariates: Age, ICV, Current IQ, Medication pIQ diff HC: No Age diff HC: No Sex diff HC: No |
| 59 | 39 SSD (22.5 ± NA, 33/6) 33 SSD FDR (22.1 ± NA, 15/18) 50 HC FDR (20.4 ± NA, 26/21) 47 HC (21.1 ± NA, 20.4) | Positive Symptoms: NA Negative Symptoms: NA | Verbal Memory/Learning, Visual Memory/Learning | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Hippocampus, Parahippocampus Neuroimaging Analysis: ROI and vertex-wise | NA | Covariates: Sex pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |
| 60 | 90 SSD (25.95 ± 8.28, 62/28) 39 Non-SSD Psychoses (23.58 ± 7.29, 25/14) 93 HC (24.75 ± 5.84, 53/40) | Positive Symptoms: NA Negative Symptoms: NA | Intelligence, Speed of Processing | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 61 | 19 SSD (34.3 ± 6.9, 14/5) 11 BD (23.7 ± 3.6, 9/2) 20 HC (27.4 ± 6.8, 18/2) | Positive Symptoms: NA Negative Symptoms: NA | Verbal Memory/Learning, Visual Memory/Learning | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Hippocampus, Amygdala Neuroimaging Analysis: ROI | NA | Covariates: ICV pIQ diff HC: NA Age diff HC: Yes (SSD) Sex diff HC: NA |
| 62 | 40 RO-SSD (22.9 ± 5.64, 18/22) 40 HC (23.13 ± 5.03, 19/21) | Positive Symptoms: Mild Negative Symptoms: Mild | Current IQ, Visual Memory/Learning, Speed of Processing, Verbal Fluency, Executive Function | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Cerebellum Neuroimaging Analysis: ROI | NA | Covariates: ICV pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 63 | 21 BD I (35.67 ± 10.68, 12/9) 21 SSD (38.38 ± 10.3, 12/9) 21 HC (36.95 ± 11.1, 12/9) | Positive Symptoms: Mild (BD & SSD) Negative Symptoms: Mild (BD & SSD) | Premorbid IQ, Verbal Memory/Learning, Visual Memory/Learning | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI and VBM | NA | Covariates: Age, Sex, Education pIQ diff HC: No Age diff HC: No Sex diff HC: No |
| 64 | 34 BD (43.93 ± 10.87, 19/15) 32 SSD (39.56 ± 10.9, 16/16) 38 HC (40.86 ± 11.91, 23/15) | Positive Symptoms: Mild (BD & SSD) Negative Symptoms: Mild (BD & SSD) | Current IQ, Speed of Processing, Executive Function | Scanner Strength: 3T MRI Morphology: Thickness Brain Region: Whole brain Neuroimaging Analysis: Vertex-wise | NA | Covariates: ICV pIQ diff HC: NA Age diff HC: No Sex diff HC: No |

| Reference | Cohort (#, Dx, Mean age \pm SD, M/F) | Symptoms | Cognitive Domain | Neuroimaging | Longitudinal Follow Up | Notes |
|-----------|--|--|---|---|------------------------|--|
| 65 | 48 BD (38.93 \pm 9.78, 23/25) 57 SSD (38.02 \pm 8.49, 29/28) 47 SSD FDR (37.22 \pm 11.13, 26/20) 57 HC (37.11 \pm 9.2, 26/31) | Positive Symptoms: Mild (BD & SSD) Negative Symptoms: Mild (BD & SSD) | Current IQ, Verbal Memory/Learning, Visual Memory/Learning, Executive Function, Speed of Processing | Scanner Strength: 3T MRI Morphology: Volume & thickness Brain Region: Frontal lobe, Basal Ganglia Neuroimaging Analysis: ROI and VBM | NA | Covariates: Age, Sex, Education pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 66 | 174 SSD (34.5 \pm 11.6, 98/76) 638 HC (33.9 \pm 12.9, 315/323) | Positive Symptoms: Mild Negative Symptoms: Mild | Premorbid IQ, Verbal Memory/Learning, Visual Memory/Learning, Attention | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Subcortical Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: Yes Age diff HC: No Sex diff HC: No Large study |
| 67 | 41 RO-BD (22.8 \pm 4.6, 24/17) 30 HC (22.9 \pm 4.7, 12/18) | Manic Symptoms: Remission Depressive Symptoms: Remission | Executive Function, Current IQ, Premorbid IQ | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI and VBM | NA | Covariates: Age, Sex, Total Grey Matter pIQ diff HC: No Age diff HC: No Sex diff HC: No |
| 68 | 84 SSD (27.3 \pm 5.53, 72/12) 116 HC (27.04 \pm 7.61, 58/58) | Positive Symptoms: Mild Negative Symptoms: Mild | Full Scale IQ | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI and vertex-wise | Follow up: 4 years | Covariates: Age, ICV, Sex pIQ diff HC: NA Age diff HC: No Sex diff HC: Yes |
| 69 | 29 SSD (27.6 \pm 6.8, 19/10) 45 HC (31.3 \pm 7.7, 19/26) | Positive Symptoms: Mild Negative Symptoms: NA | Speed of Processing, Executive Function | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Cerebellum Neuroimaging Analysis: VBM | NA | Covariates: Age, Sex, Cerebellum & Brainstem Volume, Cigarettes/day pIQ diff HC: NA Age diff HC: Yes Sex diff HC: Yes |
| 70 | 18 SSD (32.2 \pm 14.3, 13/5) 18 HC (31.9 \pm 14.3, 13/9) | Positive Symptoms: Mild Negative Symptoms: NA | Executive Function, Visual Memory/Learning, Attention | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 71 | 42 SSD (37.9 \pm 9.5, 42/0) | Positive Symptoms: Mild Negative Symptoms: Mild | Executive Function | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: VBM | NA | Covariates: None pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |
| 72 | 52 RO-SSD (16.02 \pm 2.15, 29/23) 48 HC (16.38 \pm 2.91, 30/18) | Positive Symptoms: NA Negative Symptoms: NA | Full Scale IQ, Verbal Memory/Learning, Speed of Processing, Executive Function, Attention | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Cingulate Cortex, Frontal lobe Neuroimaging Analysis: ROI | NA | Covariates: ICV pIQ diff HC: NA Age diff HC: No Sex diff HC: No |

| Reference | Cohort (#, Dx, Mean age ± SD, M/F) | Symptoms | Cognitive Domain | Neuroimaging | Longitudinal Follow Up | Notes |
|-----------|--|--|--|---|------------------------|--|
| 73 | 24 SSD (40.3 ± 8.5, 24/0) 31 HC (40.6 ± 8.7, 31/0) | Positive Symptoms: NA Negative Symptoms: NA | Verbal Memory/Learning, Visual Memory/Learning | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Hippocampus Neuroimaging Analysis: ROI | NA | Covariates: Age, Medication pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 74 | 42 RO-SSD (27.7 ± 8.8, 27/15) 20 SSD (25.3 ± 8.3, 15/5) 22 Psychosis (other) (29.9 ± 8.9, 12/10) 32 HC (29.8 ± 8.6, 14/16) | Positive Symptoms: NA Negative Symptoms: Mild | Premorbid IQ, Verbal Memory/Learning | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Hippocampus Neuroimaging Analysis: VBM | Follow up: 6 years | Covariates: Age, Sex, Baseline & Whole Brain Grey Matter pIQ diff HC: Yes (RO-SSD & HC) Age diff HC: No Sex diff HC: No |
| 75 | 93 SSD (27 ± 6.6, 57/36) 99 HC (25.8 ± 5.4, 53/46) | Positive Symptoms: Moderate Negative Symptoms: Mild | Speed of Processing, Executive Function, Memory | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: VBM | NA | Covariates: Age, Sex pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 76 | 17 SSD (38.47 ± 3.91, 7/10) 17 HC (34.12 ± 8.13, 6/11) | Positive Symptoms: Moderate Negative Symptoms: Moderate | Speed of Processing, Attention, Working Memory, Verbal Memory/Learning, Visual Memory/Learning, Executive Function | Scanner Strength: 3T MRI Morphology: Volume, thickness, & surface area Brain Region: Cingulate Cortex Neuroimaging Analysis: ROI and vertex-wise | NA | Covariates: Age, Sex pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 77 | 10 BD (46.9 ± 12.3, 3/7) 10 BD FDR (54.8 ± 20.1, 5/5) 34 MDD (NA ± NA, NA) 27 HC (48.3 ± 13, 10/17) | Manic Symptoms: Remission Depressive Symptoms: Moderate | Executive Function, Premorbid IQ | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: VBM | NA | Covariates: None pIQ diff HC: No Age diff HC: No Sex diff HC: No |
| 78 | 35 SSD (schizophrenia) (23.8 ± 5.2, 22/13) 25 Schizotypal (24.9 ± 4.5, 17/8) 19 HC (27.1 ± 6.7, 10/19) | Positive Symptoms: Mild (SSD & Schizotypal) Negative Symptoms: Mild (SSD & Schizotypal) | Verbal Memory/Learning | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Prefrontal Cortex Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 79 | 88 RO-SSD (28.90 ± 8.60, 52/36) 48 SSD (28.00 ± 8.40, 35/13) 34 Affective Psychosis (29.60 ± 8.60, 14/20) 17 BD (28.20 ± 8.60, 9/8) 17 Psychotic Depression (31.00 ± 8.70, 5/12) 86 HC (30.6 ± 8.50, 46/40) | Positive Symptoms: NA Negative Symptoms: NA | Executive Function, Working Memory, Verbal Fluency | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI and VBM | NA | Covariates: Age, Sex, Education, Diagnosis, Substance Abuse pIQ diff HC: NA Age diff HC: Yes (SSD) Sex diff HC: Yes (SSD) |
| 80 | 22 SSD (27.1 ± 6.7, 12/10) | Positive Symptoms: Moderate Negative Symptoms: Moderate | Attention, Speed of Processing, Verbal Memory/Learning, Visual Memory/Learning, Working Memory | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Dorsolateral Prefrontal Cortex Neuroimaging Analysis: ROI | NA | Covariates: Current IQ pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |

| Reference | Cohort (#, Dx, Mean age ± SD, M/F) | Symptoms | Cognitive Domain | Neuroimaging | Longitudinal Follow Up | Notes |
|-----------|--|--|--|---|------------------------|--|
| 81 | 20 BD I (41.5 ± 8.9, 10/10) 21 HC (38.5 ± 12.6, 10/11) | Manic Symptoms: Mild Depressive Symptoms: Mild | Premorbid IQ, Current IQ, Memory (other) | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: TBM | Follow up: 4 years | Covariates: Age, Sex, Interscan Interval pIQ diff HC: No Age diff HC: No Sex diff HC: No |
| 82 | 176 SSD (38.9 ± 11.5, 132/44) 173 HC (37.6 ± 11.3, 123/50) | Positive Symptoms: Mild Negative Symptoms: Mild | Attention, Speed of Processing, Working Memory, Visual Memory/Learning, Verbal Memory/Learning, Executive Function, Global Cognition | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Hippocampus, ICV Neuroimaging Analysis: ROI | NA | Covariates: Age, ICV pIQ diff HC: Yes Age diff HC: No Sex diff HC: No Large study |
| 83 | 24 SSD (39.1 ± 10.3, 24/0) 25 HC (41.1 ± 9.1, 19/6) | Positive Symptoms: NA Negative Symptoms: NA | Executive Function, Speed of Processing | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Frontal lobe Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 84 | 15 SSD (37.6 ± NA, 15/0) | Positive Symptoms: NA Negative Symptoms: NA | Executive Function, Verbal Memory/Learning, Visual Memory/Learning, Speed of Processing, Intelligence | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Temporal lobe Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |
| 85 | 21 SSD (39.79 ± 9.16, NA) 24 HC (40.64 ± 9.38, NA) | Positive Symptoms: NA Negative Symptoms: NA | Current IQ, Executive Function, Verbal Memory/Learning, Visual Memory/Learning | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Hippocampus Neuroimaging Analysis: ROI | NA | Covariates: Education pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 86 | 32 BD I (44.03 ± 10.69, 19/13) 35 HC (42.06 ± 11.45, 20/15) | Manic Symptoms: Mild Depressive Symptoms: Mild | Current IQ, Speed of Processing, Executive Function | Scanner Strength: 3T MRI Morphology: Volume & thickness Brain Region: Whole brain Neuroimaging Analysis: Vertex-wise | NA | Covariates: Age, Sex, ICV pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 87 | 27 SSD (44.19 ± 9.62, 27/0) 27 HC (41.63 ± 10.55, 27/0) | Positive Symptoms: Mild Negative Symptoms: Mild | Premorbid IQ, Executive Function | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Frontal lobe Neuroimaging Analysis: ROI | NA | Covariates: Head size pIQ diff HC: No Age diff HC: No Sex diff HC: No |
| 88 | 21 SSD (42.7 ± 8.4, 21/0) 28 HC (42 ± 7.5, 28/0) | Positive Symptoms: Mild Negative Symptoms: Mild | Visual Memory/Learning | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Fusiform Gyrus Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: No |

| Reference | Cohort (#, Dx, Mean age \pm SD, M/F) | Symptoms | Cognitive Domain | Neuroimaging | Longitudinal Follow Up | Notes |
|-----------|---|--|--|--|------------------------|--|
| 89 | 35 RO-SSD (23.57 \pm 4.95, 25/10) 54 SSD (38.61 \pm 10.87, 37/17) 20 HC (younger) (26.15 \pm 5.52, 14/7) 21 HC (older) (36.19 \pm 11.27, 15/6) | Positive Symptoms: Moderate (RO-SSD) Mild (SSD) Negative Symptoms: Mild (RO-SSD & SSD) | Executive Function, Attention, Visual Memory/Learning, Verbal Fluency, Premorbid IQ | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Prefrontal Cortex, Premotor Cortex, Temporal Lobe, Hippocampus Neuroimaging Analysis: ROI | NA | Covariates: Age piQ diff HC: NA Age diff HC: Yes (SSD & older HC) Sex diff HC: No |
| 90 | 14 SSD (29.92 \pm 7.17, 11/3) 14 HC (31.23 \pm 5.4, 8/6) | Positive Symptoms: Mild Negative Symptoms: Mild | Working Memory, Premorbid IQ, Current IQ, Speed of Processing, Executive Function, Verbal Memory/Learning | Scanner Strength: 3T MRI Morphology: Thickness Brain Region: Whole brain Neuroimaging Analysis: Vertex-wise | NA | Covariates: None piQ diff HC: Yes Age diff HC: No Sex diff HC: No |
| 91 | 51 SSD (48.9 \pm 17.9, 28/23) 49 HC (52.8 \pm 17.2, 26/23) | Positive Symptoms: Mild Negative Symptoms: Mild | Global Cognition, Verbal Memory/Learning | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Hippocampus Neuroimaging Analysis: VBM | NA | Covariates: Sex piQ diff HC: Yes Age diff HC: No Sex diff HC: No |
| 92 | 20 RO-SSD (24.39 \pm 5.14, 15/5) 26 HC (23.7 \pm 4.15, 17/9) | Positive Symptoms: Mild Negative Symptoms: Mild | Intelligence | Scanner Strength: 1.5T MRI Morphology: Thickness & surface area Brain Region: Whole brain Neuroimaging Analysis: ROI and vertex-wise | NA | Covariates: Age, Sex, Handedness, Diagnosis piQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 93 | 19 RO-SSD (22.2 \pm 3.7, 12/7) 18 HC (23.4 \pm 3.3, 11/7) | Positive Symptoms: Moderate Negative Symptoms: Moderate | Speed of Processing, Attention, Working Memory, Verbal Memory/Learning, Visual Memory/Learning, Executive Function | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: VBM | NA | Covariates: Age, Sex, Education, ICV piQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 94 | 386 RO-SSD (15.8 \pm 3, 190/196) 521 NOS (14.9 \pm 3.5, 220/301) 359 HC (15 \pm 3.9, 185/174) | Positive Symptoms: NA Negative Symptoms: NA | Global Cognition | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI | NA | Covariates: Age, Sex, ICV piQ diff HC: NA Age diff HC: Yes Sex diff HC: Yes Large study |
| 95 | 109 SSD (29.44 \pm 8.21, 66/43) 76 HC (27.8 \pm 7.73, 47/29) | Positive Symptoms: Mild Negative Symptoms: Mild | Verbal Memory/Learning, Visual Memory/Learning, Executive Function, Working Memory, Speed of Processing, Attention, Premorbid IQ | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI | Follow up: 3 years | Covariates: Age, ICV, Premorbid IQ piQ diff HC: NA Age diff HC: No Sex diff HC: No Large study |
| 96 | 109 SSD (29.44 \pm 8.21, 66/43) 76 HC (27 \pm 7.73, 47/29) | Positive Symptoms: Moderate Negative Symptoms: Mild | Verbal Memory/Learning, Visual Memory/Learning, Executive Function, Working Memory, Speed of Processing, Attention, Premorbid IQ | Scanner Strength: 1.5T MRI Morphology: Thickness Brain Region: Whole brain Neuroimaging Analysis: Vertex-wise | Follow up: 3 years | Covariates: Age piQ diff HC: NA Age diff HC: No Sex diff HC: No Large study |

| Reference | Cohort (#, Dx, Mean age ± SD, M/F) | Symptoms | Cognitive Domain | Neuroimaging | Longitudinal Follow Up | Notes |
|-----------|--|--|---|---|------------------------|--|
| 97 | 20 SSD (64.4 ± 10.6, 12/8) 24 HC (72.67 ± 6.7, 19/5) | Positive Symptoms: Mild Negative Symptoms: Mild | Executive Function, Verbal Memory/Learning, Visual Memory/Learning | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Hippocampus, Amygdala Neuroimaging Analysis: ROI | NA | Covariates: Age, Education pIQ diff HC: NA Age diff HC: Yes Sex diff HC: No |
| 98 | 13 RO-SSD (23.76 ± 5.65, 13/0) 13 HC (23.36 ± 4.58, 13/0) | Positive Symptoms: Mild Negative Symptoms: Mild | Attention | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI and VBM | NA | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 99 | 62 SSD (38.8 ± 5.3, 62/0) 27 HC (35.7 ± 8.7, 27/0) | Positive Symptoms: Mild Negative Symptoms: Mild | Intelligence, Executive Function, Memory, Verbal Fluency, Visual Memory/Learning | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI | NA | Covariates: Age, ICV pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 100 | 71 BD I (43.8 ± 11.4, 33/38) 82 HC (40.5 ± 11.6, 39/43) | Positive Symptoms: Mild Negative Symptoms: Mild | Full Scale IQ, Verbal Memory/Learning, Visual Memory/Learning, Working Memory, Memory (other), Executive Function | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: VBM | NA | Covariates: Age pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 101 | 17 BD (27 ± 6, 10/7) 12 HC (27 ± 5, 8/4) | Manic Symptoms: Mild Depressive Symptoms: NA | Attention | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Frontal lobe, Subcortical Neuroimaging Analysis: ROI | NA | Covariates: Age, Sex, Race, Substance Abuse pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 102 | 38 SSD (32.3 ± 10.6, 25/13) 29 HC (31.3 ± 9.2, 22/7) | Positive Symptoms: Mild Negative Symptoms: Mild | Full Scale IQ, Current IQ, Working Memory, Speed of Processing, Verbal Memory/Learning, Executive Function | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Hippocampus, Dorsolateral Prefrontal Cortex, Orbitofrontal Cortex Neuroimaging Analysis: ROI | NA | Covariates: Whole Brain Volume pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 103 | 40 SSD (39.1 ± 10.9, 30/10) | Positive Symptoms: Mild Negative Symptoms: Mild | Attention, Premorbid IQ, Speed of Processing, Verbal Memory/Learning, Visual Memory/Learning, Executive Function | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |
| 104 | 28 SSD (27.32 ± 4.13, 21/7) 28 HC (28.75 ± 5.36, 21/7) | Positive Symptoms: NA Negative Symptoms: NA | Current IQ, Executive Function, Working Memory, Attention, Verbal Fluency | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: VBM | NA | Covariates: ICV pIQ diff HC: NA Age diff HC: No Sex diff HC: No |

| Reference | Cohort (#, Dx, Mean age ± SD, M/F) | Symptoms | Cognitive Domain | Neuroimaging | Longitudinal Follow Up | Notes |
|-----------|--|--|--|---|------------------------|--|
| 105 | 17 SSD (33.6 ± 8.4, 14/3) | Positive Symptoms: NA Negative Symptoms: NA | Executive Function, Speed of Processing, Verbal Memory/Learning, Visual Memory/Learning, Attention, Intelligence | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Frontal lobe Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |
| 106 | 52 BD (27.1 ± 6.2, 33/19) 39 HC (31.9 ± 6.5, 22/17) | Manic Symptoms: Mild Depressive Symptoms: Mild | Working Memory, Executive Function | Scanner Strength: 3T MRI Morphology: Volume, thickness, & surface area Brain Region: Whole brain Neuroimaging Analysis: ROI | NA | Covariates: Age, Education, Sex pIQ diff HC: NA Age diff HC: Yes Sex diff HC: No |
| 107 | 21 SSD (35.1 ± 9.8, 12/9) 21 HC (34.6 ± 8.3, 12/7) | Positive Symptoms: NA Negative Symptoms: NA | Working Memory | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: VBM | NA | Covariates: Duration of illness pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 108 | 34 SSD (36.9 ± 7.8, 34/0) 47 HC (37.9 ± 9.2, NA) | Positive Symptoms: NA Negative Symptoms: NA | Executive Function, Memory, Speed of Processing | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Prefrontal, frontal, fronto-temporal, temporal-parietal, parital, parietal-occipital Neuroimaging Analysis: ROI | NA | Covariates: Age, Head size pIQ diff HC: NA Age diff HC: Yes Sex diff HC: NA |
| 109 | 13 SSD (25.9 ± 5.4, 13/0) 13 HC (29.3 ± 4.7, 13/0) | Positive Symptoms: Mild Negative Symptoms: Mild | Working Memory, Executive Function | Scanner Strength: 1.0T MRI Morphology: Volume Brain Region: Straight Gyrus, Anterior Cingulate Gyrus, Orbitofrontal Cortex, Middle Frontal Gyrus, Hippocampus Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: NA |
| 110 | 20 SSD (males) (23.3 ± 5, 20/0) 15 SSD (females) (27.5 ± 9.3, 0/15) | Positive Symptoms: NA Negative Symptoms: NA | Visual Memory/Learning, Visual Memory/Learning, Speed of Processing, Executive Function, Memory, Attention, Intelligence, Global Cognition | Scanner Strength: 1.0T MRI Morphology: Volume Brain Region: Whole brain, Frontal lobe Neuroimaging Analysis: ROI | NA | Covariates: Positive symptoms pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |
| 111 | 43 SSD (males) (24.7 ± 5.2, 43/0) 32 SSD (females) (27.3 ± 7.7, 0/32) | Positive Symptoms: NA Negative Symptoms: NA | Visual Memory/Learning, Visual Memory/Learning, Speed of Processing, Executive Function, Memory, Attention, Intelligence, Global Cognition | Scanner Strength: 1.0T MRI Morphology: Volume Brain Region: Hippocampus Neuroimaging Analysis: ROI | NA | Covariates: Total Brain Volume pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |
| 112 | 81 SSD (25.5 ± 6.6, 48/33) 23 HC (NA ± NA, 14/9) | Positive Symptoms: NA Negative Symptoms: NA | General Cognition | Scanner Strength: 1.0T MRI Morphology: Volume Brain Region: Cerebellum Neuroimaging Analysis: ROI | NA | Covariates: Total Brain Volume, Age, Parental SES pIQ diff HC: NA Age diff HC: No Sex diff HC: No |

| Reference | Cohort (#, Dx, Mean age ± SD, M/F) | Symptoms | Cognitive Domain | Neuroimaging | Longitudinal Follow Up | Notes |
|-----------|---|--|---|--|------------------------|--|
| 113 | 24 SSD (40.09 ± NA, 20/4) 24 HC (41.74 ± NA, 16/8) | Positive Symptoms: NA Negative Symptoms: NA | Intelligence, Executive Function, Verbal Memory/Learning, Visual Memory/Learning, Working Memory, Attention | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Hippocampus Neuroimaging Analysis: ROI | NA | Covariates: ICV pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 114 | 12 RO-BD (13.9 ± 0.8, 6/6) 12 HC (13.5 ± 0.7, 6/6) | Manic Symptoms: Mild Depressive Symptoms: Moderate | Intelligence | Scanner Strength: 1.0T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI | Follow up: 5 years | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 115 | 56 SSD (32.8 ± 7.7, 39/17) 90 SSD FDR (50.2 ± 15.5, 34/56) 55 HC (38.8 ± 14.1, 27/28) | Positive Symptoms: NA Negative Symptoms: NA | Verbal Memory/Learning, Visual Memory/Learning, Current IQ, Executive Function | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI | NA | Covariates: Whole Brain Volume, IQ, Handedness, Verbal Memory pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 116 | 26 SSD (38.69 ± 10.28, 16/10) 29 HC (33.76 ± 12.38, 20/9) | Positive Symptoms: NA Negative Symptoms: NA | Speed of Processing | Scanner Strength: 3T MRI Morphology: Thickness Brain Region: Whole brain Neuroimaging Analysis: SBM | NA | Covariates: Age, Sex, Mean Cortical Thickness pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 117 | 52 SSD (32.3 ± 9.1, 27/25) 38 HC (28.2 ± 9.4, 21/17) | Positive Symptoms: Mild Negative Symptoms: Mild | Verbal Memory/Learning, Visual Memory/Learning | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Temporopolar, Perihinal, & Entorhinal Cortices Neuroimaging Analysis: ROI | NA | Covariates: Age, Sex, Smoking pIQ diff HC: NA Age diff HC: Yes Sex diff HC: No |
| 118 | 28 RO-SSD (21.37 ± 2.0, 21/7) 52 SSD (38.55 ± 9.21, 38/14) 28 HC (21.96 ± 1.96, 18/10) 52 HC (39.15 ± 10.43) | Positive Symptoms: Mild (both cohorts) Negative Symptoms: Mild (both cohorts) | Current IQ, Premorbid IQ, Visual Memory/Learning | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Hippocampus Neuroimaging Analysis: ROI | NA | Covariates: Age, ICV pIQ diff HC: NA Age diff HC: Yes Sex diff HC: No |
| 119 | 15 SSD (46 ± 7.4, 15/0) 16 HC (48.2 ± 11.1, 16/0) | Positive Symptoms: NA Negative Symptoms: Mild | Memory | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Hippocampus Neuroimaging Analysis: ROI | NA | Covariates: Age, Sex pIQ diff HC: Yes Age diff HC: No Sex diff HC: No |
| 120 | 47 SSD (26.55 ± 6.71, 31/16) | Positive Symptoms: Mild Negative Symptoms: NA | Working Memory, Verbal Memory/Learning, Executive Function | Scanner Strength: 3T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI and VBM | NA | Covariates: Age, Sex, Current IQ, Duration of illness pIQ diff HC: NA Age diff HC: NA Sex diff HC: NA |

| Reference | Cohort (#, Dx, Mean age \pm SD, M/F) | Symptoms | Cognitive Domain | Neuroimaging | Longitudinal Follow Up | Notes |
|-----------|--|--|---|---|------------------------|--|
| 121 | 28 SSD (33.1 \pm 7, 20/8) 14 HC (30.9 \pm 9.5, 9/5) | Positive Symptoms: Mild Negative Symptoms: Mild | Attention, Working Memory, Executive Function | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: VBM | NA | Covariates: Age, Sex pIQ diff HC: NA Age diff HC: No Sex diff HC: Yes |
| 122 | 33 SSD (23.4 \pm 4, 19/14) 28 HC (healthy parents; 51.8 \pm 5.7, 29/31) 60 PA (parents of SSD; 50.7 \pm 5.6, 29/31) 30 HC (23.4 \pm 3.2, 18/12) | Positive Symptoms: Mild Negative Symptoms: Mild | Working Memory, Speed of Processing, Verbal Memory/Learning | Scanner Strength: 3T MRI Morphology: Thickness & surface area Brain Region: Whole brain Neuroimaging Analysis: Vertex-wise | NA | Covariates: Age, Sex pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 123 | 77 RO-SSD (26 \pm 6.6, 43/34) 82 HC (28.9 \pm 8, 41/41) | Positive Symptoms: NA Negative Symptoms: NA | Intelligence | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain Neuroimaging Analysis: ROI | NA | Covariates: Age, ICV pIQ diff HC: NA Age diff HC: No Sex diff HC: No |
| 124 | 23 SSD (46.5 \pm 4.2, 23/0) 23 HC (43.3 \pm 9.6, 23/0) | Positive Symptoms: Mild Negative Symptoms: Moderate | Intelligence, Working Memory, Executive Function | Scanner Strength: 1.5T MRI Morphology: Volume Brain Region: Whole brain, Area 46 Neuroimaging Analysis: ROI | NA | Covariates: None pIQ diff HC: NA Age diff HC: No Sex diff HC: No |

Note. Note that as symptom scales varied across studies and in an attempt to facilitate synthesis of results across studies, we report levels of positive and negative symptom severity based on the manuals of the respective symptom rating scale. #, number of studies; Age diff HC, statistically significant difference in mean age between patients and healthy controls; ARMS, at risk mental state; BD I/II, bipolar disorder type I/type II; Dx, diagnosis; F, female; FDR, first degree relative; HC, healthy controls; IQ, intelligence quotient; M, male; MDD, major depressive disorder; MRI, magnetic resonance imaging; N/A, not available/applicable; NOS, not otherwise specified; pIQ diff HC, statistically significant difference in premorbid IQ scores between patients and healthy controls; PS, psychosis-spectrum; RO-BD, recent-onset bipolar disorder; RO-SSD, recent-onset schizophrenia-spectrum disorders; ROI, region of interest; SD, standard deviation; Sex diff HC, statistically significant difference in sex between patients and healthy controls; SSD, schizophrenia-spectrum disorders; T, tesla. Note that some studies comprise samples of participants that are not included in the synthesis of findings (e.g ARMS cohorts, parents of SSD) because they do not fall within the scope of the review. ‘Large study’ refers to studies with independent patient population samples of at least 100 individuals.

Table 2: Cognition-brain morphology relationships reported from each study

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | | Reference |
|--------|--------------------|-------------------|--------------|---------------|------------|---------------------------------|------------------|-----------------------------|------------------|-----|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | | |
| BD | Attention | | Volume | Frontal | Total | Prefrontal Cortex | Positive | No | No Relationships | 101 | |
| BD | Attention | | Volume | Subcortical | Total | Caudate | No Relationships | No | No Relationships | 101 | |
| BD | Attention | | Volume | Subcortical | Total | Thalamus | No Relationships | No | No Relationships | 101 | |
| BD | Attention | | Volume | Temporal | Total | Hippocampus | Positive | No | No Relationships | 101 | |
| BD | Executive Function | | Surface area | Frontal | Total | | No Relationships | No HC | | 43 | |
| BD | Executive Function | | Thickness | Frontal | Total | Inferior Precentral Cortex | Positive | Yes | Positive | 1 | |
| BD | Executive Function | | Thickness | Frontal | Total | Lateral Prefrontal Cortex | Positive | No | No Relationships | 1 | |
| BD | Executive Function | | Thickness | Frontal | Left | Lateral Superior Frontal Cortex | Positive | No | No Relationships | 1 | |
| BD | Executive Function | | Thickness | Frontal | Right | Medial Superior Frontal Cortex | Positive | Yes | Positive | 1 | |
| BD | Executive Function | | Thickness | Frontal | Total | | No Relationships | No HC | | 43 | |
| BD | Executive Function | | Volume | Frontal | Left | Inferior Orbitofrontal Cortex | Positive | No HC | | 17 | |
| BD | Executive Function | | Volume | Frontal | Total | | No Relationships | No HC | | 43 | |
| BD | Executive Function | | Volume | Insula Cortex | Left | Insula | Positive | No | No Relationships | 77 | |
| BD | Executive Function | | Thickness | Occipital | Total | Medial Occipital Cortex | Positive | No | No Relationships | 1 | |
| BD | Executive Function | | Thickness | Parietal | Right | Precuneus | No Relationships | Yes | Positive | 86 | |
| BD | Executive Function | | Surface area | Temporal | Left | Parahippocampal Gyrus | Positive | No HC | | 106 | |
| BD | Executive Function | | Surface area | Temporal | Total | | No Relationships | No HC | | 43 | |
| BD | Executive Function | | Thickness | Temporal | Left | Superior Temporal Gyrus | Positive | No | No Relationships | 86 | |
| BD | Executive Function | | Thickness | Temporal | Total | | No Relationships | No HC | | 43 | |
| BD | Executive Function | | Volume | Temporal | Right | Hippocampus | Positive | No HC | | 106 | |
| BD | Executive Function | | Volume | Temporal | Total | | No Relationships | No HC | | 43 | |
| BD | Executive Function | | Volume | Whole Brain | Total | | No Relationships | No HC | | 9 | |
| BD | Executive Function | | Volume | Whole Brain | Total | Total Grey Matter | No Relationships | No | No Relationships | 100 | |
| BD | Intelligence | Current IQ | Volume | Cerebellum | Total | | Positive | No | No Relationships | 81 | |
| BD | Intelligence | Current IQ | Surface area | Frontal | Total | | No Relationships | No HC | | 43 | |
| BD | Intelligence | Current IQ | Thickness | Frontal | Total | | No Relationships | No HC | | 43 | |
| BD | Intelligence | Current IQ | Volume | Frontal | Total | | No Relationships | No HC | | 43 | |
| BD | Intelligence | Premorbid IQ | Surface area | Frontal | Total | Total Frontal | Positive | No HC | | 43 | |
| BD | Intelligence | Premorbid IQ | Volume | Frontal | Total | Total Frontal | Positive | No HC | | 43 | |
| BD | Intelligence | Current IQ | Volume | Temporal | Total | Amygdala | No Relationships | No HC | | 35 | |
| BD | Intelligence | Current IQ | Volume | Temporal | Total | Hippocampus | No Relationships | No HC | | 35 | |

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | | Reference |
|--------|------------------------|-------------------|--------------|-------------|------------|-----------------------|------------------|-----------------------------|------------------|-----|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | | |
| BD | Intelligence | Current IQ | Volume | Subcortical | Total | Thalamus | No Relationships | No HC | | 35 | |
| BD | Intelligence | Current IQ | Surface area | Temporal | Total | | No Relationships | No HC | | 43 | |
| BD | Intelligence | Current IQ | Thickness | Temporal | Total | | No Relationships | No HC | | 43 | |
| BD | Intelligence | Current IQ | Volume | Temporal | Total | Temporal Lobe | Positive | Yes | Positive | 81 | |
| BD | Intelligence | Current IQ | Volume | Temporal | Total | | No Relationships | No HC | | 43 | |
| BD | Intelligence | Full Scale IQ | Volume | Temporal | Total | Temporal Lobe | Positive | Yes | Positive | 81 | |
| BD | Intelligence | Global Cognition | Volume | Temporal | Total | Hippocampus Subiculum | No Relationships | No | No Relationships | 52 | |
| BD | Intelligence | Current IQ | Volume | Whole Brain | Total | | No Relationships | No HC | | 9 | |
| BD | Intelligence | Global Cognition | Volume | Whole Brain | Total | | No Relationships | No | No Relationships | 79 | |
| BD | Intelligence | Full Scale IQ | Volume | Whole Brain | Total | Total Grey Matter | No Relationships | No | No Relationships | 100 | |
| BD | Memory | General Memory | Volume | Temporal | Left | Amygdala | Positive | No | No Relationships | 61 | |
| BD | Memory | General Memory | Volume | Whole Brain | Total | | No Relationships | No | No Relationships | 81 | |
| BD | Speed of Processing | | Surface area | Temporal | Total | Inferior Temporal | Positive | No | No Relationships | 48 | |
| BD | Verbal Memory/Learning | | Volume | Temporal | Left | Amygdala | Positive | No | No Relationships | 61 | |
| BD | Verbal Memory/Learning | | Volume | Temporal | Total | Hippocampus Subiculum | Positive | Yes | Positive | 52 | |
| BD | Verbal Memory/Learning | | Volume | Temporal | Left | Hippocampus | No Relationships | No | No Relationships | 63 | |
| BD | Verbal Memory/Learning | | Volume | Temporal | Right | Hippocampus | Positive | Yes | Positive | 63 | |
| BD | Verbal Memory/Learning | | Volume | Temporal | Total | Hippocampus | No Relationships | No | No Relationships | 12 | |
| BD | Verbal Memory/Learning | | Volume | Whole Brain | Total | | No Relationships | No HC | | 9 | |
| BD | Verbal Memory/Learning | | Volume | Whole Brain | Total | Total Grey Matter | No Relationships | No | No Relationships | 100 | |
| BD | Visual Memory/Learning | | Surface area | Frontal | Total | | No Relationships | No HC | | 43 | |
| BD | Visual Memory/Learning | | Thickness | Frontal | Total | | No Relationships | No HC | | 43 | |
| BD | Visual Memory/Learning | | Volume | Frontal | Total | | No Relationships | No HC | | 43 | |
| BD | Visual Memory/Learning | | Surface area | Temporal | Total | | No Relationships | No HC | | 43 | |
| BD | Visual Memory/Learning | | Thickness | Temporal | Total | | No Relationships | No HC | | 43 | |
| BD | Visual Memory/Learning | | Volume | Temporal | Left | Hippocampus | No Relationships | No | No Relationships | 63 | |
| BD | Visual Memory/Learning | | Volume | Temporal | Right | Hippocampus | No Relationships | No | No Relationships | 63 | |
| BD | Visual Memory/Learning | | Volume | Temporal | Total | | No Relationships | No HC | | 43 | |
| BD | Visual Memory/Learning | | Volume | Whole Brain | Total | | No Relationships | No HC | | 9 | |
| BD | Visual Memory/Learning | | Volume | Whole Brain | Total | Total Grey Matter | No Relationships | No | No Relationships | 100 | |
| BD | Working Memory | | Thickness | Frontal | Total | Caudal Middle Frontal | Positive | No | No Relationships | 16 | |

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | Reference |
|--------|-----------------------------------|-------------------|--------------|------------------|------------|--------------------------|------------------|-----------------------------|------------------|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | |
| BD | Working Memory | | Thickness | Frontal | Total | Rostral Middle Frontal | Positive | No | No Relationships | 16 |
| BD | Working Memory | | Thickness | Frontal | Total | Superior Frontal | Positive | No | No Relationships | 16 |
| BD | Working Memory | | Surface area | Temporal | Left | Parahippocampal Gyrus | Positive | No HC | | 106 |
| BD | Working Memory | | Volume | Temporal | Right | Hippocampus | Positive | No HC | | 106 |
| BD | Working Memory | | Volume | Whole Brain | Total | | No Relationships | No HC | | 9 |
| BD | Working Memory | | Volume | Whole Brain | Total | Total Grey Matter | No Relationships | No | No Relationships | 100 |
| RO-BD | Attention | | Thickness | Parietal | Left | Intraparietal Sulcus | Positive | No HC | | 51 |
| RO-BD | Attention | | Thickness | Parietal | Left | Posterior Angular Gyrus | Positive | No HC | | 51 |
| RO-BD | Attention | | Thickness | Parietal | Right | Supramarginal Gyrus | Positive | No HC | | 51 |
| RO-BD | Executive Function | | Surface area | Frontal | Total | Precentral | Positive | Yes | Positive | 55 |
| RO-BD | Executive Function | | Surface area | Parietal | Total | Postcentral | Positive | Yes | Positive | 55 |
| RO-BD | Executive Function | | Volume | Subcortical | Left | Caudate | Negative | Yes | Positive | 67 |
| RO-BD | Executive Function | | Volume | Subcortical | Right | Caudate | Negative | Yes | Positive | 67 |
| RO-BD | Executive Function/Verbal Fluency | | Thickness | Parietal | Right | Supramarginal Gyrus | Positive | No HC | | 51 |
| RO-BD | Speed of Processing | | Thickness | Parietal | Right | Parieto-occipital Sulcus | Positive | No HC | | 51 |
| RO-BD | Verbal Memory/Learning | | Volume | Frontal | Right | Inferior Frontal Gyrus | Negative | Yes | Negative | 14 |
| RO-BD | Verbal Memory/Learning | | Volume | Frontal | Right | Medial Frontal Gyrus | Positive | No | No Relationships | 14 |
| RO-BD | Verbal Memory/Learning | | Volume | Frontal | Left | Superior Frontal Gyrus | Negative | No | No Relationships | 14 |
| RO-BD | Verbal Memory/Learning | | Thickness | Parietal | Left | Intraparietal Sulcus | Positive | No HC | | 51 |
| RO-BD | Verbal Memory/Learning | | Thickness | Parietal | Right | Supramarginal Gyrus | Positive | No HC | | 51 |
| RO-BD | Verbal Memory/Learning | | Thickness | Temporal | Right | Superior Temporal Gyrus | Positive | No HC | | 51 |
| RO-BD | Verbal Memory/Learning | | Volume | Temporal | Left | Hippocampus | Negative | Yes | Positive | 14 |
| RO-BD | Verbal Memory/Learning | | Volume | Temporal | Right | Hippocampus | Negative | No | No Relationships | 14 |
| RO-SSD | Attention | | Volume | Cingulate Cortex | Total | Anterior Cingulate Gyrus | No Relationships | No HC | | 72 |
| RO-SSD | Attention | | Thickness | Frontal | Right | Precentral Gyrus | Positive | No HC | | 51 |
| RO-SSD | Attention | | Volume | Frontal | Left | Inferior Frontal Gyrus | Positive | No | No Relationships | 98 |
| RO-SSD | Attention | | Volume | Frontal | Total | Orbital Frontal Gyrus | No Relationships | No HC | | 72 |
| RO-SSD | Attention | | Volume | Frontal | Total | Superior Frontal Gyrus | No Relationships | No HC | | 72 |
| RO-SSD | Attention | | Volume | Parietal | Left | Angular Gyrus | Positive | No | No Relationships | 98 |
| RO-SSD | Attention | | Volume | Parietal | Total | Postcentral Gyrus | Negative | No | No Relationships | 32 |
| RO-SSD | Attention | | Volume | Parietal | Total | Postcentral Gyrus | Positive | No | No Relationships | 98 |
| RO-SSD | Attention | | Volume | Parietal | Total | Supramarginal Gyrus | Positive | No | No Relationships | 98 |
| RO-SSD | Attention | | Volume | Subcortical | Right | Caudate | Negative | No | No Relationships | 23 |
| RO-SSD | Attention | | Volume | Subcortical | Left | Thalamic Nucleus | Positive | No | No Relationships | 98 |

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | | Reference |
|--------|-----------------------------------|-------------------|-----------|------------------|------------|-------------------------------|-----------|-----------------------------|-----------|------------------|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | | |
| RO-SSD | Attention | | Thickness | Whole Brain | Total | | | No Relationships | No | No Relationships | 96 |
| RO-SSD | Attention | | Volume | Whole Brain | Total | | | No Relationships | No HC | | 93 |
| RO-SSD | Attention | | Volume | Whole Brain | Total | | | Positive | No HC | | 72 |
| RO-SSD | Executive Function | | Volume | Basal Ganglia | Total | Globus Pallidus | | Positive | No HC | | 24 |
| RO-SSD | Executive Function | | Volume | Basal Ganglia | Right | Nucleus Accumbens | | Positive | No HC | | 24 |
| RO-SSD | Executive Function | | Volume | Basal Ganglia | Total | Nucleus Accumbens | | Positive | No | No Relationships | 31 |
| RO-SSD | Executive Function | | Volume | Brain Stem | Left | Pons | | Negative | No HC | | 24 |
| RO-SSD | Executive Function | | Volume | Brain Stem | Total | | | Negative | No HC | | 24 |
| RO-SSD | Executive Function | | Volume | Cerebellum | Right | Inferior Vermis | | Negative | No HC | | 24 |
| RO-SSD | Executive Function | | Volume | Cerebellum | Total | | | Negative | No HC | | 24 |
| RO-SSD | Executive Function | | Volume | Cingulate Cortex | Total | Anterior Cingulate | | Positive | No HC | | 110 |
| RO-SSD | Executive Function | | Volume | Cingulate Cortex | Total | Anterior Cingulate Gyrus | | No Relationships | No HC | | 72 |
| RO-SSD | Executive Function | | Volume | Frontal | Total | Orbital Frontal Gyrus | | No Relationships | No HC | | 72 |
| RO-SSD | Executive Function | | Volume | Frontal | Left | Orbital Inferior Frontal Gyri | | Positive | No | No Relationships | 40 |
| RO-SSD | Executive Function | | Volume | Frontal | Total | Superior Frontal Gyrus | | No Relationships | No HC | | 72 |
| RO-SSD | Executive Function | | Volume | Occipital | Total | Brodman Area 19 | | Negative | No HC | | 24 |
| RO-SSD | Executive Function | | Volume | Occipital | Left | Lingual Gyrus | | Negative | No HC | | 24 |
| RO-SSD | Executive Function | | Volume | Occipital | Right | Occipital Gyrus | | Negative | No HC | | 24 |
| RO-SSD | Executive Function | | Volume | Parietal | Total | Brodman Area 40 | | Positive | No HC | | 24 |
| RO-SSD | Executive Function | | Volume | Parietal | Total | Brodman Area 7 | | Positive | No HC | | 24 |
| RO-SSD | Executive Function | | Volume | Parietal | Left | Inferior Parietal Lobule | | Positive | No HC | | 24 |
| RO-SSD | Executive Function | | Volume | Parietal | Left | Superior Parietal Lobule | | Positive | No HC | | 24 |
| RO-SSD | Executive Function | | Volume | Temporal | Total | Amygdala | | Positive | No | No Relationships | 31 |
| RO-SSD | Executive Function | | Volume | Subcortical | Right | Caudate | | Negative | No | No Relationships | 23 |
| RO-SSD | Executive Function | | Volume | Subcortical | Total | Caudate | | No Relationships | Yes | Positive | 58 |
| RO-SSD | Executive Function | | Volume | Subcortical | Total | Posterior Lobe | | Negative | No HC | | 24 |
| RO-SSD | Executive Function | | Volume | Temporal | Total | Anterior Hippocampus | | Positive | No HC | | 6 |
| RO-SSD | Executive Function | | Volume | Temporal | Left | Fusiform Gyrus | | Negative | No HC | | 24 |
| RO-SSD | Executive Function | | Volume | Temporal | Left | Temporal Lobe | | Positive | No | No Relationships | 23 |
| RO-SSD | Executive Function | | Thickness | Whole Brain | Total | | | No Relationships | No | No Relationships | 96 |
| RO-SSD | Executive Function | | Volume | Whole Brain | Total | | | No Relationships | No HC | | 93 |
| RO-SSD | Executive Function | | Volume | Whole Brain | Total | | | No Relationships | No HC | | 72 |
| RO-SSD | Executive Function/Verbal Fluency | | Volume | Cerebellum | Left | Lobule VI | | Positive | No | No Relationships | 62 |
| RO-SSD | Executive Function/Verbal Fluency | | Volume | Cerebellum | Left | Lobule X | | Positive | No | No Relationships | 62 |
| RO-SSD | Executive Function/Verbal Fluency | | Volume | Frontal | Left | Medial Frontal Gyrus | | Positive | No | No Relationships | 21 |

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | | Reference |
|--------|-----------------------------------|-------------------|--------------|------------------|------------|---|-----------------|-----------------------------|-----------------|-----|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | | |
| RO-SSD | Executive Function/Verbal Fluency | | Volume | Insula Cortex | Right | Insula | No Relationship | Yes | Positive | 21 | |
| RO-SSD | Executive Function/Verbal Fluency | | Volume | Temporal | Right | Superior Temporal Gyrus | Positive | No | No Relationship | 21 | |
| RO-SSD | General Memory | | Volume | Temporal | Total | Hippocampus | No | No | No Relationship | 8 | |
| RO-SSD | Intelligence | Current IQ | Volume | Frontal | Total | Orbitofrontal Cortex | Positive | No | No Relationship | 13 | |
| RO-SSD | Intelligence | Current IQ | Volume | Frontal | Total | Rectus | Positive | No | No Relationship | 13 | |
| RO-SSD | Intelligence | Current IQ | Volume | Frontal | Total | Superior Frontal Cortex | Positive | No | No Relationship | 13 | |
| RO-SSD | Intelligence | Global Cognition | Volume | Frontal | Right | Inferior Dorsolateral Prefrontal Cortex | Positive | No | No Relationship | 79 | |
| RO-SSD | Intelligence | Global Cognition | Volume | Frontal | Right | Superior Dorsolateral Prefrontal Cortex | Positive | No | No Relationship | 79 | |
| RO-SSD | Intelligence | Global Cognition | Volume | Parietal | Left | Lateral Parietal Cortex | Positive | No | No Relationship | 79 | |
| RO-SSD | Intelligence | Global Cognition | Volume | Parietal | Right | Lateral Parietal Cortex | Positive | No | No Relationship | 79 | |
| RO-SSD | Intelligence | Global Cognition | Volume | Subcortical | Right | Caudate | Negative | No | No Relationship | 23 | |
| RO-SSD | Intelligence | Global Cognition | Volume | Temporal | Left | Entorhinal Cortex | Positive | No HC | | 94 | |
| RO-SSD | Intelligence | Global Cognition | Volume | Temporal | Right | Superior Temporal Cortex | Positive | No | No Relationship | 79 | |
| RO-SSD | Intelligence | Current IQ | Surface area | Whole Brain | Total | | No Relationship | No | No Relationship | 92 | |
| RO-SSD | Intelligence | Current IQ | Thickness | Whole Brain | Total | | No Relationship | No | No Relationship | 92 | |
| RO-SSD | Intelligence | Current IQ | Volume | Whole Brain | Total | Total Grey Matter | No Relationship | No | No Relationship | 56 | |
| RO-SSD | Intelligence | Current IQ | Volume | Whole Brain | Total | Total Grey Matter | Positive | No | No Relationship | 123 | |
| RO-SSD | Intelligence | Full Scale IQ | Volume | Whole Brain | Total | Total Brain Volume | No Relationship | No | No Relationship | 29 | |
| RO-SSD | Intelligence | Premorbid IQ | Surface area | Whole Brain | Total | Total Cortical Surface Area | Positive | No HC | | 44 | |
| RO-SSD | Intelligence | Premorbid IQ | Thickness | Whole Brain | Total | Total Cortical Thickness | Positive | No HC | | 44 | |
| RO-SSD | Intelligence | Premorbid IQ | Volume | Whole Brain | Total | Total Grey Matter | No Relationship | No | No Relationship | 123 | |
| RO-SSD | Speed of Processing | | Volume | Cerebellum | Left | Lobule VI | No Relationship | Yes | Positive | 62 | |
| RO-SSD | Speed of Processing | | Volume | Cerebellum | Left | Lobule X | Positive | No | No Relationship | 62 | |
| RO-SSD | Speed of Processing | | Volume | Cerebellum | Total | | No Relationship | No | No Relationship | 62 | |
| RO-SSD | Speed of Processing | | Volume | Cerebellum | Total | | No Relationship | No | No Relationship | 29 | |
| RO-SSD | Speed of Processing | | Volume | Cingulate Cortex | Total | Anterior Cingulate Gyrus | No Relationship | No HC | | 72 | |
| RO-SSD | Speed of Processing | | Thickness | Frontal | Right | Precentral Gyrus | Negative | No HC | | 51 | |
| RO-SSD | Speed of Processing | | Thickness | Frontal | Right | Precentral Gyrus | Negative | No HC | | 51 | |
| RO-SSD | Speed of Processing | | Volume | Frontal | Total | Orbital Frontal Gyrus | No Relationship | No HC | | 72 | |
| RO-SSD | Speed of Processing | | Volume | Frontal | Total | Superior Frontal Gyrus | No Relationship | No HC | | 72 | |
| RO-SSD | Speed of Processing | | Thickness | Parietal | Left | Intraparietal Sulcus | Negative | No HC | | 51 | |
| RO-SSD | Speed of Processing | | Volume | Temporal | Total | Anterior Hippocampus | Positive | No HC | | 6 | |

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | | Reference |
|--------|------------------------|-------------------|-----------|------------------|------------|------------------------------|------------------|-----------------------------|------------------|-----|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | | |
| RO-SSD | Speed of Processing | | Volume | Whole Brain | Total | Total Brain Volume | No Relationships | No | No Relationships | 29 | |
| RO-SSD | Speed of Processing | | Volume | Whole Brain | Total | | No Relationships | No HC | | 93 | |
| RO-SSD | Speed of Processing | | Volume | Whole Brain | Total | | Positive | No HC | | 72 | |
| RO-SSD | Verbal Memory/Learning | | Volume | Cingulate Cortex | Total | Anterior Cingulate Gyrus | No Relationships | No HC | | 72 | |
| RO-SSD | Verbal Memory/Learning | | Volume | Frontal | Total | Orbital Frontal Gyrus | No Relationships | No HC | | 72 | |
| RO-SSD | Verbal Memory/Learning | | Volume | Frontal | Total | Superior Frontal Gyrus | No Relationships | No HC | | 72 | |
| RO-SSD | Verbal Memory/Learning | | Volume | Subcortical | Total | Caudate | Negative | No | No Relationships | 58 | |
| RO-SSD | Verbal Memory/Learning | | Volume | Subcortical | Total | | No Relationships | No HC | | 27 | |
| RO-SSD | Verbal Memory/Learning | | Volume | Temporal | Left | Hippocampal Gyri | Positive | No | No Relationships | 40 | |
| RO-SSD | Verbal Memory/Learning | | Volume | Temporal | Left | Hippocampus | Positive | No | No Relationships | 74 | |
| RO-SSD | Verbal Memory/Learning | | Thickness | Whole Brain | Total | | No Relationships | No | No Relationships | 96 | |
| RO-SSD | Verbal Memory/Learning | | Volume | Whole Brain | Total | | No Relationships | No HC | | 93 | |
| RO-SSD | Verbal Memory/Learning | | Volume | Whole Brain | Total | | No Relationships | No HC | | 72 | |
| RO-SSD | Visual Memory/Learning | | Volume | Cerebellum | Total | | No Relationships | No | No Relationships | 29 | |
| RO-SSD | Visual Memory/Learning | | Volume | Parietal | Left | Presupplementary Motor Area | Positive | No | No Relationships | 29 | |
| RO-SSD | Visual Memory/Learning | | Volume | Parietal | Right | Presupplementary Motor Area | No Relationships | No | No Relationships | 29 | |
| RO-SSD | Visual Memory/Learning | | Volume | Temporal | Right | Hippocampal Gyri | Positive | No | No Relationships | 40 | |
| RO-SSD | Visual Memory/Learning | | Volume | Temporal | Total | Hippocampal Subfield (CA4DG) | Positive | No | No Relationships | 118 | |
| RO-SSD | Visual Memory/Learning | | Volume | Temporal | Total | Hippocampal Stratum | Positive | No | No Relationships | 118 | |
| RO-SSD | Visual Memory/Learning | | Thickness | Whole Brain | Total | | No Relationships | No | No Relationships | 96 | |
| RO-SSD | Visual Memory/Learning | | Volume | Whole Brain | Total | Total Brain Volume | No Relationships | No | No Relationships | 29 | |
| RO-SSD | Visual Memory/Learning | | Volume | Whole Brain | Total | | No Relationships | No HC | | 93 | |
| RO-SSD | Working Memory | | Volume | Frontal | Total | Orbitofrontal Cortex | Positive | Yes | Positive | 13 | |
| RO-SSD | Working Memory | | Volume | Frontal | Total | Superior Frontal Cortex | Positive | Yes | Positive | 13 | |
| RO-SSD | Working Memory | | Volume | Frontal | Left | Superior Frontal Gyrus | Positive | No | No Relationships | 21 | |
| RO-SSD | Working Memory | | Volume | Parietal | Left | Postcentral Gyrus | Negative | No | No Relationships | 32 | |
| RO-SSD | Working Memory | | Volume | Temporal | Left | Hippocampal Gyri | Positive | No | No Relationships | 40 | |
| RO-SSD | Working Memory | | Volume | Temporal | Right | Hippocampal Gyri | Positive | No | No Relationships | 40 | |
| RO-SSD | Working Memory | | Thickness | Whole Brain | Total | | No Relationships | No | No Relationships | 96 | |
| RO-SSD | Working Memory | | Volume | Whole Brain | Total | Total Grey Matter | No Relationships | Yes | Positive | 19 | |
| RO-SSD | Working Memory | | Volume | Whole Brain | Total | | No Relationships | No HC | | 93 | |

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | | Reference |
|--------|--------------------|---------------------------------|--------------|------------------|------------|--------------------------------|------------------|-----------------------------|------------------|-----|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | | |
| SSD | Attention | | Volume | Basal Ganglia | Right | Nucleus Accumbens | Positive | No | No Relationships | 66 | |
| SSD | Attention | | Volume | Cerebellum | Total | | No Relationships | No | No Relationships | 112 | |
| SSD | Attention | | Surface area | Frontal | Total | Prefrontal Cortex | No Relationships | No HC | | 46 | |
| SSD | Attention | | Thickness | Frontal | Right | Frontal Cortex | Negative | | | 15 | |
| SSD | Attention | | Thickness | Frontal | Left | Inferior Orbitofrontal Cortex | Positive | No | No Relationships | 26 | |
| SSD | Attention | | Thickness | Frontal | Right | Pars Opercularis | Positive | No | No Relationships | 26 | |
| SSD | Attention | | Thickness | Frontal | Total | Prefrontal Cortex | No Relationships | No HC | | 46 | |
| SSD | Attention | | Thickness | Frontal | Left | Superior Frontal Gyrus | Negative | | | 15 | |
| SSD | Attention | | Volume | Frontal | Right | Dorsolateral Prefrontal Cortex | Positive | No | No Relationships | 70 | |
| SSD | Attention | | Volume | Frontal | Left | Prefrontal Cortex | Positive | No HC | | 105 | |
| SSD | Attention | | Volume | Frontal | Total | Prefrontal Cortex | No Relationships | No HC | | 46 | |
| SSD | Attention | | Volume | Frontal | Total | Total Frontal Lobe | Positive | No HC | | 2 | |
| SSD | Attention | | Thickness | Parietal | Total | Parietal Cortex | Negative | No HC | | 20 | |
| SSD | Attention | | Volume | Parietal | Total | Total Parietal Lobe | Positive | No HC | | 2 | |
| SSD | Attention | | Volume | Subcortical | Total | Caudate | Positive | No HC | | 2 | |
| SSD | Attention | | Volume | Subcortical | Total | Thalamus | No Relationships | No | No Relationships | 45 | |
| SSD | Attention | | Thickness | Temporal | Left | Superior Temporal Gyrus | Negative | | | 15 | |
| SSD | Attention | | Thickness | Temporal | Left | Transverse Temporal Gyrus | Positive | No | No Relationships | 26 | |
| SSD | Attention | | Thickness | Temporal | Right | Transverse Temporal Gyrus | Positive | No | No Relationships | 26 | |
| SSD | Attention | | Volume | Temporal | Total | Hippocampal Tail | Positive | No HC | | 82 | |
| SSD | Attention | | Volume | Temporal | Left | Posterior Hippocampus | Negative | No | No Relationships | 113 | |
| SSD | Attention | | Volume | Temporal | Total | Superior Temporal Gyrus | No Relationships | Yes | Positive | 42 | |
| SSD | Attention | | Thickness | Whole Brain | Total | Total Cortical Thickness | Negative | No HC | | 20 | |
| SSD | Attention | | Volume | Whole Brain | Total | Total Cerebral Tissue | Positive | No HC | | 2 | |
| SSD | Attention | | Volume | Whole Brain | Total | Total Grey Matter | Positive | No | No Relationships | 41 | |
| SSD | Attention | | Volume | Whole Brain | Total | Total Grey Matter | Positive | Yes | Positive | 41 | |
| SSD | Executive Function | | Volume | Cerebellum | Total | Crus I/II | Positive | No | No Relationships | 69 | |
| SSD | Executive Function | | Volume | Cerebellum | Left | | Positive | No HC | | 103 | |
| SSD | Executive Function | | Volume | Cerebellum | Right | | Positive | No HC | | 103 | |
| SSD | Executive Function | | Volume | Cerebellum | Total | | No Relationships | Yes | Positive | 112 | |
| SSD | Executive Function | | Volume | Cingulate Cortex | Right | Anterior Cingulate | Positive | No HC | | 103 | |
| SSD | Executive Function | | Volume | Cingulate Cortex | Left | Cingulate Gyrus | Positive | No HC | | 103 | |
| SSD | Executive Function | | Volume | Cingulate Cortex | Right | Cingulate Gyrus | Positive | No HC | | 103 | |
| SSD | Executive Function | Cognitive Flexibility/Switching | Volume | Frontal | Total | Prefrontal Cortex | Positive | No | No Relationships | 5 | |
| SSD | Executive Function | Sensorimotor Gating | Volume | Frontal | Left | Dorsolateral Prefrontal Cortex | Positive | No HC | | 71 | |

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | Reference |
|--------|--------------------|---------------------|--------------|-------------|------------|----------------------------------|-----------------|-----------------------------|-----------------|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | |
| SSD | Executive Function | Sensorimotor Gating | Volume | Frontal | Right | Middle Frontal Cortex | Positive | No HC | | 71 |
| SSD | Executive Function | Sensorimotor Gating | Volume | Frontal | Right | Orbitofrontal Cortex | Positive | No HC | | 71 |
| SSD | Executive Function | | Surface area | Frontal | Total | Prefrontal Cortex | No Relationship | No HC | | 46 |
| SSD | Executive Function | | Thickness | Frontal | Right | Inferior Frontal Gyrus | Positive | Yes | Positive | 47 |
| SSD | Executive Function | | Thickness | Frontal | Total | Pars Opercularis | Positive | No | No Relationship | 64 |
| SSD | Executive Function | | Thickness | Frontal | Total | Prefrontal Cortex | No Relationship | No HC | | 46 |
| SSD | Executive Function | | Thickness | Frontal | Total | Superior Frontal Gyrus | Positive | Yes | Positive | 47 |
| SSD | Executive Function | | Volume | Frontal | Total | Dorsolateral Prefrontal Cortex | Positive | Yes | Positive | 57 |
| SSD | Executive Function | | Volume | Frontal | Left | Inferior Frontal Gyrus | Positive | No | No Relationship | 87 |
| SSD | Executive Function | | Volume | Frontal | Total | Inferior Frontal Gyrus | Positive | Yes | Positive | 57 |
| SSD | Executive Function | | Volume | Frontal | Left | Middle Frontal Gyrus | Positive | No | No Relationship | 7 |
| SSD | Executive Function | | Volume | Frontal | Left | Middle Frontal Gyrus | Positive | Yes | Positive | 65 |
| SSD | Executive Function | | Volume | Frontal | Left | Middle Orbitofrontal Gyrus | No Relationship | Yes | Positive | 83 |
| SSD | Executive Function | | Volume | Frontal | Right | Middle Orbitofrontal Gyrus | No Relationship | Yes | Positive | 83 |
| SSD | Executive Function | | Volume | Frontal | Left | Orbitofrontal Cortex | Positive | No | No Relationship | 102 |
| SSD | Executive Function | | Volume | Frontal | Left | Prefrontal Cortex | Positive | No HC | | 105 |
| SSD | Executive Function | | Volume | Frontal | Total | Prefrontal Cortex | No Relationship | No HC | | 46 |
| SSD | Executive Function | | Volume | Frontal | Total | Prefrontal Cortex | Positive | No HC | | 105 |
| SSD | Executive Function | | Volume | Frontal | Left | Inferior Frontal Gyrus | Positive | No HC | | 18 |
| SSD | Executive Function | | Volume | Frontal | Right | Inferior Frontal Gyrus | Positive | No HC | | 18 |
| SSD | Executive Function | | Volume | Occipital | Left | Occipital Lobe | Positive | No HC | | 103 |
| SSD | Executive Function | | Volume | Occipital | Right | Occipital Lobe | Positive | No HC | | 103 |
| SSD | Executive Function | | Volume | Parietal | Total | Parietal-Occipital Lobe | Positive | No | No Relationship | 108 |
| SSD | Executive Function | | Volume | Parietal | Total | Total Parietal Lobe | Positive | No HC | | 2 |
| SSD | Executive Function | | Volume | Temporal | Left | Amygdala | Positive | No | No Relationship | 97 |
| SSD | Executive Function | | Volume | Temporal | Right | Amygdala | Positive | No | No Relationship | 97 |
| SSD | Executive Function | | Volume | Subcortical | Total | Caudate | Positive | No HC | | 2 |
| SSD | Executive Function | | Volume | Subcortical | Left | Putamen | Negative | No | No Relationship | 49 |
| SSD | Executive Function | | Volume | Subcortical | Right | Putamen | Negative | No | No Relationship | 49 |
| SSD | Executive Function | | Volume | Subcortical | Total | Putamen | Positive | No HC | | 2 |
| SSD | Executive Function | | Volume | Subcortical | Total | Thalamus | No Relationship | No | No Relationship | 45 |
| SSD | Executive Function | | Volume | Subcortical | Total | Thalamus | Positive | No HC | | 2 |
| SSD | Executive Function | | Thickness | Temporal | Right | Anterior Superior Temporal Gyrus | Positive | Yes | Positive | 47 |
| SSD | Executive Function | | Thickness | Temporal | Left | Superior Temporal Gyrus | Positive | Yes | Positive | 47 |
| SSD | Executive Function | | Thickness | Temporal | Left | Temporal Pole | Positive | Yes | Positive | 47 |

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | | Reference |
|--------|-----------------------------------|-------------------|-----------|-------------|------------|-----------------------------------|------------------|-----------------------------|------------------|-----|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | | |
| SSD | Executive Function | | Volume | Temporal | Left | Anterior Hippocampus | Positive | No | No Relationships | 102 | |
| SSD | Executive Function | | Volume | Temporal | Left | Anterior Hippocampus | Positive | No | No Relationships | 53 | |
| SSD | Executive Function | | Volume | Temporal | Right | Anterior Hippocampus | Positive | No | No Relationships | 53 | |
| SSD | Executive Function | | Volume | Temporal | Total | Anterior Hippocampus | Positive | No | No Relationships | 111 | |
| SSD | Executive Function | | Volume | Temporal | Left | Hippocampus | No Relationships | Yes | Negative | 85 | |
| SSD | Executive Function | | Volume | Temporal | Left | Hippocampus | Positive | No | No Relationships | 97 | |
| SSD | Executive Function | | Volume | Temporal | Left | Hippocampus | Positive | No | No Relationships | 53 | |
| SSD | Executive Function | | Volume | Temporal | Right | Hippocampus | No Relationships | Yes | Negative | 85 | |
| SSD | Executive Function | | Volume | Temporal | Right | Hippocampus | Positive | No | No Relationships | 97 | |
| SSD | Executive Function | | Volume | Temporal | Right | Hippocampus | Positive | No | No Relationships | 53 | |
| SSD | Executive Function | | Volume | Temporal | Total | Hippocampus | Positive | Yes | Positive | 57 | |
| SSD | Executive Function | | Volume | Temporal | Left | Parahippocampal Gyrus | Positive | No HC | | 84 | |
| SSD | Executive Function | | Volume | Temporal | Right | Parahippocampal Gyrus | Positive | No HC | | 84 | |
| SSD | Executive Function | | Volume | Temporal | Total | Parahippocampal Gyrus | Positive | No HC | | 103 | |
| SSD | Executive Function | | Volume | Temporal | Left | Posterior Hippocampus | Negative | No | No Relationships | 113 | |
| SSD | Executive Function | | Volume | Temporal | Left | Posterior Hippocampus | Positive | No | No Relationships | 53 | |
| SSD | Executive Function | | Volume | Temporal | Right | Posterior Hippocampus | Positive | No | No Relationships | 53 | |
| SSD | Executive Function | | Volume | Temporal | Left | Posterior Superior Temporal Gyrus | Positive | No HC | | 84 | |
| SSD | Executive Function | | Volume | Temporal | Right | Posterior Superior Temporal Gyrus | Positive | No HC | | 84 | |
| SSD | Executive Function | | Volume | Temporal | Total | Temporal Lobe | No Relationships | Yes | Negative | 89 | |
| SSD | Executive Function | | Volume | Temporal | Total | Temporal Lobe | Positive | No HC | | 2 | |
| SSD | Executive Function | | Volume | Temporal | Total | Temporal Pole | No Relationships | Yes | Positive | 42 | |
| SSD | Executive Function | | Volume | Temporal | Right | Ventro-temporal Cortex | Positive | No | No Relationships | 70 | |
| SSD | Executive Function | | Volume | Whole Brain | Total | Total Brain Volume | No Relationships | No | No Relationships | 5 | |
| SSD | Executive Function | | Volume | Whole Brain | Total | Total Brain Volume | Positive | No HC | | 105 | |
| SSD | Executive Function | | Volume | Whole Brain | Total | Total Cerebral Tissue | Positive | No HC | | 2 | |
| SSD | Executive Function | | Volume | Whole Brain | Total | Total Grey Matter | Negative | No | No Relationships | 34 | |
| SSD | Executive Function | | Volume | Whole Brain | Total | Total Grey Matter | No Relationships | No | No Relationships | 41 | |
| SSD | Executive Function | | Volume | Whole Brain | Total | Total Grey Matter | No Relationships | Yes | Positive | 57 | |
| SSD | Executive Function | | Volume | Whole Brain | Total | Total Grey Matter | No Relationships | Yes | Positive | 41 | |
| SSD | Executive Function/Verbal Fluency | | Thickness | Frontal | Right | Inferior Frontal Gyrus | Positive | No | No Relationships | 28 | |
| SSD | Executive Function/Verbal Fluency | | Thickness | Frontal | Right | Middle Frontal Gyrus | Positive | No | No Relationships | 28 | |

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | | Reference |
|--------|-----------------------------------|-------------------|-----------|------------------|------------|---|------------------|-----------------------------|------------------|-----|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | | |
| SSD | Executive Function/Verbal Fluency | | Volume | Whole Brain | Total | Total Brain Volume | Positive | No | No Relationships | 4 | |
| SSD | Intelligence | Current IQ | Volume | Cerebellum | Total | | Positive | No HC | | 33 | |
| SSD | Intelligence | Global Cognition | Volume | Cerebellum | Total | | No Relationships | No | No Relationships | 112 | |
| SSD | Intelligence | Global Cognition | Volume | Cerebellum | Total | | Positive | No | No Relationships | 60 | |
| SSD | Intelligence | Language | Volume | Cerebellum | Total | | No Relationships | No | No Relationships | 112 | |
| SSD | Intelligence | Current IQ | Volume | Cingulate Cortex | Total | Anterior Cingulate | No Relationships | No | No Relationships | 36 | |
| SSD | Intelligence | Global Cognition | Volume | Cingulate Cortex | Right | Anterior Dorsal Cingulate Gyrus | No Relationships | Yes | Positive | 79 | |
| SSD | Intelligence | Current IQ | Volume | Frontal | Right | Middle Orbitofrontal Gyrus | No Relationships | Yes | Positive | 83 | |
| SSD | Intelligence | Current IQ | Volume | Frontal | Left | Orbitofrontal Cortex | Positive | No | No Relationships | 102 | |
| SSD | Intelligence | Current IQ | Volume | Frontal | Left | Prefrontal Cortex | Positive | No HC | | 105 | |
| SSD | Intelligence | Current IQ | Volume | Frontal | Total | Prefrontal Cortex | Positive | No HC | | 105 | |
| SSD | Intelligence | Full Scale IQ | Volume | Frontal | Left | Orbitofrontal Cortex | Positive | No | No Relationships | 102 | |
| SSD | Intelligence | Global Cognition | Volume | Frontal | Left | Anterior Dorsolateral Prefrontal Cortex | Positive | No | No Relationships | 79 | |
| SSD | Intelligence | Global Cognition | Volume | Frontal | Left | Dorsolateral Prefrontal Cortex | Positive | No | No Relationships | 60 | |
| SSD | Intelligence | Global Cognition | Volume | Frontal | Total | Dorsolateral Prefrontal Cortex | No Relationships | No | No Relationships | 57 | |
| SSD | Intelligence | Global Cognition | Volume | Frontal | Right | Inferior Dorsolateral Prefrontal Cortex | Positive | No | No Relationships | 79 | |
| SSD | Intelligence | Global Cognition | Volume | Frontal | Total | Inferior Frontal Gyrus | Positive | Yes | Positive | 57 | |
| SSD | Intelligence | Global Cognition | Volume | Frontal | Right | Lateral Prefrontal Cortex | Negative | No | No Relationships | 79 | |
| SSD | Intelligence | Premorbid IQ | Thickness | Frontal | Left | Inferior Frontal Gyrus | Positive | Yes | Positive | 47 | |
| SSD | Intelligence | Premorbid IQ | Thickness | Frontal | Left | Middle Frontal Gyrus | Positive | Yes | Positive | 47 | |
| SSD | Intelligence | Premorbid IQ | Thickness | Frontal | Right | Middle Frontal Gyrus | Positive | Yes | Positive | 47 | |
| SSD | Intelligence | Premorbid IQ | Thickness | Frontal | Right | Superior Frontal Gyrus | Positive | Yes | Positive | 47 | |
| SSD | Intelligence | Current IQ | Volume | Insula | Total | Insula Cortex | Positive | Yes | Positive | 10 | |
| SSD | Intelligence | Premorbid IQ | Thickness | Insula Cortex | Right | Insula Cortex | Positive | Yes | Positive | 47 | |
| SSD | Intelligence | Premorbid IQ | Thickness | Occipital | Left | Middle Occipital Gyrus | No Relationships | Yes | Positive | 47 | |
| SSD | Intelligence | Premorbid IQ | Thickness | Occipital | Right | Temporo-occipital Gyrus | No Relationships | Yes | Positive | 47 | |
| SSD | Intelligence | Global Cognition | Volume | Parietal | Left | Lateral Parietal Cortex | Positive | No | No Relationships | 79 | |
| SSD | Intelligence | Global Cognition | Volume | Parietal | Right | Lateral Parietal Cortex | Positive | No | No Relationships | 79 | |
| SSD | Intelligence | Current IQ | Volume | Subcortical | Left | Putamen | Positive | No HC | | 33 | |
| SSD | Intelligence | Current IQ | Volume | Temporal | Left | Anterior Hippocampus | Positive | No | No Relationships | 102 | |
| SSD | Intelligence | Current IQ | Volume | Temporal | Right | Anterior Hippocampus | Negative | No | No Relationships | 113 | |
| SSD | Intelligence | Current IQ | Volume | Temporal | Left | Hippocampus | Positive | No HC | | 33 | |

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | | Reference |
|--------|----------------|--------------------|--------------|-------------|------------|-------------------------------|-----------------|-----------------------------|-----------------|-----|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | | |
| SSD | Intelligence | Current IQ | Volume | Temporal | Right | Hippocampus | No Relationship | Yes | Negative | 85 | |
| SSD | Intelligence | Current IQ | Volume | Temporal | Right | Hippocampus | Positive | No HC | | 33 | |
| SSD | Intelligence | Current IQ | Volume | Temporal | Left | Superior Temporal Gyrus | Positive | No HC | | 18 | |
| SSD | Intelligence | Current IQ | Volume | Temporal | Left | Temporal Lobe | Positive | No HC | | 33 | |
| SSD | Intelligence | Full Scale IQ | Volume | Temporal | Left | Anterior Hippocampus | Positive | No | No Relationship | 102 | |
| SSD | Intelligence | Full Scale IQ | Volume | Temporal | Right | Hippocampus | No Relationship | Yes | Negative | 85 | |
| SSD | Intelligence | Global Cognition | Volume | Temporal | Total | Hippocampus Subiculum | No Relationship | No | No Relationship | 52 | |
| SSD | Intelligence | Global Cognition | Volume | Temporal | Total | Hippocampus | Positive | No | No Relationship | 91 | |
| SSD | Intelligence | Global Cognition | Volume | Temporal | Total | Hippocampus | Positive | Yes | Positive | 57 | |
| SSD | Intelligence | Global Cognition | Volume | Temporal | Total | Molecular Layer (Hippocampus) | Positive | No HC | | 82 | |
| SSD | Intelligence | Global Cognition | Volume | Temporal | Left | Parahippocampal Gyrus | No Relationship | Yes | Negative | 79 | |
| SSD | Intelligence | Global Cognition | Volume | Temporal | Right | Parahippocampal Gyrus | No Relationship | Yes | Negative | 79 | |
| SSD | Intelligence | Global Cognition | Volume | Temporal | Left | Superior Temporal Cortex | Positive | No | No Relationship | 79 | |
| SSD | Intelligence | Global Cognition | Volume | Temporal | Right | Superior Temporal Gyrus | Positive | No | No Relationship | 60 | |
| SSD | Intelligence | Global Cognition | Volume | Temporal | Total | Temporal Lobe | No Relationship | No | No Relationship | 25 | |
| SSD | Intelligence | Language | Volume | Temporal | Right | Parahippocampus | Negative | No HC | | 99 | |
| SSD | Intelligence | Non-verbal Ability | Volume | Temporal | Total | Temporal Pole | No Relationship | Yes | Positive | 42 | |
| SSD | Intelligence | Premorbid IQ | Thickness | Temporal | Right | Temporal Lobe | Positive | Yes | Positive | 47 | |
| SSD | Intelligence | Verbal IQ | Volume | Temporal | Left | Hippocampus | No Relationship | Yes | Positive | 115 | |
| SSD | Intelligence | Current IQ | Volume | Whole Brain | Total | Intracranial Volume | No Relationship | Yes | Positive | 113 | |
| SSD | Intelligence | Full Scale IQ | Surface area | Whole Brain | Total | | No Relationship | No | No Relationship | 68 | |
| SSD | Intelligence | Full Scale IQ | Thickness | Whole Brain | Total | Total Cortical Thickness | Positive | No | No Relationship | 68 | |
| SSD | Intelligence | Full Scale IQ | Thickness | Whole Brain | Total | | No Relationship | No | No Relationship | 68 | |
| SSD | Intelligence | Full Scale IQ | Volume | Whole Brain | Total | Total Cortical Volume | Positive | No | No Relationship | 68 | |
| SSD | Intelligence | Full Scale IQ | Volume | Whole Brain | Total | Total Grey Matter | Positive | Yes | Positive | 114 | |
| SSD | Intelligence | Full Scale IQ | Volume | Whole Brain | Total | | No Relationship | No | No Relationship | 68 | |
| SSD | Intelligence | Global Cognition | Volume | Whole Brain | Total | Total Grey Matter | Positive | No | No Relationship | 108 | |
| SSD | Intelligence | Global Cognition | Volume | Whole Brain | Total | Total Grey Matter | Positive | Yes | Positive | 57 | |
| SSD | Intelligence | Language | Volume | Whole Brain | Total | Total Brain Volume | No Relationship | No | No Relationship | 5 | |
| SSD | Intelligence | Language | Volume | Whole Brain | Total | Total Grey Matter | Positive | Yes | Positive | 41 | |
| SSD | Intelligence | Language | Volume | Whole Brain | Total | Total Grey Matter | Positive | Yes | Positive | 41 | |
| SSD | Intelligence | Non-verbal Ability | Volume | Whole Brain | Total | Total Grey Matter | No Relationship | Yes | Positive | 41 | |
| SSD | Intelligence | Non-verbal Ability | Volume | Whole Brain | Total | Total Grey Matter | Positive | Yes | Positive | 41 | |

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | Reference |
|--------|---------------------|-------------------|-----------|------------------|------------|--------------------------------|-----------------|-----------------------------|-----------------|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | |
| SSD | Intelligence | Premorbid IQ | Volume | Whole Brain | Total | Total Brain Volume | No Relationship | No | No Relationship | 5 |
| SSD | Intelligence | Premorbid IQ | Volume | Whole Brain | Total | Total Grey Matter | Positive | No | No Relationship | 4 |
| SSD | Memory | General Memory | Volume | Cerebellum | Total | | No Relationship | Yes | Positive | 112 |
| SSD | Memory | Facial Memory | Volume | Cingulate Cortex | Total | Anterior Cingulate | No Relationship | No | No Relationship | 36 |
| SSD | Memory | General Memory | Volume | Parietal | Total | Parietal-Occipital | Positive | No | No Relationship | 108 |
| SSD | Memory | Short Term Memory | Volume | Parietal | Total | Parietal-Occipital Lobe | Positive | No | No Relationship | 108 |
| SSD | Memory | Episodic Memory | Thickness | Temporal | Total | Parahippocampal Gyrus | No Relationship | No | No Relationship | 59 |
| SSD | Memory | Episodic Memory | Volume | Temporal | Total | Hippocampus | No Relationship | No | No Relationship | 59 |
| SSD | Memory | Episodic Memory | Volume | Temporal | Total | Parahippocampal Gyrus | No Relationship | No | No Relationship | 59 |
| SSD | Memory | General Memory | Volume | Temporal | Left | Hippocampus | Positive | No | No Relationship | 73 |
| SSD | Memory | General Memory | Volume | Temporal | Right | Hippocampus | Positive | No | No Relationship | 85 |
| SSD | Memory | General Memory | Volume | Temporal | Right | Hippocampus | Positive | No | No Relationship | 73 |
| SSD | Memory | General Memory | Volume | Temporal | Right | Hippocampus | Positive | No | No Relationship | 119 |
| SSD | Speed of Processing | Motor Speed | Volume | Cerebellum | Total | Cerebellum | Positive | No | No Relationship | 60 |
| SSD | Speed of Processing | | Volume | Cerebellum | Total | Cerebellum | No Relationship | No | No Relationship | 112 |
| SSD | Speed of Processing | | Volume | Cerebellum | Total | Cerebellum | Positive | No | No Relationship | 49 |
| SSD | Speed of Processing | | Volume | Cerebellum | Total | Crus I/II | No Relationship | No | No Relationship | 69 |
| SSD | Speed of Processing | | Thickness | Frontal | Left | Middle Frontal Cortex | Positive | Yes | Positive | 122 |
| SSD | Speed of Processing | | Thickness | Frontal | Total | Pars Opercularis | Positive | No | No Relationship | 64 |
| SSD | Speed of Processing | | Thickness | Frontal | Total | Superior Frontal Gyrus | No Relationship | Yes | Positive | 116 |
| SSD | Speed of Processing | | Volume | Frontal | Total | Dorsolateral Prefrontal Cortex | No Relationship | No | No Relationship | 57 |
| SSD | Speed of Processing | | Volume | Frontal | Total | Inferior Frontal Gyrus | Positive | Yes | Positive | 57 |
| SSD | Speed of Processing | | Volume | Frontal | Left | Middle Frontal Gyrus | Positive | No | No Relationship | 65 |
| SSD | Speed of Processing | | Volume | Frontal | Left | Orbitofrontal Cortex | Positive | Yes | Positive | 75 |
| SSD | Speed of Processing | | Volume | Frontal | Right | Orbitofrontal Cortex | Positive | Yes | Positive | 75 |
| SSD | Speed of Processing | | Volume | Frontal | Total | Prefrontal Cortex | Positive | Yes | Positive | 11 |
| SSD | Speed of Processing | | Volume | Insula Cortex | Total | | Positive | Yes | Positive | 75 |
| SSD | Speed of Processing | | Thickness | Occipital | Total | Calcarine Sulcus | Positive | Yes | Positive | 122 |
| SSD | Speed of Processing | Motor Speed | Volume | Subcortical | Left | Caudate | Positive | No | No Relationship | 60 |
| SSD | Speed of Processing | | Thickness | Temporal | Total | Transverse Temporal | Positive | No | No Relationship | 48 |
| SSD | Speed of Processing | | Volume | Temporal | Right | Anterior Hippocampus | Positive | No | No Relationship | 113 |
| SSD | Speed of Processing | | Volume | Temporal | Total | Anterior Hippocampus | Positive | No | No Relationship | 111 |

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | Reference |
|--------|------------------------|-----------------------|--------------|---------------|------------|--------------------------------|------------------|-----------------------------|------------------|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | |
| SSD | Speed of Processing | | Volume | Temporal | Total | Dentate Gyrus | Positive | No HC | | 82 |
| SSD | Speed of Processing | | Volume | Temporal | Total | Hippocampus | Positive | Yes | Positive | 57 |
| SSD | Speed of Processing | | Volume | Temporal | Left | Posterior Hippocampus | Negative | No | No Relations hip | 113 |
| SSD | Speed of Processing | | Volume | Temporal | Left | Temporal Pole | Positive | Yes | Positive | 75 |
| SSD | Speed of Processing | | Volume | Whole Brain | Total | Total Grey Matter | Negative | No | No Relations hip | 113 |
| SSD | Speed of Processing | | Volume | Whole Brain | Total | Total Grey Matter | No Relations hip | No | No Relations hip | 57 |
| SSD | Speed of Processing | | Volume | Whole Brain | Total | Total Grey Matter | Positive | No | No Relations hip | 4 |
| SSD | Verbal Fluency | Semantic Clustering | Volume | Frontal | Total | Inferior Frontal Gyrus | Positive | Yes | Positive | 78 |
| SSD | Verbal Fluency | Semantic Clustering | Volume | Frontal | Total | Orbitofrontal Cortex | Positive | No | No Relations hip | 78 |
| SSD | Verbal Fluency | Semantic Clustering | Volume | Frontal | Total | Straight Gyrus | No Relations hip | Yes | Positive | 78 |
| SSD | Verbal Fluency | Serial Clustering | Volume | Frontal | Total | Inferior Frontal Gyrus | No Relations hip | Yes | Negative | 78 |
| SSD | Verbal Fluency | Subjective Clustering | Volume | Frontal | Total | Inferior Frontal Gyrus | Positive | No | No Relations hip | 78 |
| SSD | Verbal Fluency | | Volume | Parietal | Total | Total Parietal Lobe | Positive | No HC | | 2 |
| SSD | Verbal Memory/Learning | | Volume | Basal Ganglia | Total | Nucleus Accumbens | Positive | No | No Relations hip | 66 |
| SSD | Verbal Memory/Learning | | Volume | Cerebellum | Total | Cerebellum | Negative | No | No Relations hip | 115 |
| SSD | Verbal Memory/Learning | | Surface area | Frontal | Right | Caudal Middle Frontal Gyrus | No Relations hip | Yes | Negative | 48 |
| SSD | Verbal Memory/Learning | | Surface area | Frontal | Total | Prefrontal Cortex | No Relations hip | No HC | | 46 |
| SSD | Verbal Memory/Learning | | Thickness | Frontal | Right | Middle Frontal Gyrus | Positive | Yes | Positive | 47 |
| SSD | Verbal Memory/Learning | | Thickness | Frontal | Total | Prefrontal Cortex | No Relations hip | No HC | | 46 |
| SSD | Verbal Memory/Learning | | Thickness | Frontal | Right | Superior Frontal Gyrus | Positive | Yes | Positive | 47 |
| SSD | Verbal Memory/Learning | | Volume | Frontal | Right | Dorsolateral Prefrontal Cortex | Positive | No HC | | 80 |
| SSD | Verbal Memory/Learning | | Volume | Frontal | Total | Dorsolateral Prefrontal Cortex | No Relations hip | No | No Relations hip | 57 |
| SSD | Verbal Memory/Learning | | Volume | Frontal | Total | Inferior Frontal Gyrus | No Relations hip | No | No Relations hip | 57 |
| SSD | Verbal Memory/Learning | | Volume | Frontal | Total | Inferior Frontal Gyrus | No Relations hip | Yes | Positive | 4 |
| SSD | Verbal Memory/Learning | | Volume | Frontal | Left | Middle Frontal Gyrus | Positive | No | No Relations hip | 65 |
| SSD | Verbal Memory/Learning | | Volume | Frontal | Total | Orbitofrontal Cortex | Positive | No | No Relations hip | 5 |
| SSD | Verbal Memory/Learning | | Volume | Frontal | Left | Prefrontal Cortex | Positive | No | No Relations hip | 5 |
| SSD | Verbal Memory/Learning | | Volume | Frontal | Left | Prefrontal Cortex | Positive | No HC | | 105 |
| SSD | Verbal Memory/Learning | | Volume | Frontal | Total | Prefrontal Cortex | No Relations hip | No HC | | 46 |
| SSD | Verbal Memory/Learning | | Volume | Frontal | Total | Prefrontal Cortex | Positive | No | No Relations hip | 5 |
| SSD | Verbal Memory/Learning | | Volume | Frontal | Total | Prefrontal Cortex | Positive | No HC | | 105 |
| SSD | Verbal Memory/Learning | | Volume | Frontal | Total | Superior Frontal Gyrus | Positive | No | No Relations hip | 65 |
| SSD | Verbal Memory/Learning | | Volume | Frontal | Total | Total Frontal Lobe | Positive | No HC | | 2 |

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | Reference |
|--------|------------------------|-------------------|--------------|---------------|------------|-------------------------|------------------|-----------------------------|------------------|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | |
| SSD | Verbal Memory/Learning | | Thickness | Insula Cortex | Right | Insula Cortex | Positive | Yes | Positive | 47 |
| SSD | Verbal Memory/Learning | | Volume | Parietal | Total | Precuneus | Positive | No | No Relationships | 4 |
| SSD | Verbal Memory/Learning | | Volume | Parietal | Total | Total Parietal Lobe | Positive | No HC | | 2 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Left | Amygdala | Negative | No | No Relationships | 61 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Left | Amygdala | Positive | No | No Relationships | 97 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Right | Amygdala | Positive | No | No Relationships | 97 |
| SSD | Verbal Memory/Learning | | Volume | Subcortical | Left | Putamen | Negative | No | No Relationships | 49 |
| SSD | Verbal Memory/Learning | | Volume | Subcortical | Right | Putamen | Negative | No | No Relationships | 49 |
| SSD | Verbal Memory/Learning | | Volume | Subcortical | Total | Thalamus | Negative | No | No Relationships | 65 |
| SSD | Verbal Memory/Learning | | Surface area | Temporal | Right | Fusiform Gyrus | No Relationships | Yes | Negative | 48 |
| SSD | Verbal Memory/Learning | | Thickness | Temporal | Right | Inferior Temporal Gyrus | Positive | Yes | Positive | 47 |
| SSD | Verbal Memory/Learning | | Thickness | Temporal | Total | Parahippocampal Gyrus | No Relationships | No | No Relationships | 59 |
| SSD | Verbal Memory/Learning | | Thickness | Temporal | Right | Superior Temporal Gyrus | Positive | Yes | Positive | 47 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Right | Anterior Hippocampus | No Relationships | Yes | Positive | 113 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Right | Anterior Hippocampus | Positive | No | No Relationships | 53 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Total | Entorhinal Cortex | No Relationships | No | No Relationships | 117 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Total | Hippocampus Subiculum | No Relationships | Yes | Positive | 52 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Left | Hippocampus | No Relationships | No | No Relationships | 97 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Left | Hippocampus | No Relationships | No | No Relationships | 63 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Left | Hippocampus | Positive | No | No Relationships | 50 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Left | Hippocampus | Positive | No | No Relationships | 85 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Left | Hippocampus | Positive | No HC | | 99 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Right | Hippocampus | Positive | No | No Relationships | 53 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Right | Hippocampus | Positive | No | No Relationships | 97 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Right | Hippocampus | Positive | No | No Relationships | 63 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Right | Hippocampus | Positive | No HC | | 99 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Total | Hippocampus | No Relationships | No | No Relationships | 59 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Total | Hippocampus | Positive | No | No Relationships | 66 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Total | Hippocampus | Positive | Yes | Positive | 42 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Total | Hippocampus | Positive | No | No Relationships | 57 |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Total | Parahippocampal Gyrus | No Relationships | No | No Relationships | 59 |

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | | Reference |
|--------|------------------------|-------------------|---------|-------------|------------|-----------------------------------|------------------|-----------------------------|------------------|-----|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | | |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Total | Perirhinal Cortex | No Relationships | No | No Relationships | 117 | |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Left | Posterior Hippocampus | No Relationships | Yes | Positive | 113 | |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Right | Posterior Hippocampus | Positive | No | No Relationships | 53 | |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Left | Posterior Superior Temporal Gyrus | Positive | No HC | | 84 | |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Total | Temporal Pole | No Relationships | Yes | Positive | 42 | |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Total | Temporopolar Cortex | No Relationships | No | No Relationships | 117 | |
| SSD | Verbal Memory/Learning | | Volume | Temporal | Total | Total Temporal Lobe | Positive | No HC | | 2 | |
| SSD | Verbal Memory/Learning | | Volume | Whole Brain | Total | Total Brain Volume | No Relationships | No | No Relationships | 5 | |
| SSD | Verbal Memory/Learning | | Volume | Whole Brain | Total | Total Cerebral Tissue | Positive | No HC | | 2 | |
| SSD | Verbal Memory/Learning | | Volume | Whole Brain | Total | Total Grey Matter | No Relationships | No | No Relationships | 57 | |
| SSD | Verbal Memory/Learning | | Volume | Whole Brain | Total | Total Grey Matter | Positive | No | No Relationships | 41 | |
| SSD | Verbal Memory/Learning | | Volume | Whole Brain | Total | Total Grey Matter | Positive | Yes | Positive | 22 | |
| SSD | Verbal Memory/Learning | | Volume | Whole Brain | Total | Total Grey Matter | Positive | Yes | Positive | 41 | |
| SSD | Verbal Memory/Learning | | Volume | Whole Brain | Total | | No Relationships | No HC | | 95 | |
| SSD | Visual Memory/Learning | | Volume | Cerebellum | Total | | No Relationships | No | No Relationships | 115 | |
| SSD | Visual Memory/Learning | | Volume | Cerebellum | Total | | No Relationships | Yes | Positive | 112 | |
| SSD | Visual Memory/Learning | Delayed recall | Volume | Frontal | Total | Prefrontal Cortex | Positive | No | No Relationships | 89 | |
| SSD | Visual Memory/Learning | Immediate recall | Volume | Frontal | Total | Prefrontal Cortex | Positive | Yes | Positive | 89 | |
| SSD | Visual Memory/Learning | | Volume | Frontal | Total | Inferior Frontal Gyrus | No Relationships | Yes | Positive | 4 | |
| SSD | Visual Memory/Learning | | Volume | Frontal | Right | Prefrontal Cortex | Positive | Yes | Positive | 5 | |
| SSD | Visual Memory/Learning | | Volume | Frontal | Total | Prefrontal Cortex | Positive | Yes | Positive | 5 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Right | Amygdala | Negative | No | No Relationships | 61 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Right | Amygdala | Positive | No | No Relationships | 97 | |
| SSD | Visual Memory/Learning | | Volume | Subcortical | Right | Thalamus | Positive | No | No Relationships | 66 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Left | Amygdala | Positive | No | No Relationships | 97 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Left | Anterior Fusiform Gyrus | Positive | No | No Relationships | 88 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Right | Anterior Fusiform Gyrus | Positive | No | No Relationships | 88 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Left | Anterior Hippocampus | No Relationships | Yes | Positive | 113 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Right | Anterior Hippocampus | Negative | No | No Relationships | 113 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Total | CA4 (Hippocampus) | Positive | No HC | | 82 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Left | Entorhinal Cortex | Positive | No | No Relationships | 70 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Total | Entorhinal Cortex | No Relationships | No | No Relationships | 117 | |

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | | Reference |
|--------|------------------------|-------------------|--------------|------------------|------------|-------------------------------|------------------|-----------------------------|------------------|-----|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Left | Hippocampus | No Relations hip | No | No Relations hip | 115 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Left | Hippocampus | No Relations hip | No | No Relations hip | 97 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Left | Hippocampus | No Relations hip | No | No Relations hip | 63 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Right | Hippocampus | No Relations hip | No | No Relations hip | 63 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Right | Hippocampus | Positive | No | No Relations hip | 97 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Total | Hippocampus | No Relations hip | Yes | Positive | 42 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Total | Hippocampus | No Relations hip | Yes | Positive | 89 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Total | Hippocampus | Positive | No | No Relations hip | 66 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Total | Hippocampus | Positive | Yes | Positive | 42 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Total | Hippocampal Subfield (CA4DG) | Positive | No | No Relations hip | 118 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Total | Hippocampal Stratum | Positive | No | No Relations hip | 118 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Right | Lateral Hippocampus | Positive | No | No Relations hip | 30 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Total | Molecular Layer (Hippocampus) | Positive | No HC | | 82 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Total | Perirhinal Cortex | No Relations hip | No | No Relations hip | 117 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Left | Posterior Fusiform Gyrus | No Relations hip | No | No Relations hip | 88 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Right | Posterior Fusiform Gyrus | No Relations hip | No | No Relations hip | 88 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Left | Posterior Hippocampus | Positive | Yes | Positive | 113 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Total | Superior Temporal Gyrus | No Relations hip | Yes | Positive | 42 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Total | Temporal Pole | No Relations hip | Yes | Positive | 42 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Right | Temporopolar | Positive | No | No Relations hip | 70 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Total | Temporopolar Cortex | No Relations hip | No | No Relations hip | 117 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Left | Ventral Temporal Cortex | Positive | No | No Relations hip | 70 | |
| SSD | Visual Memory/Learning | | Volume | Temporal | Right | Ventral Temporal Cortex | Positive | No | No Relations hip | 70 | |
| SSD | Visual Memory/Learning | | Volume | Whole Brain | Total | Total Brain Volume | No Relations hip | No | No Relations hip | 5 | |
| SSD | Visual Memory/Learning | | Volume | Whole Brain | Total | Total Grey Matter | No Relations hip | Yes | Positive | 41 | |
| SSD | Visual Memory/Learning | | Volume | Whole Brain | Total | Total Grey Matter | Positive | No | No Relations hip | 41 | |
| SSD | Working Memory | | Volume | Cerebellum | Total | | Positive | No | No Relations hip | 104 | |
| SSD | Working Memory | | Volume | Cingulate Cortex | Total | Anterior Cingulate | Positive | No | No Relations hip | 54 | |
| SSD | Working Memory | | Volume | Cingulate Cortex | Left | Posterior Cingulate Cortex | Positive | No | No Relations hip | 76 | |
| SSD | Working Memory | | Surface area | Frontal | Total | Prefrontal Cortex | No Relations hip | No HC | | 46 | |
| SSD | Working Memory | | Thickness | Frontal | Left | Caudal Middle Frontal Gyrus | No Relations hip | Yes | Positive | 28 | |

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | | Reference |
|--------|----------------|-------------------|-----------|-------------|------------|--------------------------------|------------------|-----------------------------|------------------|-----|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | | |
| SSD | Working Memory | | Thickness | Frontal | Right | Caudal Middle Frontal Gyrus | No Relationships | Yes | Positive | 28 | |
| SSD | Working Memory | | Thickness | Frontal | Total | Prefrontal Cortex | No Relationships | No HC | | 46 | |
| SSD | Working Memory | | Thickness | Frontal | Left | Rostral Middle Frontal Gyrus | No Relationships | Yes | Positive | 28 | |
| SSD | Working Memory | | Volume | Frontal | Left | Dorsolateral Prefrontal Cortex | Positive | No HC | | 120 | |
| SSD | Working Memory | | Volume | Frontal | Total | Dorsolateral Prefrontal Cortex | No Relationships | No | No Relationships | 57 | |
| SSD | Working Memory | | Volume | Frontal | Left | Frontal Lobe | Negative | No | No Relationships | 37 | |
| SSD | Working Memory | | Volume | Frontal | Right | Frontal Lobe | No Relationships | No | No Relationships | 37 | |
| SSD | Working Memory | | Volume | Frontal | Total | Frontal Lobe | Positive | No HC | | 2 | |
| SSD | Working Memory | | Volume | Frontal | Total | Inferior Frontal Gyrus | No Relationships | No | No Relationships | 57 | |
| SSD | Working Memory | | Volume | Frontal | Left | Inferior Prefrontal Cortex | Positive | No | No Relationships | 38 | |
| SSD | Working Memory | | Volume | Frontal | Total | Medial Frontal Cortex | Positive | No | No Relationships | 54 | |
| SSD | Working Memory | | Volume | Frontal | Left | Middle Frontal Gyrus | No Relationships | Yes | Negative | 124 | |
| SSD | Working Memory | | Volume | Frontal | Left | Middle Frontal Gyrus | Positive | Yes | Negative | 109 | |
| SSD | Working Memory | | Volume | Frontal | Left | Orbitofrontal Cortex | Positive | No | No Relationships | 102 | |
| SSD | Working Memory | | Volume | Frontal | Total | Prefrontal Cortex | No Relationships | No HC | | 46 | |
| SSD | Working Memory | | Volume | Frontal | Total | Prefrontal Cortex | Positive | Yes | Positive | 11 | |
| SSD | Working Memory | | Volume | Frontal | Total | Straight Gyrus | Negative | Yes | Negative | 109 | |
| SSD | Working Memory | | Volume | Frontal | Total | Superior Prefrontal Cortex | Positive | No | No Relationships | 38 | |
| SSD | Working Memory | | Volume | Parietal | Left | Parietal Lobe | No Relationships | No | No Relationships | 37 | |
| SSD | Working Memory | | Volume | Parietal | Right | Parietal Lobe | No Relationships | No | No Relationships | 37 | |
| SSD | Working Memory | | Volume | Parietal | Total | Precuneus | No Relationships | Yes | Negative | 4 | |
| SSD | Working Memory | | Volume | Parietal | Total | Total Parietal Lobe | Positive | No HC | | 2 | |
| SSD | Working Memory | | Volume | Subcortical | Left | Putamen | Negative | No | No Relationships | 49 | |
| SSD | Working Memory | | Volume | Subcortical | Right | Putamen | Negative | No | No Relationships | 49 | |
| SSD | Working Memory | | Volume | Subcortical | Left | Thalamus | No Relationships | No | No Relationships | 3 | |
| SSD | Working Memory | | Volume | Subcortical | Right | Thalamus | No Relationships | No | No Relationships | 3 | |
| SSD | Working Memory | | Volume | Subcortical | Total | Thalamus | No Relationships | No | No Relationships | 45 | |
| SSD | Working Memory | | Thickness | Temporal | Right | Middle Temporal Gyrus | Positive | No | No Relationships | 28 | |
| SSD | Working Memory | | Thickness | Temporal | Right | Superior Temporal Gyrus | Positive | No | No Relationships | 28 | |
| SSD | Working Memory | | Volume | Temporal | Left | Anterior Hippocampus | Positive | No | No Relationships | 53 | |
| SSD | Working Memory | | Volume | Temporal | Right | Anterior Hippocampus | Negative | No | No Relationships | 113 | |

| Cohort | Domain (Broad) | Domain (Specific) | Measure | Patients | | | | Healthy Controls | | Reference |
|--------|--------------------------|-------------------|-----------|-------------|------------|--------------------------------|----------------------|-----------------------------|----------------------|-----------|
| | | | | Lobe | Hemisphere | Region | Direction | Relationship present in HC? | Direction | |
| SSD | Working Memory | | Volume | Temporal | Right | Anterior Hippocampus | Positive | No | No Relationships hip | 53 |
| SSD | Working Memory | | Volume | Temporal | Right | Hippocampus | Positive | No | No Relationships hip | 53 |
| SSD | Working Memory | | Volume | Temporal | Total | Hippocampus | No Relationships hip | No | No Relationships hip | 57 |
| SSD | Working Memory | | Volume | Temporal | Right | Inferior Temporal Gyrus | Positive | No | No Relationships hip | 121 |
| SSD | Working Memory | | Volume | Temporal | Right | Posterior Hippocampus | No Relationships hip | Yes | Positive | 113 |
| SSD | Working Memory | | Volume | Temporal | Left | Temporal Lobe | Negative | No | No Relationships hip | 37 |
| SSD | Working Memory | | Volume | Temporal | Right | Temporal Lobe | Negative | No | No Relationships hip | 37 |
| SSD | Working Memory | | Volume | Temporal | Total | Total Temporal Lobe | Positive | No HC | | 2 |
| SSD | Working Memory | | Thickness | Whole Brain | Total | Total Cortical Thickness | Positive | No HC | | 90 |
| SSD | Working Memory | | Volume | Whole Brain | Total | Intracranial Volume | No Relationships hip | No | No Relationships hip | 37 |
| SSD | Working Memory | | Volume | Whole Brain | Total | Total Cerebral Tissue | Positive | No HC | | 2 |
| SSD | Working Memory | | Volume | Whole Brain | Total | Total Grey Matter | No Relationships hip | Yes | Positive | 57 |
| SSD | Working Memory | | Volume | Whole Brain | Total | Total Grey Matter | No Relationships hip | No | No Relationships hip | 107 |
| SSD | Working Memory/Attention | | Volume | Frontal | Right | Dorsolateral Prefrontal Cortex | Positive | No HC | | 80 |

Note. Findings presented here are from what is reported in each paper. In the case that ‘whole brain’ was the lobe of investigation, the region column is blank, and no relationship was identified, it reflects that the study did not find region or cluster of significance across the entirety of the brain, rather than referring to ‘total brain volume’, which is labelled accordingly; both the hippocampus and amygdala were considered to be temporal given their placement deep within the anterior lobe, rather than the centre of the brain; rows are banded to increase readability; BD, bipolar disorder; HC, healthy control; RO, recent-onset; SSD, schizophrenia-spectrum disorder.

Table 3. Brain regions implicated for each cognition domain and diagnosis

| | | Attention | Speed of processing | General memory | Verbal memory/learning | Visual memory/learning | Working Memory |
|-------------|----------|---|--|--------------------------|---|--|---|
| RO-SSD | Broad | ✓: Frontal (2) ✓: Parietal (2*) ✓: Subcortical (2*) | ✗: Cerebellum (2) | - | ✓: Temporal (2) ✗: Whole brain (2; V) | ✗: Whole brain (2; V) | ✓: Frontal (2) |
| | Specific | ✓: Postcentral gyrus (2*) | - | - | - | - | ✓: Superior frontal (2) |
| SSD | Broad | ✓: Frontal (5*) ✓: Temporal (4*) ✓: Parietal (2*) | ✓: Temporal (6) ✓: Frontal (5) ✓: Cerebellum (2) ✓: Total grey matter (2) | ✓: Temporal (3) | ✓: Temporal (13) ✓: Frontal (6) ✓: Subcortical (2*) ✓: Parietal (2) ✓: Total grey matter volume (2) | ✓: Temporal (10*^) ✓: Frontal (2) ✗: Cerebellum (2) | ✓: Frontal (9*) ✓: Temporal (6*) ✓: Cingulate cortex (2) ✗: Total grey matter (2) |
| | Specific | - | ✓: Cerebellum (2) ✓: Left middle frontal (2) | ✓: Right hippocampus (3) | ✓: Hippocampus (9) ✓: Left amygdala (2*) ✓: Left prefrontal cortex (2) | ✓: Prefrontal cortex (2) ✓: Right amygdala (2*) ✓: Hippocampus (2) ✗: Left hippocampus (3) | ✓: Right anterior hippocampus (2*) ✗: Thalamus (2) |
| | Specific | - | - | - | - | - | - |
| RO-BD | Broad | - | - | - | ✓: Temporal (2*) | - | - |
| | Specific | - | - | - | - | - | - |
| BD | Broad | - | - | - | ✓: Temporal (3) | ✗: Temporal (2) | - |
| | Specific | - | - | - | - | - | - |
| HC (RO) | Broad | ✗: Parietal (2) ✗: Subcortical (2) | ✗: Cerebellum (2) | - | ✗: Temporal (3) | - | - |
| | Specific | ✗: Postcentral gyrus (2) | - | - | - | - | - |
| HC (SSD/BD) | Broad | ✗: Frontal (3) ✗: Temporal (3) ✗: Subcortical (2) | ✓: Frontal (4) ✗: Cerebellum (4) ✗: Temporal (3) ✗: Total grey matter (3) | ✗: Temporal (4) | ✗: Temporal (12) ✗: Frontal (3) ✗: Total grey matter volume (3) | ✓: Frontal (3) ✗: Temporal (10) ✗: Total grey matter volume (2) | ✗: Frontal (7) ✗: Temporal (6) ✗: Subcortical (3) ✗: Cingulate cortex (2) ✗: Total grey matter volume (2) |
| | Specific | - | - | ✗: Right hippocampus (3) | ✗: Left hippocampus (5) ✗: Right hippocampus (4) ✗: Left amygdala (2) | ✓: Prefrontal cortex (2) ✗: Left hippocampus (3) ✗: Right amygdala (2) ✗: Right hippocampus (2) | ✓: Left middle frontal gyrus (2*) ✗: Right anterior hippocampus (2) |
| | Specific | - | - | - | - | - | - |

Note. Only findings **replicated** across *at least 2* independent studies are reported in Table 3. For example, in

the table above the '9' listed in parenthesis next to hippocampus in the verbal memory column for SSD

indicates that 9 *independent* studies observed an association between this domain and brain region. For the

domains where lower numbers, such as a 2 or 3, are indicated in parenthesis next to brain regions (e.g.

attention), it suggests that amongst the available studies for that given domain, there was only minimal

consistency in findings across studies. For a summary of *all* cognition-brain morphology relationships reported

from each study, see Table 2.

The cognitive domain of 'verbal fluency' was omitted from Table 3 for brevity, as there was insufficient

findings across all domains to enable replication. 'Broad' rows refer to findings at the level of the lobe (rather

than *total* volume [or thickness or surface area] of the lobe itself). 'Specific' rows indicate specific subregions

consistently implicated; ✓ indicates an association with the given region; ✕ indicates a region in which there no association found; & indicates the region comprised negative associations only; but note the directionality of the association is positive unless otherwise marked; * indicates the region comprised a combination of positive and negative associations; ^ indicates an equal number of studies suggested both an association and no association with this region; - indicates the evidence was too inconsistent or insufficient to form conclusions; BD, bipolar disorder; HC, healthy controls; SSD, schizophrenia-spectrum disorders; V, volume.

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A systematic review of cognition–brain morphology relationships on the schizophrenia–bipolar disorder spectrum

Supplementary Material

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Search terms

At stage one, titles, abstracts and keywords were screened by SC and included if they met the appropriate criteria. During this stage, if the relevance of a paper was in question, JKs and TVR were included in the screening process. At stage two, both JK and SC screened full-text articles. Any discrepancies at this stage were passed to both TVR and VC for deliberation, and were discussed until a consensus was reached. Furthermore, authors JK and TVR were involved in conceptualization and writing of the review, and authors SC, MH, VC, SR, CP, and CW were heavily involved in both writing and review feedback processes.

Search terms were based on three concepts: diagnosis, cognition, and brain morphology. For diagnosis, the terms included: *schizophrenia, schizoaffective, schizophrenia spectrum, bipolar disorder, bipolar disorder, bipolar, manic, euthymic, bipolar depression, psychosis, first-episode psychosis, first episode/recent onset bipolar, first episode/recent onset schizophrenia* and *psychotic disorders*.

For cognition: *cognition, cognitive, cognition disorders, neurocognitive, neurocognition, neuropsychology, neuropsychological, cognitive deficit, cognitive function, cognitive ability, cognitive dysfunction, cognitive impairment, intelligence, IQ, intellect, memory, learning, attention, vigilance, speed of processing, executive, flexibility, reasoning, problem solving, and decision making*.

For brain morphology: *brain volume, brain surface area, brain thickness, brain structure, brain morphology, cortical volume, cortical surface area, cortical thickness, cortical structure, cortical morphology, grey matter, MRI, magnetic resonance, neuroimaging, voxel-based morphology, and VBM*.

It should be noted that this review was conducted in the context of providing literature for several systematic reviews (Karantonis et al., in preparation), hence terminology relevant

to neuropsychological subgroups were included in the search terms, but were not part of the inclusion criteria for this study.

Search Strategy (PubMed database)

("schizophrenia spectrum and other psychotic disorders"[MeSH Terms] OR "bipolar and related disorders"[MeSH Terms] OR schizophrenia[Title/Abstract] OR schizophrenic[Title/Abstract] OR bipolar[Title/Abstract] OR schizoaffective[Title/Abstract] OR "first episode psychosis"[Title/Abstract] OR "psychosis"[Title/Abstract] OR "first-episode psychosis"[Title/Abstract] OR "paediatric bipolar disorder" [Title/Abstract] OR "pediatric bipolar disorder" [Title/Abstract] OR "first episode bipolar disorder"[Title/Abstract] OR "first episode mania"[Title/Abstract] OR "recent onset bipolar disorder" [Title/Abstract])

AND

("cognition"[MeSH Terms] OR "cognition disorders"[MeSH Terms] OR "cognitive dysfunction"[MeSH Terms] OR cognit*[Title/Abstract] OR neuropsychol*[Title/Abstract] OR neurocognit*[Title/Abstract] OR "cognitive cluster"[Title/Abstract] OR "cognitive subgroup"[Title/Abstract] OR "cognitive subtype"[Title/Abstract] OR "cognitive heterogeneity"[Title/Abstract] OR "neuropsychological subgroup"[Title/Abstract] OR "neurocognitive subgroup"[Title/Abstract] OR "cluster analysis"[Title/Abstract] OR "clustering analyses"[Title/Abstract] OR intellectual[Title/Abstract] OR intelligence[Title/Abstract] OR memory[Title/Abstract] OR learning[Title/Abstract] OR attention[Title/Abstract] OR "speed of processing"[Title/Abstract] OR "processing speed"[Title/Abstract] OR "executive function"[Title/Abstract] OR "cognitive flexibility"[Title/Abstract] OR "problem solving"[Title/Abstract] OR "cognitive reserve"[Title/Abstract] OR "executive control"[Title/Abstract] OR recognition[Title/Abstract] OR priming[Title/Abstract] OR "inhibition"[Title/Abstract] OR "psychomotor speed"[Title/Abstract] OR "fluency"[Title/Abstract] OR "comprehension"[Title/Abstract] OR "IQ"[Title/Abstract] OR "WAIS"[Title/Abstract] OR "Weschler" OR "visuospatial"[Title/Abstract] OR "arithmetic"[Title/Abstract] OR "motor functioning"[Title/Abstract] OR "executive dysfunction"[Title/Abstract])

AND

(("cortical"[Title/Abstract] OR "brain"[Title/Abstract] OR "whole brain"[Title/Abstract] OR "whole-brain"[Title/Abstract] OR "cortex"[Title/Abstract] OR "grey matter"[Title/Abstract] OR "gray matter"[Title/Abstract] OR neocortical[Title/Abstract] OR neocortex[Title/Abstract] OR neuroanatomical[Title/Abstract] OR hippocampal[Title/Abstract] OR cerebral[Title/Abstract] OR hippocampus[Title/Abstract] OR cerebellum[Title/Abstract] OR cerebellar[Title/Abstract] OR "brain tissue"[Title/Abstract] or lobe[Title/Abstract] OR subcortical[Title/Abstract])

AND

("thickness"[Title/Abstract] OR "surface area"[Title/Abstract] OR "volume"[Title/Abstract] OR "structure"[Title/Abstract] OR "structural"[Title/Abstract] OR "morphology"[Title/Abstract] OR "thinning"[Title/Abstract] OR "volumetric"[Title/Abstract] OR size[Title/Abstract] OR MRI[Title/Abstract] OR "magnetic resonance imag*"[Title/Abstract] OR gyrification[Title/Abstract] OR "voxel-based"[Title/Abstract] OR "mean curvature"[Title/Abstract] OR "freesurfer"[Title/Abstract]

“abnormalities”[Title/Abstract] OR “intracranial volume”[Title/Abstract] OR “sulcal width”[Title/Abstract] OR size[Title/Abstract])

AND

("1990"[Date - Publication]: "3000"[Date - Publication]) NOT “systematic review”[Publication Type] NOT review[Publication Type]

Search Strategy (Scopus database)

TITLE-ABS (schizophrenia OR schizophrenic OR schizoaffective OR psychosis OR paediatric AND bipolar AND disorder OR pediatric AND bipolar AND disorder OR first AND episode AND bipolar AND disorder OR bipolar OR first AND episode AND NOT rat AND mice) AND TITLE-ABS (cognit* OR neuropsychol* OR neurocognit* OR "cognitive cluster" OR "cognitive subgroup" OR "cognitive subtype" OR "cognitive heterogeneity" OR "neuropsychological subgroup" OR "neurocognitive subgroup" OR "cluster analysis" OR "clustering analyses" OR intellectual OR intelligence OR memory OR learning OR attention OR "speed of processing" OR "processing speed" OR "executive function" OR "cognitive flexibility" OR "problem solving" OR "cognitive reserve" OR "executive control" OR recognition OR priming OR inhibition OR "psychomotor speed" OR "fluency" OR comprehension OR iq OR visuospatial OR arithmetic OR "motor functioning" OR "executive dysfunction") AND (TITLE-ABS ("cortical" OR "brain" OR "whole brain" OR "whole-brain" OR "cortex" OR "grey matter" OR "gray matter" OR neocortical OR neocortex OR neuroanatomical OR hippocampal OR cerebral OR hippocampus OR cerebellum OR cerebellar OR lobe OR subcortical) AND TITLE-ABS ("thickness" OR "surface area" OR "volume" OR "structure" OR "structural" OR "morphology" OR "thinning" OR "volumetric" OR mri OR "magnetic resonance imag*" OR gyrification OR "voxel-based" OR "freesurfer" "abnormalities" OR "intracranial volume")) AND DOCTYPE (ar) AND PUBYEAR > 1990

Rationale for study eligibility for inclusion in this review and stratification of results.

It can be argued that the inclusion criteria for this review were very broad, as few limitations were placed on demographic and clinical factors including the mood state of BD patients. These factors were also not used to stratify the results. The rationale for this is as follows. In an initial scan of the literature, we found that demographic and clinical factors were not consistently reported amongst studies. This influenced our decision making as we did not want to exclude studies that were relevant to the topic, but which failed to report particular factors. We ultimately decided on broad inclusion criteria to ensure the review was comprehensive. Further, because the number of relevant BD studies was relatively low, we felt that the removal of studies based on specific criteria regarding mood state in BD would weaken the review. We also decided not to stratify the results on the basis of clinical/demographic factors for the following reasons. Firstly, the vast majority, if not all BD studies, had participants who demonstrated mild mood symptoms, or were considered euthymic/in remission (as indicated in Table 1); further, 83% of the SSD studies reporting symptom severity indicated either mild positive or negative symptoms in their SSD samples. Secondly, we felt that further classification beyond disorder/illness duration/cognitive domain/brain index would make the review too complex and tedious for the readers. However, demographic and clinical factors such as mean age, symptom severity, neuroimaging parameters and analysis covariates are detailed in Table 1 for further reference.

Additionally, in the instance that a sample had been analysed more than once, the article was only included if it involved a different brain measure (i.e. two papers with the same sample were accepted if one examined volume whilst the other examined cortical thickness). If a sample was published with overlapping methodologies and brain measures across papers, only the most comprehensive analysis was included in the review, if eligible

(i.e. if one paper examined volume, and the other examined volume and thickness, the second paper was included and the first excluded).

Study Quality Evaluation

Given that available study quality evaluation tools tend to be tailored to studies with experimental designs unlike those included in this review (i.e. randomized controlled trials), we devised our own evaluation tool based on criteria of direct relevance to this field. This tool was based on consensus between JK, SC and TVR that the following criteria were of importance in evaluating study quality in this topic area: (1) statistical correction for multiple comparisons was applied where appropriate, (2) standardised (automated) methods for imaging analyses were used, (3) healthy control comparison groups were included in the sample, (4) the analysis of cognition-brain morphology relationships were the primary aim or focus of the paper, and (5) if the imaging parameters/protocol and (6) cognitive measures/protocol were clearly described to enable replication. Either a zero or one was awarded for each of the respective six checks of quality, and the overall average score was 5.37, indicating a high quality generally to the studies included in this review. The main indicators of a reduction in quality were inadequate application of statistical correction (1), an absence of control group (3), or the analysis of cognition-brain morphology associations representing a secondary aim (4). Study quality criteria were initially assessed by authors JK and SC (supplementary Table 1). In the instance that a given criterion could not be confidently and accurately determined, TVR independently assessed the criterion. Any discrepancies in ratings between authors were discussed until a consensus was reached.

Supplementary Table 1: *Evaluation of the quality of studies*

| Reference | Was statistical correction applied where appropriate? | Were automated methods for imaging analyses used? | Was a healthy comparison group included? | Was the analysis of brain structure-cognition relationships the primary aim/focus of the paper? | Were the imaging parameters/protocol clearly described to enable replication? | Were the cognitive measures/protocol clearly described to enable replication? | Total quality check score |
|---------------------------------|---|---|--|---|---|---|---------------------------|
| (Abé et al., 2018) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Andreasen et al., 2011) | 0 | 1 | 1 | 1 | 1 | 0 | 4 |
| (Andrews et al., 2006) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Antonova et al., 2005) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Baaré et al., 1999) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Bilder et al., 1995) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Briend et al., 2020) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Bonilha et al., 2008) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Bruno et al., 2006) | 1 | 1 | 0 | 1 | 1 | 1 | 5 |
| (Caldirolì et al., 2018) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Cannon et al., 2005) | 1 | 1 | 1 | 0 | 1 | 1 | 5 |
| (Cao et al., 2016) | 1 | 1 | 1 | 0 | 1 | 1 | 5 |
| (Castro-Fornieles et al., 2018) | 1 | 1 | 1 | 1 | 0 | 0 | 4 |
| (Chakrabarty et al., 2015) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Chen et al., 2018) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Cho & Goghari, 2020) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Chung et al., 2013) | 0 | 1 | 0 | 0 | 1 | 1 | 3 |
| (Cobia et al., 2012) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Cocchi et al., 2009) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Crespo-Facorro et al., 2011) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Cunha et al., 2013) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Czepielewski et al., 2018) | 0 | 1 | 1 | 0 | 1 | 1 | 4 |
| (DeLisi et al., 1995) | 0 | 0 | 1 | 0 | 1 | 0 | 2 |
| (Dempster et al., 2017) | 1 | 1 | 1 | 0 | 1 | 1 | 5 |

| Reference | Was statistical correction applied where appropriate? | Were automated methods for imaging analyses used? | Was a healthy comparison group included? | Was the analysis of brain structure-cognition relationships the primary aim/focus of the paper? | Were the imaging parameters/protocol clearly described to enable replication? | Were the cognitive measures/protocol clearly described to enable replication? | Total quality check score |
|--------------------------------|--|--|---|--|--|--|----------------------------------|
| (Di Michele et al., 1992) | 0 | 0 | 1 | 1 | 1 | 1 | 4 |
| (Edgar et al., 2012) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Egloff et al., 2019) | 1 | 1 | 0 | 1 | 1 | 1 | 5 |
| (Ehrlich et al., 2012) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Exner et al., 2006) | 0 | 0 | 1 | 1 | 1 | 1 | 4 |
| (Exner et al., 2008) | 1 | 0 | 1 | 1 | 1 | 1 | 5 |
| (Fan et al., 2019) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Ferro et al., 2015) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Flaum et al., 1994) | 0 | 0 | 1 | 1 | 1 | 1 | 4 |
| (Frascarelli et al., 2015) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Frazier et al., 2005) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Fujiwara et al., 2007) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Garlinghouse et al., 2010) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Goghari et al., 2014) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Goldberg et al., 1994) | 0 | 1 | 0 | 1 | 1 | 1 | 4 |
| (Guo et al., 2014) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Gur et al., 1999) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Gur et al., 2000) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Gutierrez-Galve et al., 2012) | 1 | 1 | 0 | 1 | 1 | 1 | 5 |
| (Gutiérrez-Galve et al., 2014) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Harms et al., 2007) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Harms et al., 2010) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Hartberg et al., 2010) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Hartberg et al., 2011a) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Hartberg et al., 2011b) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |

| Reference | Was statistical correction applied where appropriate? | Were automated methods for imaging analyses used? | Was a healthy comparison group included? | Was the analysis of brain structure-cognition relationships the primary aim/focus of the paper? | Were the imaging parameters/protocol clearly described to enable replication? | Were the cognitive measures/protocol clearly described to enable replication? | Total quality check score |
|-------------------------------|---|---|--|---|---|---|---------------------------|
| (Hasan et al., 2014) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Hatton et al., 2013) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Haukvik et al., 2015) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Herold et al., 2015) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Hidese et al., 2017) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Jalbrzikowski et al., 2019) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Jensen et al., 2019) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Jirsaraie et al., 2018) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Juuhl-Langseth et al., 2015) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Karnik-Henry et al., 2012) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Keshavan et al., 2003) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Killgore et al., 2009) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Kim et al., 2018) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Knöchel et al., 2014) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Knöchel et al., 2016a) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Knöchel et al., 2016b) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Koshiyama et al., 2018) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Kozicky et al., 2013) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Kubota et al., 2015) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Kuhn et al., 2012) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Kumarasinghe et al., 2014) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Kumari et al., 2008) | 1 | 0 | 0 | 1 | 1 | 1 | 4 |
| (Kumra et al., 2011) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Kuroki et al., 2006) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Lappin et al., 2014) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |

| Reference | Was statistical correction applied where appropriate? | Were automated methods for imaging analyses used? | Was a healthy comparison group included? | Was the analysis of brain structure-cognition relationships the primary aim/focus of the paper? | Were the imaging parameters/protocol clearly described to enable replication? | Were the cognitive measures/protocol clearly described to enable replication? | Total quality check score |
|---------------------------------|---|---|--|---|---|---|---------------------------|
| (Liao et al., 2015) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Liu et al., 2016) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Matsubara et al., 2016) | 1 | 1 | 1 | 0 | 1 | 1 | 5 |
| (Matsui et al., 2008) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Minatogawa-Chang et al., 2009) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Molina et al., 2009) | 0 | 1 | 0 | 1 | 1 | 1 | 4 |
| (Moorhead et al., 2007) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Nakahara et al., 2019) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Nakamura et al., 2008) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Nestor et al., 1993) | 0 | 0 | 0 | 1 | 1 | 1 | 3 |
| (Nestor et al., 2007) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Oertel-Knochel et al., 2015) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Ohtani et al., 2014) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Onitsuka et al., 2003) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Premkumar et al., 2008) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Pujol et al., 2013) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Pujol et al., 2014) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Rais et al., 2012) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Rigucci et al., 2013) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Roalf et al., 2017) | 0 | 1 | 1 | 1 | 1 | 0 | 4 |
| (Roiz-Santiáñez et al., 2014) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Roiz-Santiáñez et al., 2015) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Sachdev et al., 2000) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Salgado-Pineda et al., 2003) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Sanfilipo et al., 2002) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |

| Reference | Was statistical correction applied where appropriate? | Were automated methods for imaging analyses used? | Was a healthy comparison group included? | Was the analysis of brain structure-cognition relationships the primary aim/focus of the paper? | Were the imaging parameters/protocol clearly described to enable replication? | Were the cognitive measures/protocol clearly described to enable replication? | Total quality check score |
|----------------------------|---|---|--|---|---|---|---------------------------|
| (Sarnicola et al., 2009) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Sax et al., 1999) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Schobel et al., 2009) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Schretlen et al., 2010) | 0 | 1 | 0 | 0 | 1 | 1 | 3 |
| (Segarra et al., 2008) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Seidman et al., 1994) | 0 | 0 | 0 | 1 | 1 | 1 | 3 |
| (Shi et al., 2018) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Spalletta et al., 2008) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Sullivan et al., 1996) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Szendi et al., 2006) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Szeszko et al., 2000) | 1 | 1 | 0 | 1 | 1 | 1 | 5 |
| (Szeszko et al., 2002) | 1 | 1 | 0 | 1 | 1 | 1 | 5 |
| (Szeszko et al., 2003) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Thoma et al., 2009) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Thompson et al., 2001) | 0 | 1 | 1 | 1 | 1 | 0 | 4 |
| (Toulopoulou et al., 2004) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Tully et al., 2014) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Turetsky et al., 2003) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Wannan et al., 2018) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Weiss et al., 2004) | 0 | 1 | 1 | 1 | 1 | 1 | 5 |
| (Wojtalik et al., 2012) | 1 | 1 | 1 | 0 | 1 | 1 | 5 |
| (Wolf et al., 2008) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Yan et al., 2019) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Zipursky, 1998) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |
| (Zuffante et al., 2001) | 1 | 1 | 1 | 1 | 1 | 1 | 6 |

Supplementary Table 2: *Recategorization of cognitive measures based on most common use*

| Number of studies | Cognitive Measure | Cognitive Domains Broad | Cognitive Domains Specific |
|-------------------|--|-----------------------------------|--|
| 11 | Animal Naming (Controlled Oral Word Association Test, Category Fluency Test) | Speed of Processing | Speed of Processing |
| 1 | Antisaccade Task: correct reaction time | Speed of Processing | Reaction Time |
| 1 | Antisaccade Task: error rate | Executive Function/Working Memory | Inhibition/Working Memory |
| 5 | Arithmetic subtest, Wechsler Adult Intelligence Scale | Working Memory/Attention | Working Memory/Attention |
| 1 | Associate Learning, Wechsler Memory Scale | Verbal Memory/Learning | Verbal Memory/Learning |
| 1 | Auditory Trigrams Test | Working Memory | Working Memory |
| 1 | Benton Facial Recognition Test | Memory | Facial Memory |
| 1 | Benton Line Orientation Test | Intelligence | Non-verbal Ability |
| 2 | Benton Visual Retention Test | Visual Memory/Learning | Visual Memory/Learning |
| 1 | Bielefelder Famous Faces Test | Memory | Semantic Memory |
| 1 | Bimanual Coordination | Executive Function | Executive Function |
| 8 | Block Design, Wechsler Adult Intelligence Scale | Intelligence | Non-verbal Ability |
| 3 | Boston Naming Test | Verbal Fluency | Verbal Fluency |
| 1 | Brief Assessment of Cognition in Schizophrenia (Japanese) | Intelligence | Cognitive Battery |
| 3 | Brief Test of Attention | Attention | Attention |
| 7 | Brief Visuo-spatial Memory Test - Revised | Visual Memory/Learning | Visual Memory/Learning |
| 1 | Brown-Petersen Distractor Task | Memory | Short Term Memory |
| 1 | Brown-Petersen Dual Task Paradigm | Attention | Divided Attention |
| 2 | Buschke Verbal Selective Reminding Test | Verbal Memory/Learning | Verbal Memory/Learning |
| 19 | Californian Verbal Learning Test | Verbal Memory/Learning | Verbal Memory/Learning |
| 8 | Category and Verbal Fluency Task | Executive Function | Executive Function |
| 1 | Competing Programs | Executive Function | Executive Function |
| 1 | Comprehension subtest, Wechsler Adult Intelligence Scale | Intelligence | Verbal Ability/Language |
| 1 | Computerised Divided Attention Task | Attention | Tonic/Phasic Alertness/Divided Attention |
| 1 | Computerized Multiphasic Interactive Neurocognitive Dual Display System | Intelligence | Cognitive Battery |
| 1 | Computerized Neurocognitive Battery | Intelligence | Global Cognition |
| 1 | Computerised Visuospatial Working Memory Task | Working Memory | Working Memory |
| 1 | Continuous Paired Associate Task | Verbal Memory/Learning | Verbal Memory/Learning |
| 23 | Continuous Performance Test (Degraded Stimulus, AX, Identical Pairs, II) | Attention | Attention |
| 9 | Controlled Oral Word Association Test | Executive Function/Verbal Fluency | Executive Function/Verbal Fluency |
| 1 | D2 Test | Attention | Attention |
| 1 | Danish Adult Reading Test | Intelligence | Premorbid IQ |
| 1 | Delayed Recall Index, Wechsler Memory Scale - Revised | Verbal & Visual Memory/Learning | Verbal & Visual Memory/Learning |
| 2 | Delis-Kaplan Executive Functions System | Executive Function/Verbal Fluency | Executive Function/Verbal Fluency |
| 2 | Design Reproduction: delayed recall, Wechsler Adult Intelligence Scale - Revised | Visual Memory/Learning | Visual Memory/Learning |
| 2 | Design Reproduction: immediate recall, Wechsler Adult Intelligence Scale - Revised | Visual Memory/Learning | Visual Memory/Learning |
| 1 | Detection Task | Verbal Memory/Learning | Verbal Memory/Learning |
| 17 | Digit Span Backward, Wechsler Memory Scale | Working Memory | Working Memory |

| Number of studies | Cognitive Measure | Cognitive Domains Broad | Cognitive Domains Specific |
|-------------------|---|-------------------------|---------------------------------|
| 11 | Digit Span Forward, Wechsler Memory Scale | Working Memory | Working Memory |
| 13 | Digit Span Total, Wechsler Memory Scale/Wechsler Adult Intelligence Scale - Revised | Working Memory | Working Memory |
| 1 | Digit Span, Repeatable Battery for the Assessment of Neuropsychological Status | Attention | Attention |
| 18 | Digit Symbol Coding (Wechsler Adult Intelligence Scale, Brief Assessment of Cognition in Schizophrenia, Repeatable Battery for the Assessment of Neuropsychological Status) | Speed of Processing | Speed of Processing |
| 4 | Digital Sequencing (Wechsler Memory Scale, Brief Assessment of Cognition in Schizophrenia) | Working Memory | Working Memory |
| 3 | Doors and People Test | Visual Memory/Learning | Visual Memory/Learning |
| 1 | Dot Pattern Expectancy Task: BX-AY | Executive Function | Inhibition |
| 1 | Dot Pattern Expectancy Task: correct reaction time | Speed of Processing | Reaction Time |
| 1 | Dot Pattern Expectancy Task: D-prime | Speed of Processing | Signal Detection |
| 1 | Dynamic Praxis | Executive Function | Executive Function |
| 1 | Executive Golf | Executive Function | Spatial Ability/Planning |
| 1 | Face Recognition, Wechsler Memory Scale - III | Visual Memory/Learning | Visual Memory/Learning |
| 4 | Family Pictures, Wechsler Memory Scale | Memory | Episodic Memory |
| 5 | FAS Fluency Task | Executive Function | Executive Function |
| 1 | Figural Memory, Wechsler Memory Scale - Revised | Visual Memory/Learning | Visual Memory/Learning |
| 1 | Figure Copy, Repeatable Battery for the Assessment of Neuropsychological Status | Visual Memory/Learning | Visual Memory/Learning |
| 1 | Figure Recall, Repeatable Battery for the Assessment of Neuropsychological Status | Memory | Delayed Memory |
| 5 | Finger Tapping Test | Speed of Processing | Motor Speed |
| 1 | General Cognitive Index, Wechsler Memory Scale - Revised | Intelligence | Global Cognition |
| 4 | Groove Pegboard Test | Speed of Processing | Motor Speed |
| 1 | Groton Maze Chase Task | Speed of Processing | Speed of Processing |
| 1 | Groton Maze Learning Task | Executive Function | Executive Function |
| 1 | Groton Maze Learning Task: delayed recall | Executive Function | Executive Function |
| 1 | Hayling Sentence Completion Task | Executive Function | Inhibition |
| 1 | Hopkins Adult Reading Test Form B | Intelligence | Premorbid IQ |
| 8 | Hopkins Verbal Learning Test - Revised | Verbal Memory/Learning | Verbal Memory/Learning |
| 1 | Identification Task | Attention | Attention |
| 2 | Information subtest, Wechsler Adult Intelligence Scale | Verbal Fluency | Verbal Comprehension |
| 1 | Intentional Encoding Task | Speed of Processing | Motor Speed |
| 1 | International Shopping List: delayed recall | Verbal Memory/Learning | Verbal Memory/Learning |
| 1 | International Shopping List: immediate recall | Working Memory | Spatial Working Memory |
| 4 | Intra/extradimensional Set Shifting Task, Cambridge Neuropsychological Test Automated Battery | Executive Function | Cognitive Flexibility/Switching |
| 1 | Iowa Gambling Task | Executive Function | Executive Function |
| 1 | Japanese Verbal Learning Test | Verbal Fluency | Semantic Clustering |
| 2 | Kaufman Brief Intelligence Test | Intelligence | Current IQ |
| 1 | Korean-Auditory Verbal Learning Test | Attention | Attention |
| 9 | Letter Number Span/Sequencing, Wechsler Adult Intelligence Scale/Wechsler Memory Scale | Working Memory | Working Memory |
| 3 | List Learning Task | Verbal Memory/Learning | Verbal Memory/Learning |
| 19 | Logical Memory I: immediate recall, Wechsler Memory Scale | Verbal Memory/Learning | Verbal Memory/Learning |
| 16 | Logical Memory II: delayed recall, Wechsler Memory Scale | Verbal Memory/Learning | Verbal Memory/Learning |

| Number of studies | Cognitive Measure | Cognitive Domains Broad | Cognitive Domains Specific |
|-------------------|---|-------------------------|---|
| 2 | Logical Memory: recognition, Wechsler Memory Scale | Memory | Semantic Memory |
| 3 | Matrix Reasoning, Wechsler Adult Intelligence Scale - III | Executive Function | Executive Function |
| 1 | Mazes subtest, Wechsler Intelligence Scale for Children - Revised | Executive Function | Executive Function |
| 1 | Mesulam-Weintraub Cancellation | Attention | Attention |
| 1 | Mini Mental State Examination | Intelligence | Global Cognition |
| 1 | Modified Card Sorting Test | Executive Function | Executive Function |
| 3 | N-Back (0-3) | Working Memory | Working Memory |
| 9 | National Adult Reading Test | Intelligence | Premorbid IQ |
| 1 | Neurological Evaluation Scale | Speed of Processing | Motor Speed |
| 5 | Neuropsychological Assessment Battery: Mazes | Executive Function | Reasoning and Problem Solving Working Memory |
| 1 | Nonword Repetition Test | Working Memory | Working Memory |
| 2 | North American Adult Reading Test | Premorbid IQ | Premorbid IQ |
| 1 | Object Assembly, Wechsler Adult Intelligence Scale - Revised | Visual Memory/Learning | Visual Memory/Learning |
| 1 | Old-New Recognition Task | Memory | General Memory |
| 1 | One-card Learning Task | Visual Memory/Learning | Visual Memory/Learning |
| 1 | Paced Auditory Serial Addition Task | Working Memory | Working Memory |
| 2 | Paired Associate Learning Test | Verbal Memory/Learning | Verbal Memory/Learning |
| 4 | Paired Associates I: verbal immediate recall, Wechsler Memory Scale - Revised | Verbal Memory/Learning | Verbal Memory/Learning |
| 2 | Paired Associates I: visual immediate recall, Wechsler Memory Scale - Revised | Visual Memory/Learning | Visual Memory/Learning |
| 4 | Paired Associates II: verbal delayed recall, Wechsler Memory Scale - Revised | Verbal Memory/Learning | Verbal Memory/Learning |
| 2 | Paired Associates II: visual delayed recall, Wechsler Memory Scale - Revised | Visual Memory/Learning | Visual Memory/Learning |
| 1 | Penn Computerised Neurocognitive Battery | Executive Function | Language Reasoning |
| 1 | Picture Arrangement | Executive Function | Executive Function |
| 1 | Posner Paradigm | Speed of Processing | Reaction Time |
| 1 | Prepulse Inhibition Task | Executive Function | Sensorimotor Gating |
| 1 | Prose Recall, Wechsler Memory Scale | Verbal Memory/Learning | Verbal Memory/Learning |
| 1 | Quick Test | Intelligence | Current IQ |
| 1 | Rapid Visual Information Processing Task | Attention | Visual Attention |
| 1 | Reaction and Movement Time, Cambridge Neuropsychological Test Automated Battery | Speed of Processing | Reaction Time |
| 1 | Reading Sentences and Paragraphs | Intelligence | Verbal Ability/Language |
| 1 | Reading subtest, Wide Range Achievement Test | Attention | Attention |
| 1 | Recognition Memory Test | Verbal Memory/Learning | Verbal Memory/Learning |
| 8 | Rey Auditory Verbal Learning Test | Verbal Memory/Learning | Verbal Memory/Learning |
| 6 | Rey Complex Figure Test | Visual Memory/Learning | Visual Memory/Learning |
| 3 | Rey-Osterreich Complex Figure Test | Visual Memory/Learning | Visual Memory/Learning |
| 1 | Rivermead Behavioural Memory Test - Extended | Memory | General Memory |
| 1 | Rosen Drawing Test | Intelligence | Non-verbal Ability |
| 1 | Seashore Rhythm | Attention | Attention |
| 2 | Self-Ordered Pointing Task | Executive Function | Self-Generated Ordering/Action Verbal Ability/Language |
| 1 | Sentence Repetition Test | Intelligence | Verbal Ability/Language |
| 1 | Serial Reaction Time Task | Speed of Processing | Reaction Time |

| Number of studies | Cognitive Measure | Cognitive Domains Broad | Cognitive Domains Specific |
|-------------------|---|-------------------------|-----------------------------------|
| 1 | Set Shifting Task | Executive Function | Executive Function |
| 2 | Shipley Institute of Living Scale | Intelligence | Current IQ |
| 4 | Similarities, Wechsler Adult Intelligence Scale - III | Executive Function | Executive Function |
| 1 | Spatial Delayed Response Task | Working Memory | Working Memory |
| 6 | Spatial Span Backward, Wechsler Memory Scale | Working Memory | Working Memory |
| 6 | Spatial Span Forward, Wechsler Memory Scale | Working Memory | Working Memory |
| 3 | Spatial Span Total, Wechsler Memory Scale | Working Memory | Spatial Working Memory |
| 1 | Spatial Working Memory Task | Working Memory | Spatial Working Memory |
| 5 | Spatial Working Memory, Cambridge Neuropsychological Test Automated Battery | Executive Function | Executive Function |
| 3 | Spot The Word Test | Intelligence | Crystallised Intelligence |
| 1 | Stanford-Binet Word Fluency Task | Verbal Fluency | Verbal Fluency |
| 1 | Stereognosis | Intelligence | Sensory Ability |
| 1 | Sternberg Item Recognition Paradigm | Working Memory | Working Memory |
| 3 | Stocking of Cambridge, Cambridge Neuropsychological Test Automated Battery | Executive Function | Executive Function |
| 1 | Stories A and B, Wechsler Memory Scale | Verbal Memory/Learning | Verbal Memory/Learning |
| 3 | Stroop Word-Colour Interference Test | Executive Function | Executive Function |
| 5 | Stroop Word-Colour Interference Test: colour | Speed of Processing | Speed of Processing |
| 4 | Stroop Word-Colour Interference Test: inhibition | Executive Function | Interference Control |
| 2 | Stroop Word-Colour Interference Test: interference | Executive Function | Executive Function |
| 5 | Stroop Word-Colour Interference Test: word | Speed of Processing | Speed of Processing |
| 1 | Subjective Ordering Task | Executive Function | Self-Generated Ordering/Action |
| 1 | Tapping subtest, Halstead-Reitan Battery | Speed of Processing | Motor Speed |
| 2 | TAVEC | Verbal Memory/Learning | Verbal Memory/Learning |
| 2 | Token Test | Intelligence | Verbal Ability/Language |
| 1 | Toulouse-Pièron Task | Attention | Attention |
| 1 | Tower of Hanoi | Executive Function | Executive Function |
| 4 | Tower of London | Executive Function | Executive Function |
| 1 | Trail Making Test (1-5) | Executive Function | Executive Function |
| 26 | Trail Making Test A | Speed of Processing | Speed of Processing |
| 27 | Trail Making Test B | Executive Function | Executive Function |
| 2 | Trail Making Test B - A Differential Score | Speed of Processing | Motor Speed |
| 1 | Two Word Fluency Test: Naming Animals, Naming 'S' | Attention | Concentration/Sustained Attention |
| 6 | Verbal Fluency Test | Executive Function | Cognitive Flexibility/Switching |
| 1 | Verbal Memory Index, Wechsler Memory Scale - Revised | Memory | Verbal Episodic Memory |
| 1 | Verbal Memory, Brief Assessment of Cognition in Schizophrenia | Attention | Visual Attention |
| 1 | Visual Figure Reproduction, Wechsler Memory Scale | Visual Memory/Learning | Visual Memory/Learning |
| 1 | Visual Memory Index, Wechsler Memory Scale - Revised | Attention | Visual Attention |
| 1 | Visual Paired Associates, Wechsler Memory Scale | Visual Memory/Learning | Visual Memory/Learning |
| 1 | Visual Patterns Test | Working Memory | Spatial Working Memory |
| 11 | Visual Reproduction I: immediate recall, Wechsler Memory Scale | Visual Memory/Learning | Visual Memory/Learning |
| 11 | Visual Reproduction II: delayed recall, Wechsler Memory Scale | Visual Memory/Learning | Visual Memory/Learning |

| Number of studies | Cognitive Measure | Cognitive Domains Broad | Cognitive Domains Specific |
|-------------------|---|---------------------------------|---------------------------------|
| 1 | Visual Span, Wechsler Memory Scale | Visual Memory/Learning | Visual Memory/Learning |
| 12 | Vocabulary subtest, Wechsler Adult Intelligence Scale | Intelligence | Premorbid IQ |
| 2 | Vocabulary, Wechsler Abbreviated Scale of Intelligence | Intelligence | Verbal IQ |
| 2 | Wechsler Abbreviated Scale of Intelligence | Intelligence | Global Cognition |
| 1 | Wechsler Adult Intelligence Scale - (vocabulary, digit span, arithmetic, similarities, picture arrangement, picture completion, block design) | Intelligence | Full Scale IQ |
| 3 | Wechsler Adult Intelligence Scale - III | Intelligence | Performance IQ |
| 2 | Wechsler Adult Intelligence Scale - III (digit-symbol coding, information, arithmetic, block design) | Intelligence | Current IQ |
| 1 | Wechsler Adult Intelligence Scale - III (information, digit span, similarities, picture completion, block design, arithmetic, and coding) | Intelligence | Full Scale IQ |
| 2 | Wechsler Adult Intelligence Scale - III (vocabulary, similarities, block design, and matrix reasoning) | Intelligence | Current IQ |
| 7 | Wechsler Adult Intelligence Scale - Revised | Intelligence | Full Scale IQ |
| 1 | Wechsler Adult Intelligence Scale - Revised (vocabulary, block design, object assembly, comprehension, similarities) | Intelligence | Current IQ |
| 1 | Wechsler Adult Intelligence Scale - Revised (vocabulary, block design) | Intelligence | Current IQ |
| 1 | Wechsler Adult Intelligence Scale - Short | Intelligence | Current IQ |
| 1 | Wechsler Intelligence Scale for Children - III (vocabulary, similarities, picture completion, block design, arithmetic, and coding) | Intelligence | Full Scale IQ |
| 2 | Wechsler Memory Scale - III | Verbal & Visual Memory/Learning | Verbal & Visual Memory/Learning |
| 3 | Wechsler Memory Scale - Revised | Memory | Verbal Declarative Memory |
| 3 | Wechsler Test of Adult Reading | Intelligence | Premorbid IQ |
| 1 | Wechsler Intelligence Scale for Children | Intelligence | Verbal IQ |
| 3 | Wide Range Achievement Test - III | Intelligence | Premorbid IQ |
| 1 | Wide Range Achievement Test - Revised | Intelligence | Premorbid IQ |
| 26 | Wisconsin Card Sorting Test | Executive Function | Executive Function |
| 1 | Working Memory Manipulation, Cambridge Neuropsychological Test Automated Battery | Executive Function | Executive Function |
| 1 | Working Memory Span, Cambridge Neuropsychological Test Automated Battery | Executive Function | Executive Function |
| 2 | Yes/No Recognition Task | Visual Memory/Learning | Visual Memory/Learning |

Note. Number of studies column refers to the total number of studies which employed each measure from the reviewed literature, and the broad and specific cognitive columns are reflective of the most commonly purported domain. If two cognitive domains are listed in the one column, it reflects equal reporting of two different cognitive domains; in each case, the relevant findings were reported under the higher order domain (e.g. working memory/attention would be reported under working memory).

Supplementary Table 3: *Cognitive assessments used in each study*

| Reference | Cognitive Measures |
|---------------------------------|---|
| (Abé et al., 2018) | Colour-Word Interference Test, Trail Making Test, Design Fluency Test |
| (Andreasen et al., 2011) | Cognitive Battery |
| (Andrews et al., 2006) | N-back Task, Intentional Encoding Task, Yes/No Recognition Task |
| (Antonova et al., 2005) | National Adult Reading Test, Wechsler Adult Intelligence Scale (vocabulary), Hopkins Verbal Learning Test, Benton Visual Retention Test, Buschke Selective Reminding Test, Wechsler Memory Scale - III, Letter Number Span, Trail Making Test A & B, Wisconsin Card Sorting Test, Continuous Performance Task Identical Pairs, Stroop, Letter and Category Verbal Fluency, Finger Tapping Test, Grooved Pegboard Task |
| (Baaré et al., 1999) | Californian Verbal Learning Test, Wechsler Memory Scale - Revised (visual reproduction), Subjective Ordering Task, Verbal Fluency Task, Wechsler Adult Intelligence Scale (comprehension, vocabulary) |
| (Bilder et al., 1995) | Cognitive Battery (refer to paper) |
| (Bonilha et al., 2008) | Trail Making Test A & B, Controlled Oral Word Association Test, Wisconsin Card Sorting Test |
| (Briend et al., 2020) | Repeatable Battery for the Assessment of Neuropsychological Status |
| (Bruno et al., 2006) | National Adult Reading Test, Wechsler Adult Intelligence Scale - Revised (vocabulary, digit span, arithmetic, similarities) Rey-Osterreich Complex Figure Test, Doors and People Test, Spatial Working Memory Test, Interdimensional/Extradimensional Shift Test, Modified Card Sorting Test |
| (Caldiroli et al., 2018) | Wechsler Adult Intelligence Scale - III (arithmetic, digit symbol coding, block design, verbal comprehension) |
| (Cannon et al., 2005) | Wechsler Memory Scale - III (spatial span), Brown-Petersen Dual Paradigm Task, Posner Paradigm, Californian Verbal Learning Test, Wechsler Adult Intelligence Scale - III (block design, digit symbol), Halstead-Reitan Battery (tapping subtest) |
| (Cao et al., 2016) | Wechsler Abbreviated Scale of Intelligence, Wechsler Test of Adult Reading, California Verbal Learning Test |
| (Castro-Fornieles et al., 2018) | Wechsler Adult Intelligence Scale - III (digit span forwards & backwards, number letter sequencing), Trail Making Test A & B, Stroop, Continuous Performance Test, TAVEC, Controlled Oral Word Association Test, Wisconsin Card Sorting Test |
| (Chakrabarty et al., 2015) | Californian Verbal Learning Test |
| (Chen et al., 2018) | Continuous Performance Test |
| (Cho & Goghari, 2020) | Computerized Visuospatial Working Memory Task, Wechsler Test of Adult Reading |
| (Chung et al., 2013) | Wisconsin Card Sorting Test |
| (Cobia et al., 2012) | MATRICES Consensus Cognitive Battery |
| (Cocchi et al., 2009) | Cambridge Neuropsychological Test Automated Battery |
| (Crespo-Facorro et al., 2011) | Trail Making Test B, Wechsler Adult Intelligence Scale (backwards digits, digit symbol, vocabulary) Continuous Performance Test Degraded Stimulus, Rey Complex Figure Test |
| (Cunha et al., 2013) | Wechsler Memory Scale - III (digit span forwards & backwards), Controlled Oral Word Association Test |
| (Czepielewski et al., 2018) | Hopkins Verbal Learning Test |
| (DeLisi et al., 1995) | Not adequately described |
| (Dempster et al., 2017) | Wisconsin Card Sorting Test, Trail Making Test B |
| (Di Michele et al., 1992) | Luria Nebraska Neuropsychological Battery |
| (Edgar et al., 2012) | Shipley Institute of Living Scale, Trail Making Test A, Continuous Performance Test |
| (Egloff et al., 2019) | Californian Verbal Learning Test |
| (Ehrlich et al., 2012) | Wechsler Adult Intelligence Scale - III (similarities, block design), Delis-Kaplan Executive Function System, Hopkins Verbal Learning Test - Revised, Benton Visual Retention Test, Wechsler Memory Scale - III (face recognition, logical memory), Wide Range Achievement Test - III |

| Reference | Cognitive Measures |
|--------------------------------|--|
| (Exner et al., 2006) | Wechsler Adult Intelligence Scale (full scale IQ), Wechsler Memory Scale (block span, visual reproduction), Trail Making Test A & B |
| (Exner et al., 2008) | Wechsler Memory Scale - Revised (logical memory, visual reproduction) |
| (Fan et al., 2019) | MATRICES Consensus Cognitive Battery |
| (Ferro et al., 2015) | Rey Auditory Verbal Learning Test, Rey Complex Figure Test, Trail Making Test B, Wechsler Adult Intelligence Scale - III (digit symbol, vocabulary), Continuous Performance Test Degraded Stimulus |
| (Flaum et al., 1994) | Wechsler Adult Intelligence Scale - Revised |
| (Frascarelli et al., 2015) | Wisconsin Card Sorting Test |
| (Frazier et al., 2005) | Wechsler Intelligence Scale for Children - III (verbal IQ) |
| (Fujiwara et al., 2007) | Wechsler Adult Intelligence Scale - Revised (Japanese; vocabulary, block design), Benton Facial Recognition Test |
| (Garlinghouse et al., 2010) | Wechsler Adult Intelligence Scale - III (digit span backwards) |
| (Goghari et al., 2014) | Spatial Working Memory Task, Wechsler Abbreviated Intelligence Scale (vocabulary, block design) |
| (Goldberg et al., 1994) | Wechsler Memory Scale (logical memory, visual reproduction, paired associates), Trail Making Test A, Stroop Colour reading, Wisconsin Card Sorting Test, FAS Verbal Fluency, Continuous Performance Test, Wechsler Adult Intelligence Scale - Revised |
| (Guo et al., 2014) | Category Fluency Animal Naming Task, Brief Assessment of Cognition in Schizophrenia - Symbol Coding, Trail Making Test A, Wechsler Memory Scale - III (spatial span), Hopkins Verbal Learning Test - Revised, Brief Visual Memory Test - Revised, Stroop Colour and Word Test |
| (Gur et al., 1999) | Wisconsin Card Sorting Test, Seashore Rhythm, Trail Making Test, Digit Span, Digit Symbol, Continuous Performance Test, Logical Memory, Californian Verbal Learning Test, Design Reproduction, Controlled Oral Word Association Test, Reading Sentences and Paragraphs, Token Test, Benton Line Orientation Test, Block Design, Stereognosis, Finger tapping |
| (Gur et al., 2000) | Wisconsin Card Sorting Test, Seashore Rhythm, Trail Making Test, Digit Span, Digit Symbol, Continuous Performance Test, Logical Memory, Californian Verbal Learning Test, Design Reproduction, Controlled Oral Word Association Test, Reading Sentences and Paragraphs, Token Test, Benton Line Orientation Test, Block Design, Stereognosis, Finger tapping |
| (Gutierrez-Galve et al., 2012) | National Adult Reading Test, Wechsler Adult Intelligence Scale - Revised (vocabulary, digit span, arithmetic, similarities, picture complete, picture arrangement, block design), Rey-Osterreich Complex Figure Test, Doors and People Test, Spatial Working Memory Test |
| (Gutiérrez-Galve et al., 2014) | National Adult Reading Test, Wechsler Adult Intelligence Scale - III, Cambridge Neuropsychological Test Automated Battery, Rey Auditory Verbal Learning Test |
| (Harms et al., 2007) | Continuous Performance Test, Wechsler Memory Scale, Wisconsin Card Sorting Test |
| (Harms et al., 2010) | Wechsler Memory Scale - III, N-back, Californian Verbal Learning Test, Wechsler Abbreviated Scale of Intelligence, Continuous Performance Test - Degraded Stimulus |
| (Hartberg et al., 2010) | Rey Auditory Verbal Learning Test, Trail Making Test B, Wechsler Adult Intelligence Scale - III (letter-number sequence), Wechsler Abbreviated Intelligence Scale (vocabulary) Wisconsin Card Sorting Test |
| (Hartberg et al., 2011a) | National Adult Reading Test (Norwegian), Californian Verbal Learning Test - II, Wechsler Adult Intelligence Scale - III (digit symbol, digit span), Colour-Word Inference Test, Verbal Fluency Test, Wechsler Abbreviated Scale of Intelligence (vocabulary) |
| (Hartberg et al., 2011b) | National Adult Reading Test (Norwegian), Californian Verbal Learning Test - II, Wechsler Adult Intelligence Scale - III (digit symbol, digit span), Colour-Word Inference Test, Verbal Fluency Test, Wechsler Abbreviated Scale of Intelligence (vocabulary) |
| (Hasan et al., 2014) | Boston Naming Test (German), Rey Auditory Verbal Learning Test (German), Self-Ordering Point Task, Wisconsin Card Sorting Test |
| (Hatton et al., 2013) | Rapid Visual Information Processing Task, Trail Making Test, Interdimensional/Extradimensional Task, Rey Auditory Verbal Learning Test, Controlled Oral Word Association Test |
| (Haukvik et al., 2015) | Californian Verbal Learning Test, Wechsler Abbreviated Scale of Intelligence |
| (Herold et al., 2015) | Wechsler Memory Scale - III (logical memory, digit span forward & backward), Trail Making Test A & B, Bielefelder Famous Faces Test |
| (Hidese et al., 2017) | Brief Assessment of Cognition in Schizophrenia (Japanese) |

| Reference | Cognitive Measures |
|---------------------------------|---|
| (Jalbrzikowski et al., 2019) | Penn Computerized Neurocognitive Battery |
| (Jensen et al., 2019) | Wechsler Adult Intelligence Scale - III |
| (Jirsaraie et al., 2018) | Brief Assessment of Cognition in Schizophrenia |
| (Juuhl-Langseth et al., 2015) | MATRICES Consensus Cognitive Battery, Wechsler Abbreviated Scale of Intelligence |
| (Karnik-Henry et al., 2012) | Wechsler Memory Scale - III (logical memory, family pictures), Californian Verbal Learning Test |
| (Keshavan et al., 2003) | Neurological Evaluation Scale |
| (Killgore et al., 2009) | Wechsler Memory Scale - Revised (prose recall, visual paired associates, figure reproduction, total memory quotient score) |
| (Kim et al., 2018) | Wechsler Adult Intelligence Scale, Trail Making Test A & B, Rey-Osterreith Complex Figure Test, Controlled Oral Word Association Test, Wisconsin Card Sorting Test |
| (Knöchel et al., 2014) | Spot-the-Word Test (German), Hopkins Verbal Learning Test - Revised, Brief Visuospatial Memory Test - Revised |
| (Knöchel et al., 2016a) | Spot-the-Word Test, Trail Making Test A & B |
| (Knöchel et al., 2016b) | Hopkins Verbal Learning Test, Brief Visuospatial Memory Test - Revised, Trail Making Test A & B |
| (Koshiyama et al., 2018) | National Adult Reading Test (Japanese), Wechsler Memory Scale - Revised |
| (Kozicky et al., 2013) | Spatial Working Memory Task, Stockings of Cambridge, Interdimensional/Extradimensional Shift Task, North American Adult Reading Test, Kaufman Brief Intelligence Test |
| (Kubota et al., 2015) | Wechsler Adult Intelligence Scale - III |
| (Kuhn et al., 2012) | Trail Making Test A & B |
| (Kumarasinghe et al., 2014) | Repeatable Battery For The Assessment Of Neuropsychological Status |
| (Kumari et al., 2008) | Pre-pulse Inhibition |
| (Kumra et al., 2011) | Wechsler Intelligence Scale for Children - III (vocabulary, similarities, picture completion, block design, arithmetic, coding), Wechsler Adult Intelligence Scale - III (similarities, picture completion, block design, arithmetic, coding, information, digit span), Californian Verbal Learning Test, Finger tapping Test, Grooved Pegboard Test, Wisconsin Card Sorting Test, Continuous Performance Test, Identical Pairs |
| (Kuroki et al., 2006) | Wechsler Memory Scale - III |
| (Lappin et al., 2014) | National Adult Reading Test, Rey Auditory Verbal Learning Test |
| (Liao et al., 2015) | Digit Symbol Substitution Test, Category Fluency Test - Animal Naming, Wechsler Memory Scale - Revised |
| (Liu et al., 2016) | MATRICES Consensus Cognitive Battery |
| (Matsubara et al., 2016) | Trail Making Test A & B, Japanese Adult Reading Inventory |
| (Matsui et al., 2008) | Japanese Verbal Learning Test |
| (Minatogawa-Chang et al., 2009) | Wechsler Memory Scale - III (digit span forwards & backwards), Controlled Oral Word Association Test |
| (Molina et al., 2009) | Wechsler Adult Intelligence Scale (digit symbol, arithmetic), Trail Making Test A, Toulouse Pieron total score, Californian Verbal Learning Test (Spanish; TAVEC), Rey-Osterreith Complex Figure Test, Wisconsin Card Sorting Test |
| (Moorhead et al., 2007) | National Adult Reading Test, Wechsler Abbreviated Scale of Intelligence (performance & verbal IQ), Extended Rivermead Behavioural Memory Test |
| (Nakahara et al., 2019) | Computerized Multiphasic Interactive Neurocognitive Dual Display System |
| (Nakamura et al., 2008) | Wechsler Adult Intelligence Scale - III, Wisconsin Card Sorting Test, Trail Making Test, Iowa Gambling Task |
| (Nestor et al., 1993) | Wechsler Adult Intelligence Scale (similarities, block design), Wisconsin Card Sorting Test, Wechsler Memory Scale - Revised (logical memory, visual reproduction, paired associates), Finger Tapping Test, |

| Reference | Cognitive Measures |
|-------------------------------|---|
| (Nestor et al., 2007) | Wechsler Adult Intelligence Scale - II (full scale, verbal & performance IQ), Wisconsin Card Sorting Test, Doors and People Test |
| (Oertel-Knochel et al., 2015) | Spot-the-Word Test, Trail Making Test A, Tower of London |
| (Ohtani et al., 2014) | Wide Range Achievement Test, Word Fluency Task |
| (Onitsuka et al., 2003) | Wechsler Memory Scale - III (facial memory) |
| (Premkumar et al., 2008) | National Adult Reading Test, Wisconsin Card Sorting Test, Wechsler Memory Scale (visual reproduction), Verbal Fluency Letters, Trail Making Test - B |
| (Pujol et al., 2013) | Wechsler Adult Intelligence Scale - III (vocabulary, block design, similarities, digit span, letter-number, arithmetic), Trail Making Test A & B, Wechsler Memory Scale - III (logical memory), Wisconsin Card Sorting Test, Tower of London |
| (Pujol et al., 2014) | Wechsler Adult Intelligence Scale - III (vocabulary), Rey Auditory Verbal Learning Test |
| (Rais et al., 2012) | Wechsler Adult Intelligence Scale - III (information, arithmetic, block design, digit symbol coding; Dutch) |
| (Rigucci et al., 2013) | Stroop Word Reading, Wisconsin Card Sorting Test, Trail Making Test A & B, Buschke Verbal Selective Reminding Test, Rey-Osterrieth Complex Figure |
| (Roalf et al., 2017) | Computerized Neurocognitive Battery |
| (Roiz-Santiáñez et al., 2014) | Rey Auditory Verbal Learning Test, Rey Complex Figure Test, Trail Making Test B, Wechsler Adult Intelligence Scale - III (digit symbol, vocabulary, digit span backwards), Continuous Performance Test Degraded Stimulus, Brief Test of Attention |
| (Roiz-Santiáñez et al., 2015) | Rey Auditory Verbal Learning Test, Rey Complex Figure Test, Trail Making Test B, Wechsler Adult Intelligence Scale - III (digit symbol, vocabulary, digit span backwards), Continuous Performance Test Degraded Stimulus, Brief Test of Attention |
| (Sachdev et al., 2000) | Wisconsin Card Sorting Test, Wechsler Adult Intelligence Scale (similarities), Controlled Oral Word Association Test, Wechsler Intelligence Scale for Children - Revised (mazes), Wechsler Memory Scale (logical memory, verbal paired associates, visual reproduction) |
| (Salgado-Pineda et al., 2003) | Continuous Performance Test |
| (Sanfilipo et al., 2002) | Wechsler Adult Intelligence Scale - Revised (vocabulary, information, similarities, logical memory, digit symbol), Wisconsin Card Sorting Test, Buschke Verbal Selective Reminding Test, Category and Verbal Fluency Task, Controlled Oral Word Association Test, Wechsler Memory Scale - Revised (visual reproduction) |
| (Sarnicola et al., 2009) | Wechsler Adult Intelligence Scale - Revised, Hayling Sentence Completion Task, Wisconsin Card Sorting Task |
| (Sax et al., 1999) | Continuous Performance Test |
| (Schobel et al., 2009) | Wechsler Adult Intelligence Scale - Revised, Wechsler Memory Scale - Revised, Wisconsin Card Sorting Test, Trail Making Test B |
| (Schretlen et al., 2010) | Hopkins Adult Reading Test - B, Trail Making Test A & B, Brief Test of Attention, Hopkins Verbal Learning Test - Revised, Brief Visuospatial Memory Test - Revised, Wisconsin Card Sorting Test |
| (Segarra et al., 2008) | Wechsler Adult Intelligence Scale - III (vocabulary, digit span, letter number sequencing, arithmetic), Trail Making Test, Controlled Oral Word Examination, Wisconsin Card Sorting Test |
| (Seidman et al., 1994) | Wisconsin Card Sorting Test, Wechsler Adult Intelligence Scale - Revised (similarities, vocabulary, block design), Auditory Continuous Performance Test, Finger Tapping, Wechsler Memory Scale (logical memory, visual reproduction) |
| (Shi et al., 2018) | NAB: Mazes, Spatial Span Test, Digital Sequencing Test |
| (Spalletta et al., 2008) | N-back Task |
| (Sullivan et al., 1996) | Self-Ordered Pointing, Wisconsin Card Sorting Test, Brown Peterson Distractor Task, Letter/Design Fluency, Fine Finger Movements, Wechsler Memory Scale, |
| (Szendi et al., 2006) | Digit Span Forwards & Backwards, Nonword Repetition Test (Hungarian), Corsi Blocks, Visual Patterns Test, Wisconsin Card Sorting Test, Tower of Hanoi, Letter Fluency, Category Fluency |
| (Szeszko et al., 2000) | Cognitive Battery (refer to paper) |
| (Szeszko et al., 2002) | Cognitive Battery (refer to paper) |
| (Szeszko et al., 2003) | Cognitive Battery (refer to paper) |

| Reference | Cognitive Measures |
|----------------------------|---|
| (Thoma et al., 2009) | Shipley Institute of Living Scale, Trail Making Test A & B, Continuous Performance Test, Auditory Consonant Trigrams Test, Digit Span Forward & Backwards, Wechsler Memory Scale - Revised (logical memory & visual reproduction) |
| (Thompson et al., 2001) | Not adequately described |
| (Toulopoulou et al., 2004) | Wechsler Memory Scale (logical memory, visual reproduction, associate learning), Wechsler Adult Intelligence Scale (block design, object assembly, vocabulary, comprehension, similarities) Executive Golf, Tower of London |
| (Tully et al., 2014) | Category Fluency Animal Naming Task |
| (Turetsky et al., 2003) | Wechsler Adult Intelligence Scale - Revised (logical memory, design reproduction), Californian Verbal Learning Test |
| (Wannan et al., 2018) | Wechsler Adult Intelligence Scale (Matrix Reasoning and Vocabulary), Wechsler Test of Adult Reading, Visuospatial Paired-Associate Learning Task |
| (Weiss et al., 2004) | Old-New Recognition Test |
| (Wojtalik et al., 2012) | Wechsler Memory Scale - Revised (stories A & B), Californian Verbal Learning Test, Wechsler Adult Intelligence Scale - Revised, Wisconsin Card Sorting Test |
| (Wolf et al., 2008) | Computerized Divided Attention Task, Corsi Block, Digit Span, Wisconsin Card Sorting Test, Stroop Word-Color Interference Test |
| (Yan et al., 2019) | Trail Making Test A, Category Fluency Test: Animal Naming, Digit Span Forwards, Logical Memory |
| (Zipursky, 1998) | National Adult Reading Test, Quick Test |
| (Zuffante et al., 2001) | Wechsler Adult Intelligence Scale - Revised, Spatial Delayed Response Task, Self-Ordered Pointing Task |

1. Comprehensive review of the literature

We summarize the results of the included studies, organized by diagnosis, beginning with findings from samples of recent-onset schizophrenia-spectrum disorders (RO-SSD) and established schizophrenia-spectrum disorders (SSD) followed by recent-onset bipolar disorder (RO-BD) and established bipolar disorder (BD). For clarity, we report morphology-cognition relationships arranged by cognitive domain and beginning with findings pertaining to grey matter volume followed by thickness and surface area. All relationships identified in the current literature between cognition and morphology are summarized and organized alphabetically by diagnosis and cognitive domain in Supplementary Table 5. Furthermore, a visual summary of the number of studies examining each index of morphology for each cognitive domain and diagnosis can be seen in Figure 2.

As mentioned in the main text, the terms *positive* and *negative* associations are used frequently throughout this section to describe the relationship between cognition and brain morphology. A positive association suggests that as cognitive performance increases, brain volume (or thickness or surface area) increases (i.e. better performance is associated with larger volumes). In turn, a negative association suggests that as cognitive performance decreases, brain morphology increases (i.e. worse performance is associated with thicker cortices). It should be noted that the direction of the relationship reported here may be different to that stated in the original manuscript for some studies. In these instances, we have reversed the direction for ease of interpretation and comparability across measures, since better cognitive performance is represented by low scores on some cognitive tests and high scores on others.

1.1 Recent-Onset Schizophrenia-Spectrum Disorders (RO-SSD)

Twenty-six studies examined the relationship between cognition and brain morphology in RO-SSD, of which 22 were cross-sectional studies, and four longitudinal in design.

1.1.1 Attention

Five studies examined attention and *volume* in RO-SSD. In the frontal region, the left inferior frontal gyrus was positively associated with attentional performance uniquely in patients (Salgado-Pineda et al., 2003), whilst no relationship was observed in the neighboring structures of the superior and orbital frontal gyri (Kumra et al., 2011). Furthermore, Kumra et al. (2011) noted no relationship between anterior cingulate gyrus volume and attention when analyzing patients-only. In the parietal lobe, positive associations with attention were identified with volume of the left angular, postcentral, and supramarginal gyri uniquely in patients (Salgado-Pineda et al., 2003). Similarly, a study by Ferro et al. (2015) observed a correlation with the postcentral gyrus in patients at a one-year follow up (absent at baseline), however this relationship was negative in direction and absent in healthy controls. In subcortical structures, studies have observed in patients but not healthy controls, a positive association with volume of the left thalamic nucleus (Salgado-Pineda et al., 2003) and a negative association with the right caudate in a four-year longitudinal study (DeLisi et al., 1995). In correlational analyses of RO-SSD patients only, Kumra et al. (2011) reported positive associations between whole brain volume and attentional performance, whilst Rigucci et al. (2013) observed no relationship between these two variables.

No studies examined attentional performance in relation to *cortical surface area*, and two studies examined attentional performance and *cortical thickness*. Here, one study showed a positive association between parietal lobe thickness and performance, specifically in the right precentral gyrus in a sample comprising only patients (Hatton et al., 2013). In contrast, a longitudinal study by Roiz-Santiáñez et al. (2015) found no association between cortical

thinning and attentional performance change in either patients or healthy controls over a three-year follow up.

1.1.2 *Speed of Processing*

Five RO-SSD studies examined speed of processing and *volume*. In the frontal lobe, one study found no association with orbital and superior frontal gyri volumes in their analyses of RO-SSD patients only (Kumra et al., 2011). Furthermore, no relationship between volume and speed of processing was found in the anterior cingulate gyrus (Kumra et al., 2011). In the temporal lobe, a single positive association was identified with anterior hippocampal volume in another study comprising a patient-only sample (Bilder et al., 1995). Another study showed that within the cerebellum, lobule X was positively correlated with speed of processing in patients but not controls, whilst lobule VI was positively correlated in healthy controls but not in patients (Kim et al., 2018). From this study, total cerebellum volume was not associated with speed of processing in either patients or healthy controls, a finding replicating that observed in earlier work by Exner et al. (2006). There were mixed findings in the studies examining whole brain volume, with both a positive association (Kumra et al., 2011) and no association (Exner et al., 2006; Rigucci et al., 2013) observed in RO-SSD.

No studies investigated speed of processing in relation to *cortical surface area* in RO-SSD, and only one study investigated speed of processing and *cortical thickness*. This study analyzed correlations in RO-SSD patients only and found a negative association in the right precentral gyrus and the left intraparietal sulcus (Hatton et al., 2013).

1.1.3 *General Memory*

A single study by Briend et al. (2020) investigated general memory performance in RO-SSD, to which they found no association between hippocampal volumes and short and long term memory in either patients or healthy controls.

1.1.4 Verbal Memory/Learning

Six studies investigated verbal memory/learning performance and volume in RO-SSD patients. Positive relationships were observed in RO-SSD patients in the hippocampal region, specifically with left hippocampal volume over a six-year period (Lappin et al., 2014), and left hippocampal gyri volume cross-sectionally (Guo et al., 2014); these associations were absent in the respective healthy control groups of these studies. A single study by Juuhl-Langseth et al. (2015) identified a negative association between verbal memory/learning and caudate volume, which was absent in the healthy control group. The remaining studies investigating verbal memory/learning did not find significant associations (in their analyses of patients-only) in regions such as the orbital and superior frontal gyrus, the anterior cingulate gyrus (Kumra et al., 2011), subcortical structures (Egloff et al., 2019), or across the whole brain (Kumra et al., 2011; Rigucci et al., 2013).

No studies investigated the relationship between verbal memory/learning and *cortical surface area* in RO-SSD, but one study examined the relationship with *cortical thickness*. This study found no association with verbal memory/learning across the entire brain in either patients or healthy controls after a three-year follow up (Roiz-Santiáñez et al., 2015).

1.1.5 Visual Memory/Learning

Four studies examined visual memory/learning performance and *volume*; findings suggested positive associations unique to RO-SSD patients in the left presupplementary motor area (Exner et al., 2006) and right hippocampal gyrus (Guo et al., 2014). No significant

relationship was found with the right presupplementary motor area, cerebellum volume, or total brain volume in patients or healthy controls (Exner et al., 2006), or with any cluster across the brain in a patient-only sample (Rigucci et al., 2013). Wannan et al. (2018) identified a positive association unique to established SSD patients between hippocampal subfield volumes (CA4DG) and stratum, and visual memory/learning performance in patients. In the sole study examining *cortical thickness*, Roiz-Santiáñez et al. (2015) reported no relationship with visual memory/learning across the entire brain after a three-year follow up period. No studies investigated visual memory/learning in relation to *cortical surface area*.

1.1.6 Working Memory

Six studies investigated working memory and *volume*; positive associations were observed uniquely in RO-SSD patients in the left superior frontal gyrus (Cunha et al., 2013), and in both patients and healthy controls in the superior frontal and orbitofrontal cortex, bilaterally, at a two-year follow up (Castro-Fornieles et al., 2018). Further positive associations were observed in both left and right hippocampal gyri in RO-SSD patients uniquely (Guo et al., 2014). A single negative association was found at a one-year follow up in the left postcentral gyrus in a patient-only sample; this was not evident at baseline (Ferro et al., 2015). With regards to global measures of volume, Cocchi et al. (2009) identified no association with total grey matter volume in RO-SSD patients, but a positive association in healthy controls. Rigucci et al. (2013) also reported an absence of any association between volume and working memory across the entire brain in analyses of patients-only. Similarly, Roiz-Santiáñez et al. (2015) did not find a significant association with *cortical thickness* across the entire brain in either patients or healthy controls, after a three-year follow up. No studies investigated working memory in relation to *cortical surface area*.

1.1.7 Executive Function

Eleven studies examined executive function and *volume* in RO-SSD; studies by Cunha et al. (2013) and Guo et al. (2014) identified positive relationships unique to their RO-SSD patient groups between executive performance and volume of the left medial frontal and left orbital inferior frontal gyrus, respectively, whilst Kumra et al. (2011) observed no relationship with orbital frontal gyrus volume. Furthermore, Kumra et al. also found no association with superior frontal gyri volume, in analyses of RO-SSD patients-only. In the temporal lobe, volumes of the anterior hippocampus (Bilder et al., 1995), right superior temporal gyrus (Cunha et al., 2013), amygdala (Fan et al., 2019), and left hemisphere of the temporal lobe (DeLisi et al., 1995) were found to be positively associated with executive function performance in RO-SSD, whilst a negative association was observed with the left fusiform gyrus (Dempster et al., 2017). At baseline in their longitudinal study, Dempster et al. (2017) observed positive associations with parietal regions such as Brodmann Areas 40 and 7, and the left inferior and superior parietal lobules, and negative associations with occipital regions such as Brodmann Area 19, the left lingual gyrus, and right occipital gyrus, in their patient only sample. These associations were not present at follow up after six years.

In the examination of subcortical regions and executive function, negative associations with right caudate and posterior lobe volume (DeLisi et al., 1995; Dempster et al., 2017) and no association with total caudate volume (Juuhl-Langseth et al., 2015) was found in RO-SSD. In the basal ganglia, the globus pallidus (Dempster et al., 2017), right and total nucleus accumbens (Dempster et al., 2017; Fan et al., 2019), left lobule VI and X (Kim et al., 2018), and anterior cingulate volumes (Szeszko et al., 2000) were all positively associated with executive function performance. Conversely, negative associations between volume and executive function were identified in the left pons, brain stem, right inferior

vermis, and cerebellum (Dempster et al., 2017). Furthermore, there were also other regions in which no relationships between volume and executive function performance were reported, such as the anterior cingulate gyrus (Kumra et al., 2011), right insula (Cunha et al., 2013), and whole brain volume (Kumra et al., 2011; Rigucci et al., 2013). Of all the studies examining volume with healthy control samples, only that of Juuhl-Langseth et al. (2015) and Cunha et al. (2013) identified a relationship in their healthy control samples; they observed positive relationships between caudate volume and right insula volume (respectively) and executive function—associations that were absent in their respective RO-SSD samples.

Only one study examined *cortical thickness* in relation to executive function; Roiz-Santiáñez et al. (2015) did not find any regions of significance across their analyses of the entire brain in either patients or healthy controls. No studies investigated executive function in relation to *cortical surface area*.

1.1.8 Intelligence/global cognition

Seven studies investigated *volume* in relation to current IQ or global cognition in RO-SSD samples. Positive associations unique to patients were observed in frontal regions such as the orbitofrontal and superior frontal cortex, rectus (Castro-Fornieles et al., 2018), and right inferior and superior dorsolateral prefrontal cortex (Minatogawa-Chang et al., 2009). In the temporal region, positive associations were found with the left entorhinal (Roalf et al., 2017) and right superior temporal cortex (Minatogawa-Chang et al., 2009). Additionally, positive associations were identified with the left and right lateral parietal cortex (Minatogawa-Chang et al., 2009), and total grey matter volume (Zipursky, 1998). A single negative association was observed longitudinally (four years) between right caudate volume and global cognition in a RO-SSD sample, to which no association was observed in the corresponding healthy control cohort (DeLisi et al., 1995). Contrary to the findings of

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Zipursky (1998), Jensen et al. (2019) and Exner et al. (2006) observed no relationship between total grey matter volume and current IQ. Of the studies examining intelligence, the majority contained healthy control samples; notably, none identified any relationship in healthy controls between morphology and measures of intelligence.

One study investigated the relationship between current IQ and *cortical thickness* and *surface area*, to which Rais et al. (2012) observed no relationship between cortical thickness or cortical surface area and current IQ in their RO-SSD patients or healthy controls. Two studies investigated *premorbid IQ* and brain morphology in RO-SSD samples. Zipursky (1998) identified no relationship between total grey matter *volume* and premorbid IQ scores in either patients or healthy controls, whilst Gutiérrez-Galve et al. (2014) observed positive associations between total *cortical thickness* and total *cortical surface area* in their RO-SSD patient-only sample. Notably, Gutiérrez-Galve et al. (2014) reported that these associations were present at baseline and at follow up two years later.

1.2 Established Schizophrenia-Spectrum Disorders (SSD)

Seventy-nine studies investigated the relationship between cognition and brain morphology in SSD; of these studies, 76 were cross-sectional and three were longitudinal.

1.2.1 Attention

Eleven studies examined attentional performance and *volume* in established SSD patients. Three studies observed positive associations in the frontal lobe, namely with left prefrontal (Seidman et al., 1994), right dorsolateral prefrontal (Kumarasinghe et al., 2014), and total frontal lobe volume (Andreasen et al., 2011). Of these studies, only a single study showed no relationship with total prefrontal cortex volume (Harms et al., 2010). Further, only Kumarasinghe et al. (2014) included healthy controls in their correlational analyses, to which

they found the association with right dorsolateral prefrontal volume to be unique to their patient sample.

In the temporal lobe, two studies showed attention was positively associated with volume of the hippocampal tail and negatively associated with left posterior hippocampal volume in analyses of SSD patients only (Nakahara et al., 2019; Thoma et al., 2009), while superior temporal gyrus volume was not associated with attentional performance in either patients or healthy controls in another study (Gur et al., 2000). With regards to volume of subcortical structures, the caudate was positively associated with attentional performance in a study analyzing correlations in SSD patients only (Andreasen et al., 2011), whilst no association was found with the thalamus in either patients or healthy controls in other work (Harms et al., 2007).

Other findings pertaining to attentional performance include: a positive relationship unique to patients with volume of the right nucleus accumbens (Koshiyama et al., 2018), a positive relationship with total parietal lobe volume in analyses of SSD patients only (Andreasen et al., 2011), and no significant relationships in either patients and healthy controls with cerebellum volume (Szeszko et al., 2003). In global assessments of volume, positive relationships were identified with total brain volume in a study analyzing correlations in SSD patients only (Andreasen et al., 2011) and total grey matter volume in both SSD patients and male healthy controls (Gur et al., 1999).

Four studies examined the relationship between attentional performance and *cortical thickness*. In the frontal region, positive associations unique to SSD patients were observed with the left inferior orbitofrontal cortex and right pars opercularis (Edgar et al., 2012), negative associations were identified in the left superior frontal gyrus and right frontal cortex in a combined SSD and healthy control sample (Chen et al., 2018), and no association was

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observed in the prefrontal cortex in a study analyzing correlations in SSD patients-only (Harms et al., 2010).

In other regions, unique positive associations between cortical thickness and attentional performance were reported in the left and right transverse temporal gyrus (Edgar et al., 2012), whilst two studies analyzing correlations in only SSD patients reported negative associations in both the left superior temporal gyrus (Chen et al., 2018) and across the parietal lobe (Crespo-Facorro et al., 2011). With respect to global measures, total cortical thickness was negatively associated with attentional performance in analyses of SSD patients-only (Crespo-Facorro et al., 2011). A single study examining *surface area* and analyzing SSD patients-only, observed no relationship between attentional performance and surface area of the prefrontal cortex (Harms et al., 2010).

1.2.2 *Speed of Processing*

Twelve studies of established SSD investigated the relationship between speed of processing and *volume*. Positive associations were observed with volume of the inferior frontal gyrus (Jirsaraie et al., 2018), left middle frontal gyrus (Knöchel et al., 2016b), bilateral orbitofrontal cortex (Liao et al., 2015) and prefrontal cortex globally (Cannon et al., 2005). One study suggested no association with dorsolateral prefrontal cortex volume (Jirsaraie et al., 2018). All of these studies of speed of processing included healthy controls in their analyses, where the finding pertaining to volume of the middle frontal gyrus (Knöchel et al., 2016b) was unique to the patient group.

In the temporal lobe, positive relationships were observed with total volume of the hippocampus (Jirsaraie et al., 2018), anterior hippocampus (Szeszko et al., 2002), right hemisphere of the anterior hippocampus (Thoma et al., 2009), dentate gyrus (Nakahara et al., 2019) and left temporal pole (Liao et al., 2015). Negative associations were limited to volume

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of the left posterior hippocampus (Thoma et al., 2009). Except for the findings pertaining to hippocampal volume (Jirsaraie et al., 2018), all findings in the temporal lobe were unique to the SSD patients.

In other analyses of speed of processing and volume, positive associations were observed with the left caudate (Keshavan et al., 2003) and insula cortex (Liao et al., 2015). In the cerebellum, findings showed either positive associations with volume (Hartberg et al., 2011b; Keshavan et al., 2003), or an absence of significant associations between cerebellum Crus I and II volumes (Kuhn et al., 2012; Szeszko et al., 2003) and speed of processing. There was mixed evidence pertaining to total grey matter volume, with reports of positive (Antonova et al., 2005), negative (Thoma et al., 2009), or an absence of (Jirsaraie et al., 2018) relationships with speed of processing. All of these findings were unique to SSD patients except for that of the insula cortex (Liao et al., 2015), for which a similar association with speed of processing was also observed in a healthy comparison group sample.

In the four studies examining *cortical thickness*, positive associations were identified with the left middle frontal cortex and calcarine sulcus in both patients and healthy controls (Yan et al., 2019), and the pars opercularis (Knöchel et al., 2016a) and transverse temporal region (Hartberg et al., 2011a) in SSD-only samples. One study by Tully et al. (2014) noted no significant association with cortical thickness of the superior frontal gyrus in their patient group, but observed a positive association in their healthy control sample. No studies examined *cortical surface area* with respect to speed of processing performance.

1.2.3 General Memory

Six studies of established SSD examined general memory performance and *volume*. Positive correlations were found with both left (Kuroki et al., 2006) and right hippocampal volume (Kuroki et al., 2006; Nestor et al., 2007; Weiss et al., 2004), in addition to volume of

the parietal-occipital region (Sullivan et al., 1996). These relationships were unique to SSD patients and absent in healthy controls. On the contrary, Szeszko et al. (2003) observed a positive relationship between general memory performance and volume of the cerebellum, which was present in healthy controls and absent in SSD patients.

Three studies examined different facets of memory and brain morphology in SSD. Sullivan et al. (1996) identified a positive relationship between parietal-occipital lobe volume and short term memory. Karnik-Henry et al. (2012) observed no relationship in either patients or healthy controls between episodic memory performance and hippocampal and parahippocampal gyrus volume, as well as *cortical thickness* of the parahippocampal gyrus. Lastly, Fujiwara et al. (2007) observed no relationship between facial memory and volume of the anterior cingulate. These findings were each unique to the patient groups and were not observed in healthy control groups within these studies. No studies examined *cortical surface area* with respect to general memory performance.

1.2.4 Verbal Memory/Learning

Twenty-seven studies examined verbal memory/learning and *volume* in established SSD cohorts. Positive associations were often observed across the frontal region, specifically in the left middle frontal gyrus (Knöchel et al., 2016b), orbitofrontal cortex (Baaré et al., 1999), total and left prefrontal cortex (Baaré et al., 1999; Seidman et al., 1994), right dorsolateral prefrontal cortex (Molina et al., 2009), superior frontal gyrus (Knöchel et al., 2016b), and with total frontal lobe volume (Andreasen et al., 2011). Of these studies, those that included healthy controls in their analyses (Baaré et al., 1999; Knöchel et al., 2016b) reported these relationships as unique to SSD patients. There were a handful of studies indicating an absence of a relationship between verbal memory/learning and volume of the inferior frontal gyrus (Antonova et al., 2005; Jirsaraie et al., 2018), dorsolateral prefrontal

cortex (Jirsaraie et al., 2018), and prefrontal cortex globally (Harms et al., 2010), although one study did find a positive association unique to its healthy control sample in the inferior frontal gyrus (Antonova et al., 2005).

In the temporal lobe, regions positively related to verbal memory/learning but unique to the patient group, included left (Hasan et al., 2014; Nestor et al., 2007; Sanfilipo et al., 2002), right (Herold et al., 2015; Knöchel et al., 2014; Sachdev et al., 2000; Sanfilipo et al., 2002), right anterior and posterior (Herold et al., 2015), and total hippocampal volume (Jirsaraie et al., 2018; Koshiyama et al., 2018; Sanfilipo et al., 2002), left posterior superior temporal gyri volume (Nestor et al., 1993), left and right amygdala (Sachdev et al., 2000) and total temporal lobe volume (Andreasen et al., 2011). Conversely, left amygdala volume was observed to be negatively associated with volume in patients-only (Killgore et al., 2009). In contrast, some studies reported no association in either patients or healthy control in regions such as the temporopolar, perirhinal, and entorhinal cortex (Turetsky et al., 2003), left hippocampus (Knöchel et al., 2014; Sachdev et al., 2000), hippocampus as a whole, and parahippocampal gyrus (Karnik-Henry et al., 2012). Furthermore, a handful of studies also indicated an absence of relationships between verbal memory/learning and the hippocampus subiculum (Haukvik et al., 2015), left posterior and right anterior hippocampus (Thoma et al., 2009) and temporal pole (Gur et al., 2000) in SSD patients that were in turn present and positive in direction in healthy comparison samples.

Other studies showed positive associations with verbal memory/learning in the patient group in the precuneus (Antonova et al., 2005) and parietal lobe (Andreasen et al., 2011), unique to SSD-patients. Negative associations were unique to the patient group were evident in the in the cerebellum (Toulopoulou et al., 2004) and subcortical structures such as left and right putamen (Hartberg et al., 2011b), and thalamus (Knöchel et al., 2016b).

Further, positive relationships were observed between verbal memory/learning and total grey matter volume in patients and healthy controls (Czepielewski et al., 2018; Gur et al., 1999), as well as total brain volume in a study analyzing SSD patients only (Andreasen et al., 2011). Conversely, some studies identified no relationship with total brain volume (Baaré et al., 1999) and total grey matter volume (Jirsaraie et al., 2018) in both patients and healthy controls, or across the entire brain in a study of only SSD (Roiz-Santiáñez et al., 2014).

Three studies examined the relationship between *cortical thickness* and verbal memory/learning in both SSD and healthy comparison groups. Positive associations were identified controls in the right middle and superior frontal gyrus, right insula cortex, right inferior and superior temporal gyrus (Hartberg et al., 2010) in both groups. In contrast, there was no association between verbal memory/learning and cortical thickness of the prefrontal cortex (Harms et al., 2010) or parahippocampal gyrus (Karnik-Henry et al., 2012) in either group.

Two studies also investigated verbal memory/learning and *cortical surface area*, but did not identify any relationship between the prefrontal cortex (Harms et al., 2010), right caudal middle frontal gyrus, or right fusiform gyrus (Hartberg et al., 2011a) in SSD patients. Notably, the relationships pertaining to the prefrontal cortex and right caudal middle frontal gyrus were present in healthy controls and were negative in direction.

1.2.5 *Visual Memory/Learning*

Eighteen studies examined the relationship between visual memory/learning and *volume* in established SSD. Visual learning was positively associated with volume of the right (Baaré et al., 1999) and total prefrontal cortex (Baaré et al., 1999; Premkumar et al., 2008) in both patients and healthy controls. A study by Antonova et al. (2005) observed a

positive relationship between inferior frontal gyrus volume and visual memory/learning performance in healthy controls, whilst this association was absent in their patient group.

In the temporal lobe, volume of both left and right anterior fusiform gyri were positively associated with visual memory/learning uniquely in patients in a fusiform region of interest study by Onitsuka et al. (2003), whilst an absence of association was observed with left and right posterior fusiform gyrus volume in the same sample of patients and healthy controls. Other positive associations with volume were evident in neighboring regions such as the left and right ventral temporal cortex, left entorhinal cortex, and right temporopolar cortex in SSD patients but not controls (Kumarasinghe et al., 2014). In contrast, Turetsky et al. (2003) found no association with volume of the entorhinal cortex, perirhinal cortex, and temporopolar cortex in either patients or healthy controls, whilst Gur et al. (2000) identified positive associations with volume in the temporal pole and superior temporal gyrus in healthy controls only. Wannan et al. (2018) identified a positive association unique to established SSD patients between hippocampal subfield volumes (CA4DG) and stratum, and visual memory/learning performance in patients. Conversely, a negative association was observed between right CA2CA3 volume and visual memory/learning performance in healthy controls and not patients.

Positive associations with visual memory/learning were also observed with the left posterior hippocampus in patients and healthy controls (Thoma et al., 2009) and left and right amygdala (Sachdev et al., 2000), total right and right lateral hippocampal volume uniquely in patients (Exner et al., 2008; Sachdev et al., 2000). A negative association unique to patients was also observed in the right anterior portion of the hippocampus (Thoma et al., 2009) and right amygdala volume (Killgore et al., 2009). Contrary to these findings, no association was found with right (Knöchel et al., 2014) or left hippocampal volume in either patients or healthy controls (Knöchel et al., 2014; Sachdev et al., 2000; Touloupoulou et al., 2004), or

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volume of the left anterior hippocampus in patients (Thoma et al., 2009). Notably, the relationship between left anterior hippocampal volume and visual memory/learning performance was present and positive in direction in healthy controls.

With respect to total hippocampal volume specifically, a positive association was identified in a sample of female SSD patients (Gur et al., 2000) and in a combined sample of males and females (Koshiyama et al., 2018), whilst no association was observed in either male patients (Gur et al., 2000) or in another combined patient sample (Premkumar et al., 2008). Notably, positive associations of visual memory/learning with total hippocampal volume were observed in the healthy control comparison samples in two studies (Gur et al., 2000; Premkumar et al., 2008). Positive associations were also identified in hippocampal subfield CA4 and the molecular layer in study analysing SSD-only (Nakahara et al., 2019).

In other subcortical regions, positive associations with visual memory/learning performance were observed with right thalamus volume (Koshiyama et al., 2018) uniquely in patients. Volume of the cerebellum was investigated in two studies, both of which found no association with visual memory/learning in SSD patients (Szeszko et al., 2003; Toulopoulou et al., 2004). Notably, Szeszko et al. (2003) observed a positive association with cerebellum volume in their healthy control sample.

In global analyses of volume, a study by Gur et al. (1999) identified a positive association between total grey matter volume and visual learning/memory uniquely in male patients; the opposite was observed in females, with a positive association absent in patients but present in healthy controls. No relationship between visual memory/learning and total brain volume in either patients or healthy controls was reported in a study by Baaré et al. (1999). Further, no studies investigated visual memory/learning in relation to either *cortical thickness* or *surface area*.

1.2.6 *Working Memory*

Twenty-two studies examined the relationship between working memory and *volume* in established SSD samples. In the frontal region, positive associations were observed with both left (Wojtalik et al., 2012) and right dorsolateral prefrontal cortex volume (Molina et al., 2009) in studies analyzing SSD but not healthy control samples. However, global estimates of dorsolateral prefrontal cortex volume were not associated with working memory in either SSD patients or healthy controls (Jirsaraie et al., 2018). One study indicated that the inferior and superior portions of the prefrontal cortex were positively associated with working memory uniquely in patients (Goghari et al., 2014), and another reported a positive association with total prefrontal cortex volume in both patients and healthy controls (Cannon et al., 2005). In contrast, a further study of only SSD patients did not observe a relationship of total prefrontal cortex volume and working memory (Harms et al., 2010).

A study by Szendi et al. (2006) observed a positive relationship between working memory and left middle frontal gyrus volume in patients, and a negative relationship in their healthy controls. Similarly, a study by Zuffante et al. (2001) also identified a negative association in their healthy control sample, however, no association was found in the SSD sample. Other findings pertaining to the frontal lobe and unique to SSD include positive relationships with medial frontal (Hidese et al., 2017) and left orbitofrontal cortex volume (Schobel et al., 2009), and a negative relationship with straight gyrus volume (Szendi et al., 2006). A further study found no relationship with inferior frontal gyrus volume in patients and healthy controls (Jirsaraie et al., 2018).

For global estimates of frontal volume, a negative association was observed in the left hemisphere uniquely in patients, whilst no relationship was observed in the right hemisphere in either patients or healthy controls (Garlinghouse et al., 2010). Lastly, Andreasen et al.

(2011) observed a positive relationship between working memory and total frontal lobe volume when analyzing a SSD-only sample.

In the temporal region, as positive relationship with temporal lobe volume was observed in a sample comprising only SSD patients (Andreasen et al., 2011). The anterior portion of the hippocampus was also found to be both positively (Herold et al., 2015) and negatively (Thoma et al., 2009) associated with working memory performance in patients, but not healthy controls. In the posterior portion, no relationship was observed in patients, whilst a positive relationship was identified in healthy controls (Thoma et al., 2009). With regards to total hippocampal volume, Herold et al. (2015) analyzed only SSD patients and identified a positive association. In contrast, Jirsaraie et al. (2018) observed no association of total hippocampal volume and working memory performance in either patients or healthy controls. A further study by Wolf et al. (2008) reported that inferior temporal gyrus volume positively correlated with working memory performance in patients but not healthy controls. Negative associations in a SSD-only study were also evident between working memory performance and temporal volume bilaterally (Garlinghouse et al., 2010).

In the parietal lobe, both left and right parietal lobe volume were not associated with working memory performance in either patients or healthy controls (Garlinghouse et al., 2010). Similarly, one study indicated no relationship with precuneus volume in SSD patients, although a negative association was observed in the healthy control sample (Antonova et al., 2005). In contrast, total parietal lobe volume was positively associated with working memory a sample of SSD-only in another study (Andreasen et al., 2011).

In subcortical regions, working memory performance was negatively associated with left, right, and total putamen volume (Hartberg et al., 2011b) and positively associated with volume of the cerebellum (Segarra et al., 2008), anterior cingulate (Hidese et al., 2017) and left posterior cingulate cortex (Liu et al., 2016) in SSD patients, but not healthy controls. In

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contrast left, right (Andrews et al., 2006), and total (Harms et al., 2007) thalamus volume was not related to performance in either patients or healthy controls.

In global analyses of volume, a positive association with working memory performance was found with total brain volume in a sample of SSD patients (Andreasen et al., 2011), whilst no associations with working memory in SSD were evident in relation to intracranial volume (Garlinghouse et al., 2010) and total grey matter volume (Jirsaraie et al., 2018; Spalletta et al., 2008). Of these studies, the only significant association in a healthy control sample was observed by Jirsaraie et al. (2018), who reported a positive correlation with total grey matter volume and working memory

Three studies investigated the association between working memory and *cortical thickness*, of which one also examined *cortical surface area*. Ehrlich et al. (2012) investigated thickness of the caudal middle, and rostral middle frontal gyri bilaterally, and found that while these regions were not significantly associated with working memory performance in SSD patients, they were positively associated in healthy controls. In a study by Harms et al. (2010), neither cortical thickness nor cortical surface area of the prefrontal cortex were associated with working memory performance in their SSD only sample. In the temporal lobe, Ehrlich et al. (2012) observed a positive association unique to patients with cortical thickness of the right middle and superior temporal gyrus. Finally, in global analyses, Pujol et al. (2013) identified a positive association between working memory performance and total cortical thickness.

1.2.7 Verbal Fluency

Two studies investigated verbal fluency and *volume* in established SSD patients. Andreasen et al. (2011) observed a positive association between verbal fluency and total parietal volume in a patient-only sample. Matsui et al. (2008) also reported positive

associations between semantic and subjective fluency, and inferior and orbitofrontal gyrus volume in patients. These were evident in the context of an absence of relationships between serial clustering and inferior frontal gyrus, and serial clustering and the straight gyrus. Only the relationship between the inferior frontal gyrus and semantic clustering in SSD patients was also evident in healthy controls, who in contrast, displayed a positive relationship between semantic fluency and the straight gyrus, and a negative relationship with subjective clustering. No studies investigated verbal fluency in relation to either *cortical thickness* or *surface area*.

1.2.8 Executive Function

Thirty studies examined the relationship between executive function and *volume*. In the frontal region, executive function performance in SSD patients was positively associated with left (Kumari et al., 2008) and total (Jirsaraie et al., 2018) dorsolateral prefrontal cortex volume, left (Seidman et al., 1994) and total (Baaré et al., 1999; Seidman et al., 1994) prefrontal cortex volume, left (Cobia et al., 2012; Ohtani et al., 2014), right (Cobia et al., 2012) and total inferior frontal gyrus volume (Jirsaraie et al., 2018), left middle frontal gyrus volume (Bonilha et al., 2008; Knöchel et al., 2016b) and right middle frontal cortex volume (Kumari et al., 2008). Further, two studies observed positive associations with left (Schobel et al., 2009) and right (Kumari et al., 2008) orbitofrontal cortex volume in patients only. These positive associations in the frontal region in SSD were also reflected in some of healthy control samples, specifically for associations with the dorsolateral prefrontal cortex, inferior frontal gyrus (Jirsaraie et al., 2018), and left middle frontal gyrus (Knöchel et al., 2016b); the remaining studies either found no association or did not include a healthy control sample. One study did not identify a relationship between executive function and prefrontal cortex volume in its SSD-only sample (Harms et al., 2010). Another study found no

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association between executive function and left or right middle orbitofrontal gyrus

(Nakamura et al., 2008) in SSD patients, although a relationship was present and positive in the healthy control group.

In the temporal region, positive associations were identified with left (Herold et al., 2015; Szeszko et al., 2002), right (Herold et al., 2015), and total (Schobel et al., 2009) anterior hippocampus volume as well as left, right (Herold et al., 2015; Sachdev et al., 2000) and total hippocampus volume (Jirsaraie et al., 2018), and left and right amygdala (Sachdev et al., 2000). With the exception of total hippocampus volume, these associations were not reflected in the healthy control samples of their respective studies. A study by Herold et al. (2015) analyzing a SSD-only sample observed positive associations between left and right posterior hippocampus volumes and executive function, while a study by Thoma et al. (2009) identified a negative association with left posterior hippocampus volume in their patient sample; no association was observed in this region in their healthy controls. Nestor et al. (2007) on the other hand, observed no relationship between executive function and left and right hippocampus volume in SSD patients, but identified a negative association between these regions and executive function in their healthy controls. However, positive associations with left and right parahippocampal (Nestor et al., 1993), total parahippocampal (Schretlen et al., 2010) superior temporal gyrus volume (Nestor et al., 1993), and total temporal lobe volume (Andreasen et al., 2011) were observed in studies consisting of SSD patients only. Conversely, another study observed no association between executive function and total temporal lobe or temporal pole volume in SSD patients (Premkumar et al., 2008), although associations in these regions were present in the healthy control sample.

In subcortical regions, studies have indicated positive associations between executive function and volume in the caudate (Andreasen et al., 2011), and putamen and thalamus (Andreasen et al., 2011) in SSD. In direct contrast to these findings, other studies have

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reported negative associations in the putamen bilaterally (Hartberg et al., 2011b) and no association in the thalamus (Harms et al., 2007). Of the studies which included healthy controls in their analyses (Harms et al., 2007; Hartberg et al., 2011b; Sachdev et al., 2000), none identified a relationship between executive function and volume.

Other findings regarding the relationship between executive function and volume in SSD patients suggest positive associations with right anterior cingulate, bilateral cingulate gyrus, left and right cerebellum, and occipital lobe volume (Schretlen et al., 2010), total parietal lobe volume (Andreasen et al., 2011), total parietal-occipital lobe volume (Sullivan et al., 1996), and Crus I and II volume (Kuhn et al., 2012). The majority of these findings are reported in studies that did not contain healthy control samples, and in those that did, the relationships were not observed in healthy individuals. In contrast to the findings pertaining to the cerebellum, one study by Szeszko et al. (2003) did not find an association between total cerebellum volume and executive function in its patient sample, but identified a positive association in its healthy control sample.

In analyses of global volume estimates, executive function was positively associated with total brain volume in three studies of SSD patients (Andreasen et al., 2011; Antonova et al., 2005; Seidman et al., 1994), whilst no association was found in another study in either patients or healthy controls (Baaré et al., 1999). A further study showed a negative association between total grey matter volume and executive function (Frascarelli et al., 2015), but there was also evidence of no relationship in others (Gur et al., 1999; Jirsaraie et al., 2018). Only two studies identified associations between global volume estimates, specifically total grey matter volume, and executive function in healthy controls (Gur et al., 1999; Jirsaraie et al., 2018).

Only four studies examined executive function and *cortical thickness* and *surface area* in established SSD. In the frontal lobe, positive associations were found with cortical

thickness of the right middle frontal gyrus (Ehrlich et al., 2012), right inferior frontal gyrus (Ehrlich et al., 2012; Hartberg et al., 2010), superior frontal gyrus (Hartberg et al., 2010) and pars opercularis (Knöchel et al., 2016a) in SSD patients. With regards to the prefrontal cortex, one study by Harms et al. (2010) found no relationship between executive function and either cortical thickness or surface area in their sample of SSD patients-only. In the temporal lobe, Hartberg et al. (2010) identified positive associations with cortical thickness of the right anterior superior temporal gyrus, left superior temporal gyrus, and left temporal pole, and these findings were also replicated in their healthy control sample. Relationships between executive function and cortical thickness or surface area of other brain regions were not examined or reported.

1.2.9 Intelligence/global cognition

Twenty-six studies of established SSD examined the relationship between premorbid or current intelligence/global cognition and *volume*. SSD-unique positive associations with current intelligence/global cognition were identified in areas including the left anterior and right inferior dorsolateral prefrontal cortex (Minatogawa-Chang et al., 2009), left dorsolateral prefrontal cortex (Keshavan et al., 2003), left orbitofrontal cortex (Schobel et al., 2009) and left and total prefrontal cortex (Seidman et al., 1994). A positive association was also observed between current intelligence/global cognition and volume of the inferior frontal gyrus in both SSD patients and healthy controls (Jirsaraie et al., 2018), while a single negative association unique to SSD patients was observed with volume of the right lateral dorsolateral prefrontal cortex (Minatogawa-Chang et al., 2009). Two further studies reported no association between current intelligence/global cognition and total dorsolateral prefrontal cortex volume in either patients or healthy controls (Jirsaraie et al., 2018), as well as the middle orbitofrontal gyrus in patients (Nakamura et al., 2008). In the latter study, the

relationship with the middle orbitofrontal gyrus was present and positive in direction in healthy controls.

In the temporal region and in SSD patients uniquely, a positive association between current intelligence/global cognition and brain volume was observed in the left anterior hippocampus (Schobel et al., 2009), whilst a negative association was identified in the right anterior hippocampus (Thoma et al., 2009). On both the left and right sides of the hippocampus, Flaum et al. (1994) identified a positive association with intelligence in their SSD-only sample. In contrast, a study by Touloupoulou et al. (2004) observed no relationship between left hippocampal volume and current intelligence/global cognition in patients, but did find a positive association in their healthy control sample. Similarly, a study by Nestor et al. (2007) found no relationship with the right side of the hippocampus in patients, however, they identified a negative association in healthy controls.

Two studies identified a positive association between total hippocampus volume specifically and current intelligence/global cognition in their SSD samples (Jirsaraie et al., 2018; Pujol et al., 2014), although only one study observed this positive association in their healthy control sample. In other hippocampus-related structures, the molecular layer was positively associated with current intelligence/global cognition in a SSD-only sample in one study (Nakahara et al., 2019), whilst no relationship was found with the hippocampus subiculum in either patients or healthy controls in another (Haukvik et al., 2015).

Two studies investigated parahippocampal volume in relation to current intelligence/global cognition. One found a negative association with right parahippocampal volume in a patient-only sample (Sanfilipo et al., 2002), whilst another found no association with left and right parahippocampal gyrus volume in patients, but negative associations with these regions in healthy controls (Minatogawa-Chang et al., 2009). Current intelligence/global cognition was also positively associated with both left (Cobia et al., 2012;

Minatogawa-Chang et al., 2009) and right (Keshavan et al., 2003) hemispheres of the superior temporal region in patients only. A study by Gur et al. (2000) observed no relationship between intelligence and volume of the temporal pole in patients, however, a positive association was found in the healthy control sample. Finally, a positive association was observed with left temporal lobe volume in study of SSD patients only (Flaum et al., 1994), while another study reported no relationship with the temporal lobe as a whole in either patients or healthy controls (Di Michele et al., 1992).

In the cingulate cortex, no association between current intelligence/global cognition and volume of the anterior cingulate or right anterior dorsal cingulate gyrus was evident in patients (Fujiwara et al., 2007), however the latter association was present and positive in healthy controls (Minatogawa-Chang et al., 2009). Across the brain, positive associations were observed in the insula cortex in both patients and healthy controls (Caldiroli et al., 2018), the lateral parietal cortex in patients uniquely (Minatogawa-Chang et al., 2009), and in the left putamen in study of only SSD-patients (Flaum et al., 1994). In the cerebellum, two studies identified a positive association with volume and current intelligence/global cognition unique to patients (Flaum et al., 1994; Keshavan et al., 2003), whilst another observed no relationship in either patients or healthy controls (Szeszko et al., 2003).

In analyses of global brain volume, total grey matter volume was found to be positively associated with current intelligence/global cognition in both patients and healthy controls in one study (Jirsaraie et al., 2018) and in patients only in another (Sullivan et al., 1996). In contrast, a positive relationship between current intelligence/global cognition and intracranial volume was found to be unique to healthy controls in a study by Thoma et al. (2009). A single longitudinal study by Kubota et al. (2015) showed no relationship between current intelligence and global measures of volume at baseline. However, a positive association of current intelligence and total cortical volume was observed after four years.

In regards to premorbid intelligence, one study indicated a positive association with total grey matter volume in patients uniquely (Antonova et al., 2005), but another indicated no association with total brain volume in either patients or healthy controls (Baaré et al., 1999). In a study by Gur et al. (1999), language ability was positively associated with total grey matter volume in both patients and healthy controls, while non-verbal intelligence was positively associated with total grey matter uniquely in male SSD patients, and positively associated with total grey matter volume in both male and female healthy controls.

Two studies of established SSD also investigated *cortical thickness* and one *surface area* in relation to premorbid and current intelligence in established SSD. In the cross-sectional study, Hartberg et al. (2010) observed a positive association between premorbid intelligence and cortical thickness of the left inferior and middle frontal gyrus, right middle and superior frontal gyrus, right temporal lobe, right temporo-occipital gyrus, left middle occipital gyrus, and right insula cortex in both SSD patients and controls. Positive associations of the left middle occipital gyrus and right temporo-occipital gyrus were also evident in healthy controls but not patients in this study. In contrast, Kubota et al. (2015) reported no association at baseline with current intelligence and cortical thickness and surface area in SSD patients across the entire brain in a longitudinal study. However, after four years, a positive association with total cortical thickness emerged, and was found to be unique to SSD patients.

1.3 Recent-onset bipolar disorder (RO-BD)

Five studies investigated the relationship between cognition and brain morphology in RO-BD; of which four were cross-sectional.

1.3.1 Attention

A single study examined attentional performance and *cortical thickness* in RO-BD patients; thickness of the parietal lobe, specifically in the left intraparietal sulcus, left posterior angular gyrus, and right supramarginal gyrus, was positively associated with performance in a sample analyzing correlations in only patients (Hatton et al., 2013). No other studies investigated either *volume* or *surface area*.

1.3.2 *Speed of Processing*

Only one study analyzing correlations in only patients investigated speed of processing and *cortical thickness*; a positive association was identified in the right parieto-occipital sulcus (Hatton et al., 2013). No other studies investigated either *volume* or *surface area*.

1.3.3 *Verbal Memory/Learning*

Two studies investigated verbal memory/learning and morphology in RO-BD; positive correlations were observed with *volume* of the right medial frontal gyrus in patients only, whilst negative associations were identified in the left superior frontal gyrus in patients only, and in the right inferior frontal gyrus in patients and healthy controls (Chakrabarty et al., 2015). In the temporal lobe, negative associations were observed with left and right hippocampal volume in patients, and positive associations with left hippocampal volume in healthy controls (Chakrabarty et al., 2015). Regarding *cortical thickness*, Hatton et al. (2013) reported positive associations with the right superior temporal gyrus, left intraparietal sulcus, and right supramarginal gyrus in correlational analyses of patients-only.

1.3.4 *Executive Function*

Three studies examined executive function in RO-BD, each examining volume, cortical thickness, or cortical surface area respectively. Bilateral caudate *volume* was negatively correlated with executive function in RO-BD patients, and positively in healthy controls in one study (Kozicky et al., 2013). Another study that did not include healthy controls in their analyses identified a positive association with the right supramarginal gyrus *thickness* in RO-BD (Hatton et al., 2013). The third study identified a positive association with postcentral *surface area* in both RO-BD patients and healthy controls (Jalbrzikowski et al., 2019).

1.3.5 Intelligence/global cognition

One study investigated full scale IQ and *volume* in RO-BD; total grey matter volume was positively associated in both patients and healthy controls after a five year follow up period—a relationship notably absent at baseline (Thompson et al., 2001). No studies have investigated *cortical thickness* or *surface area* in a RO-BD sample.

1.4 Established bipolar disorder (BD)

Eighteen studies investigated the relationship between cognition and brain morphology in established-BD; all of which were cross-sectional.

1.4.1 Attention

A single study by Sax et al. (1999) investigated attention and *volume* in established BD. Total prefrontal cortex and hippocampal volume were positively correlated with attentional performance, while no significant relationship was observed in the subcortical volumes of the caudate and thalamus. These associations were unique to the BD patients, and

not observed in healthy controls. No studies investigated attentional performance in relation to either *cortical thickness* or *surface area*.

1.4.2 *Speed of Processing*

A single study by Hartberg et al. (2011a) investigated speed of processing in established BD, and their study identified a positive association with *cortical surface area* of the inferior temporal region. This relationship was unique to the BD patients, and not evident in healthy controls. No studies investigated speed of processing in relation to either *volume* or *cortical thickness*.

1.4.3 *General Memory*

Two studies examined the relationship between general assessments of memory and *volume* in established BD. These found a positive association between left amygdala volume and general memory in patients only (Killgore et al., 2009), and no association with whole brain volume in either patients or healthy controls (Moorhead et al., 2007). No studies investigated general memory in relation to either *cortical thickness* or *surface area*.

1.4.4 *Verbal Memory/Learning*

Six studies examined verbal memory/learning and *volume* in established BD. In the temporal lobe, Knöchel et al. (2014) reported positive associations with right hippocampal volume, whilst no association was observed with left hippocampal volume. Furthermore, a positive association with hippocampal subiculum volume was reported (Haukvik et al., 2015), as was an absence of an association with total hippocampal volume (Cao et al., 2016). The association with total hippocampal volume was unique to patients, and the finding pertaining to the hippocampus subiculum, and left and right hippocampal volume were

positively associated in healthy controls. In the left amygdala, a positive association with verbal memory/learning was identified in BD patients, and not in healthy controls. Lastly, there was no evidence for relationships between verbal memory/learning and global measures such as whole brain volume (Bruno et al., 2006) and total grey matter volume (Sarnicola et al., 2009). Regarding global measures, only the study by Sarnicola et al. (2009) analyzed a healthy control sample, with similar findings to their patient sample. No studies examined *cortical thickness* or *surface area* in relation to verbal memory/learning.

1.4.5 Visual Memory/Learning

Across the four studies examining visual memory/learning in established BD, there was no evidence of an association with *volume, thickness or surface area*. Specifically, three studies indicated no association of visual learning/memory and volume of the bilateral hippocampus (Knöchel et al., 2014), total grey matter volume (Sarnicola et al., 2009), volume of any brain region (Bruno et al., 2006). No associations of the frontal or other temporal lobe regions were evident across measures of volume, cortical thickness, and cortical surface area in the fourth study (Gutierrez-Galve et al., 2012). Only the studies by Knöchel et al. (2014) and Sarnicola et al. (2009) included healthy controls in their analyses, and the relationships between bilateral hippocampal volumes and total grey matter volume were also not significant in their healthy controls.

1.4.6 Working Memory

Four studies have investigated working memory performance in established BD. Shi et al. (2018) identified positive associations with both right hippocampal *volume* and left parahippocampal gyri *surface area*, uniquely in patients. Cho and Goghari (2020) reported positive associations with *thickness* of the caudal middle, rostral middle, and superior regions

of the frontal lobe, similarly absent in healthy controls. In global analyses, Sarnicola et al. (2009) found no relationship with total grey matter in either BD patients or healthy controls, while Bruno et al. (2006) found no associations in any brain region in their analysis of a BD-only sample.

1.4.7 Executive Function

Seven studies of established BD examined executive function and *volume*. Specific frontal and temporal structures such as the left inferior orbitofrontal cortex (Chung et al., 2013) and right hippocampus (Shi et al., 2018) were positively associated with executive function. In contrast, no associations between executive function and volume were observed in analyses of broader measures including total frontal and temporal volume (Gutierrez-Galve et al., 2012), and in global analyses of total grey matter volume (Sarnicola et al., 2009) or in any region across the entire brain (Bruno et al., 2006). It should be noted that of these studies, only that of Sarnicola et al. (2009) included healthy controls in their analyses, to which they found no association between executive function and total grey matter volume in healthy controls. Additionally, left insula volume was significantly positively correlated with executive function uniquely in BD patients (Matsubara et al., 2016).

Three studies of established BD examined the relationship between *cortical thickness* and executive function. Positive associations have been observed for thickness of the inferior prefrontal cortex and right medial superior frontal cortex in both BD patients and healthy controls. Further, positive associations with cortical thickness in both lateral prefrontal and right medial superior frontal cortices were also observed, albeit in patients only (Abé et al., 2018). Other regions positively associated with BD patients—and not with healthy controls—include the medial occipital cortex (Abé et al., 2018) and left superior temporal gyrus (Oertel-Knochel et al., 2015). Conversely, a positive association unique to healthy controls

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was observed with the right precuneus (Oertel-Knochel et al., 2015). As with volume, broader assessments of cortical thickness such as total frontal and temporal thickness were not associated with executive function (Gutierrez-Galve et al., 2012).

Two studies investigated the relationship between executive function and *surface area*. Gutierrez-Galve et al. (2012) did not find an association with total surface area of the frontal and temporal lobes. In contrast, Shi et al. (2018) reported a positive relationship in the left parahippocampal gyrus. As mentioned previously, neither of these studies included healthy control samples in their analyses.

1.4.8 *Intelligence/global cognition*

Seven studies examined premorbid or current intelligence/global cognition and *volume* in established BD. Positive associations were observed with cerebellum and temporal lobe volume in both patients and healthy controls (Moorhead et al., 2007). In contrast, a collection of studies observed no relationships with volumes of the amygdala, thalamus, hippocampus subiculum and total hippocampus (Frazier et al., 2005; Haukvik et al., 2015), as well as total frontal, total temporal, total grey matter (Sarnicola et al., 2009) and whole brain volume (Gutierrez-Galve et al., 2012; Minatogawa-Chang et al., 2009). Similarly, there were no significant relationships between current intelligence and frontal or temporal lobe *cortical thickness* and *surface area* in a study of only BD-patients (Gutierrez-Galve et al., 2012), although this study showed a positive relationship between premorbid IQ and total frontal surface area (Gutierrez-Galve et al., 2012). Of the studies mentioned, only that by Moorhead et al. (2007) included a healthy control group in their analyses.

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