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Resting regional brain activity correlates of verbal learning deficit in major depressive disorder

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ABSTRACT

Memory deficits are reported in major depressive disorder (MDD). Prefrontal cortical and mesiotemporal cortical (MTC)/subcortical regions are involved in the Buschke Selective Reminding Task (SRT), a verbal list-learning task. To determine whether depression-related changes in resting brain metabolism explain (in part) the deficits in SRT performance found in MDD, statistical correlation maps were calculated between SRT total recall score (TR) and relative regional cerebral metabolic rate for glucose (rCMRglu), measured by [^{18}F]-flourodeoxyglucose (FDG) positron emission tomography (PET), in unmedicated, depressed MDD patients (*N = 29*). Subsequently, to explore hypothesized loss of top-down control in MDD, we compared the correlations between rCMRglu of SRT-relevant regions of the dorsolateral prefrontal cortex (dlPFC) and amygdala in a larger cohort of MDD (*N = 60; 29 inclusive*) *versus* healthy controls (HC) (*N = 43*). SRT performance of patients is on average 0.5 standard deviation below published normative mean. TR and rCMRglu *positively* correlate in bilateral dorsomedial PFC, dlPFC, dorsal anterior cingulate; *negatively* correlate in bilateral MTC/subcortical regions, and cerebellum. rCMRglu in dlPFC correlates negatively with that in amygdala in HC but not in MDD. Depression-related changes present in FDG-PET measured resting brain activity may be in part responsible for memory deficit found in MDD.

1. Introduction

Verbal learning deficits have been reported in major depressive disorder (MDD) (Baune et al., 2010; Boeker et al., 2012; Kaneda, 2009; Marvel and Paradiso, 2004). These deficits have been observed in free recall (Taconnat et al., 2010), paragraph recall (Zubieta et al., 2001) and word list recall (Austin et al., 1992; Gourovitch et al., 1999; Paradiso et al., 1997; van Gorp et al., 1999); non-declarative memory appears to be unaffected (Ilsley et al., 1995). Verbal learning deficits in depression are not fully explained by attentional deficits, motor slowing (Hermens et al., 2010; Snyder, 2013), or insufficient effort (Christensen et al., 1997; Kindermann and Brown, 1997), potentially indicating that deficits in episodic verbal memory processes are, at least in part, independent of other cognitive and affective symptoms in MDD (Gruber et al., 2011).

Neuroimaging studies suggest that MDD is associated with brain-wide, anomalous resting state brain activity, thought to reflect the state of dysfunctional brain networks involved in affect and cognition (Diener et al., 2012; Dutta et al., 2014; Murray et al., 2011; Palmer et al., 2014). We have previously shown that depression severity correlates *negatively* with resting relative regional cerebral metabolic rate for glucose (rCMRglu) in cortical regions, such as the dorsolateral prefrontal cortex (dlPFC), but *positively* with rCMRglu of subcortical and mesiotemporal regions, such as the hippocampus and amygdala, in severely depressed MDD patients (Milak et al., 2005; Palmer et al., 2014). This is in agreement with the top-down disconnectivity model of MDD, which posits that depression symptomatology is related to a ``loss of control" of hypoactive cortical regions over hyperactive, subcortical ones (Mayberg, 1997; Mayberg et al., 1999).

Certain dimensions or components of clinical psychopathology as identified by factor analysis of the Hamilton Depression Rating Scale (HDRS) or the Beck Depression Inventory (BDI) correlate with rCMRglu

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in unique brain regions specific to each of those above-mentioned dimensions, suggesting that resting rCMRglu is associated with dimensions of MDD psychopathology in a regionally specific manner (Milak et al., 2010b, 2005).

Few studies, however, have specifically examined regional brain metabolic correlates of depression-related deficits in verbal learning, or how depression-related metabolic changes may be related to the severity of memory and learning deficit (Harper et al., 2017; Ottowitz et al., 2010; Shan et al., 2017). Systematic evaluation of the brain for resting rCMRglu correlates of memory performance deficit severity in MDD, as well as the interregional rCMRglu correlations among these regions in healthy volunteers vs. depressed MDD patients (Korgaonkar et al., 2012), should help identify the structures and their functional connections where depression-related activity interferes with verbal learning performance.

Therefore, we sought to (1) identify the resting rCMRglu correlates of the cognitive deficit captured by the Buschke Selective Reminding Task (SRT) (Buschke, 1973; Buschke and Fuld, 1974), a 12-trial, verbal list-learning task that is sensitive to memory deficit in depression (Keilp et al., 2001; Zakzanis et al., 1998), in medication-free, DSM-IV MDD patients; (2) examine the correlations between rCMRglu from SRT-related cortical and subcortical regions of interest (ROIs) in a larger group of MDD patients, and compare to the correlation of the same regions in healthy control (HC) subjects.

2. Methods

2.1. Subjects

A total of 60 MDD and 43 HC, aged 18 to 60 years old, male and female subjects underwent [^{18}F]-flourodeoxyglucose ([^{18}F]-FDG) positron emission tomography (PET). Data from a subgroup of 29 MDD subjects who had both PET and SRT were used for the correlation analysis between rCMRglu and SRT Total Recall (TR) score detailed in *Image Analysis*. We have previously published data from subgroups of this cohort (Anderson et al., 2004; Kegeles et al., 2003; Milak et al., 2010, 2005; Nobler et al., 2001; Oquendo et al., 2005, 2003).

All MDD subjects were diagnosed with the Structured Clinical Interview for DSM-IV, Patient version (SCID-P) (Williams, 1992) and scored 16 or more on the 17-item HDRS (Hamilton, 1960, 1967) at screening. Participants provided written informed consent as approved by the local Institutional Review Board. Depression severity was assessed using the 24-item HDRS and BDI. Demographics, past psychiatric and medical histories, and developmental and family histories were recorded on the Columbia Baseline Demographic Form. Subjects in the HC group were administered the Non-Patient version of SCID (SCID-NP) to confirm their eligibility as healthy volunteers. Subjects were excluded if one or more of the following criteria was recorded in their history, physical exam and/or laboratory tests; medical condition(s) deemed to be active and clinically significant (e.g., likely to be the cause of symptoms or laboratory abnormalities at the time of enrollment), presence of metal implants, being unable to provide a consent; meeting SCID-IV criteria for eating disorders and/or substance abuse in the 2 months before enrollment, substance dependence in the 6 months before enrollment, any history of mania or hypomania, primary psychotic disorder or major depressive episode (MDE) with psychotic features (see Table 1 for additional characteristics of sample).

Because antidepressants are known to impact resting brain metabolism (Bellani et al., 2011), patients underwent a minimum of 14 days of psychotropic medication washout (6 weeks in the case of fluoxetine and one month in the case of oral antipsychotics), with the exception of lorazepam. Patients were allowed up to 3 mg daily of lorazepam during the washout period, except in the three days prior to PET scanning. In practice, no patient received lorazepam for at least 9 days prior to scanning.

2.2. Memory assessment

A standard 12-word, 12-trial version of the SRT with a delayed free recall 30 min after the conclusion of the learning phase was administered to the subgroup of 29 depressed MDD subjects. The SRT differs from other list-learning tasks in that subjects are only ``selectively reminded" of words that they did not recall after each learning trial (other tasks present the full list on every trial). This increases the demand to actively encode the words recalled on each trial—since they will not be repeated on the subsequent trial in the reminding procedure—and makes the task sensitive to these encoding failures.

The SRT was administered 1-3 days prior to imaging, when all subjects were free of psychotropic medication. Scores for TR, Long Term Storage (LTS), Long Term Retrieval (LTR), Short Term Retrieval (STR), Consistent Long Term Retrieval (CLTR), Delayed Recall (DR) and Intrusion (INTR) were recorded and adjusted for standard sex effects. They were converted to *z*-scores based on published age-adjusted norms (Spreen and Strauss, 1998) prior to statistical analyses.

Cognitive ability, reaction time and processing speed were evaluated with Choice Reaction Time (CTR), Weschsler Adult Intelligence Scale (WAIS) – Digit Symbol and Trail Making Parts A and B.

2.3. PET studies

Imaging acquisition details have been described previously (Milak et al., 2005). A bolus injection of approximately 370 MBq [^{18}F]-FDG was administered intravenously. Subjects gazed at crosshairs in a dimmed, quiet room during the first 15 min following [^{18}F]-FDG injection. They then rested quietly for another 15 min before moving to the scanner, where the head was positioned so that the lowest scanning plane was parallel to and approximately 1.0 cm above the canthomeatal line. A Siemens ECAT Exact 47 scanner (in plane spatial resolution 5.8 mm, axial resolution 4.3 mm full width at half maximum at center) was used to acquire a 60 min emission scan in 2D mode in a series of twelve 5 min frames beginning about 45 min after tracer injection. An attenuation map was obtained from a 15 min ^{68}Ge/^{68}Ga transmission scan. Images were reconstructed with a Shepp radial filter, cutoff frequency of 35 cycles per projection rays and a ramp axial filter cutoff frequency of 0.5 S.

2.4. Image analysis

The 12 PET frames were aligned using Automated Image Registration (Woods et al., 1998) and summed. Statistical analysis was performed using Statistical Parametric Mapping (SPM12) (Institute of Neurology, University College of London, UK) implemented in Matlab 2015 (Mathworks Inc., USA) (Friston and Robert, 1994). The summed reconstructed frames were spatially normalized into the MNI (Montreal Neurological Institute, McGill University, CA) standard template to remove the inter-subject variabilities in anatomy and head positioning (Worsley et al., 1995). Spatially normalized images were smoothed by convolution with an isotropic Gaussian kernel of 12 mm to increase the signal-to-noise ratio and to accommodate the subtle variations in anatomical structures. The effects of global uptake were controlled by normalizing the counts in each voxel to the total gray matter counts in the brain (proportional scaling in SPM).

To determine the regions where brain activity correlates with performance on the SRT, a voxel-level correlation analysis between SRT total recall score and rCMRglu in the sample of 29 MDD patients was performed using the general linear model. Height threshold was set *a priori* to $p < 0.01$ and the extent threshold was set to $p < 0.05$ after Family Wise Error (FWE) correction for multiple comparisons by SPM. Stereotaxic coordinates reported are in Talairach Atlas (Talairach et al., 1988) coordinates, converted from MNI coordinates (Brett et al., 1999; Calder et al., 2001; Duncan et al., 2000). Identical height threshold, extent threshold, and statistical correction routine in SPM were used in

the analysis between the rate of verbal list-learning and rCMRglu.

To examine depression-related failure of top-down control, resting rCMRglu averages of the dlPFC were correlated with that of the amygdalar in depressed MDD ($N = 60$, including the SRT subgroup) *and compared to correlations between the same ROIs in* HC subjects ($N = 43$). The ROIs are comprised exclusively of voxels where rCMRglu correlates with TR within atlas-based anatomical limits of the dlPFC and amygdala, two structures selected *a priori* due to their posited relationship and role in memory and its deficits in depression. Anatomical limits were defined using the Wake Forest University Pickatlas and the Tailarach Daemon database (Ardekani et al., 2005; Duvernoy et al., 1991; Kates et al., 1997; Killiany et al., 1997; Klein et al., 2009; Maldjian et al., 2004, 2003; Talairach et al., 1988). All operations were conducted in SPM12, including extraction of rCMRglu averages from ROIs. Control ROIs were identical in coordinates and voxel count to those of the MDD group. Partial correlation analysis between the log-transformed rCMRglu average of each ROI (which met criteria for normality of distribution as indicated by the Kolmogorov-Smirnov test) was performed in IBM SPSS Statistics for Macintosh, Version 24.0, controlling for age.

3. Results

3.1. SRT performance in the depressed MDD (N = 29)

In patients administered the SRT, mean performance on the subscales of the SRT (expressed as *z*-scores) is approximately 0.5 of a standard deviation below normative data (Spreen et al., 1998) (Fig. 1): TR: −0.55; STR: −0.44; LTS: −0.34; LTR: 0.15; CLTR: −0.53; DR: −0.66; INTR: 0.64. The subscale scores of the SRT correlate highly with one another and with TR. They yield regional patterns of correlations with rCMRglu similar to that of TR in our sample (Spreen et al., 1998; Strauss et al., 2006; Westerveld et al., 1994). Depression severity, as measured by the BDI total score, but not as measured by the HDRS, correlates with TR ($R^2 = 0.167$, $df = 1,25$, $p = 0.035$ and $R^2 = 0.229$, $df = 1,25$, $p = 0.241$, respectively).

There is no correlation between TR and CRT ($p = 0.185$), WAIS-DS ($p = 0.210$), TMA ($p = 0.081$), or Trail Making Part B ($p = 0.263$) in this sample.

3.2. Prefrontal cortical rCMRglu correlations with Total Recall in depressed MDD (N = 29)

Two clusters of 2903 and 3499 contiguous voxels are identified where rCMRglu correlates *positively* with TR (cluster level $p = 0.027$ and 0.012 after FWE by SPM12; $R^2 = 0.54$ and 0.37 at the clusters' local maxima: −52, 4, 46 and 38, 4, 54 Talairach (*x, y, z*) coordinates, respectively; Fig. 2, Supplementary Figs. 1A and B). These clusters are located in frontal brain regions: bilateral inferior frontal gyrus, middle frontal gyrus, precentral gyrus, medial frontal gyrus, superior frontal gyrus (approximate Brodmann areas (BA): 6, 8, 9, 32, 46), and left middle frontal gyrus (BA: 6, 8, 9), extending bilaterally into the anterior cingulate (BA: 32). Prefrontal correlations of TR and rCMRglu survive the removal of the variance of TR explained by HDRS from TR, but not the removal of the variance explained by BDI.

3.3. Mesiotemporal and subcortical rCMRglu correlations with Total Recall in depressed MDD (N = 29)

A single cluster of 14033 contiguous voxels was identified where rCMRglu correlates *negatively* with TR (cluster level $p < 0.0001$, $R^2 = 0.51$; local maximum at Talairach (*x, y, z*) coordinates −22, 8, 2; Fig. 2 and Supplementary Fig. 1C, after FWE by SPM12). This cluster (BA: 3) includes mostly ventral temporal lobe and subcortical structures, such as bilateral mesiotemporal cortex (amygdala, hippocampus, BA: 20, 28, 34, 35, 36, 37), hypothalamus, and parts of cerebellum.

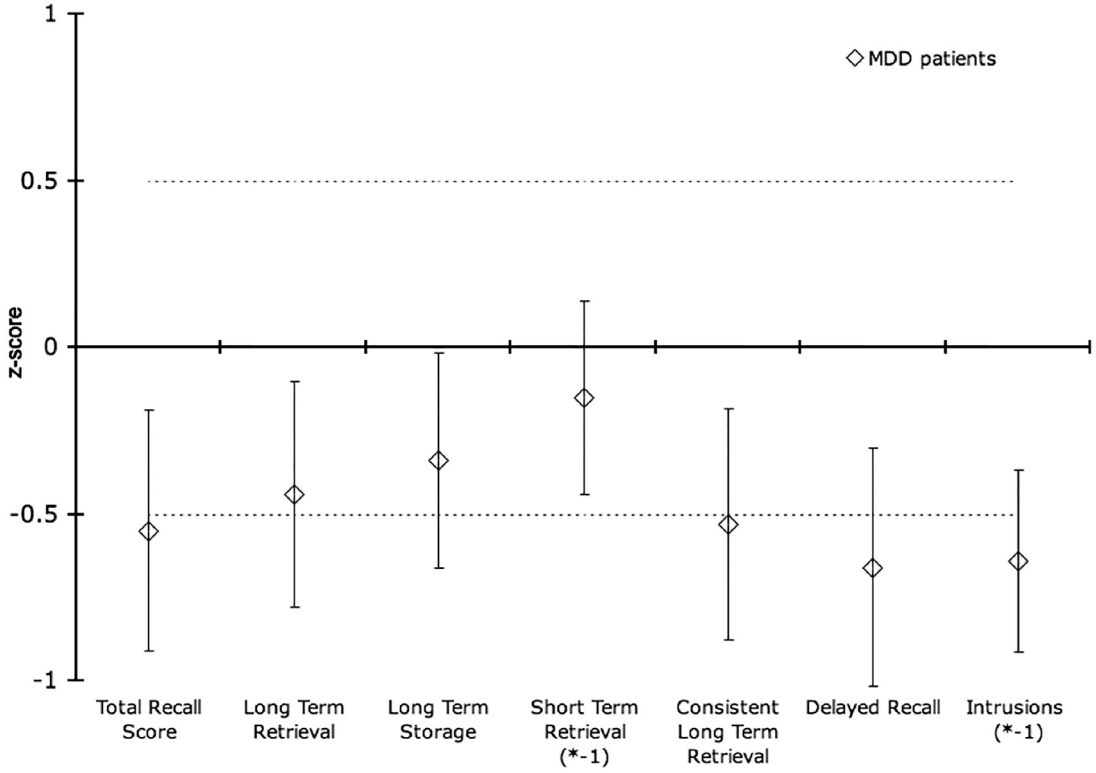

Fig. 1. Mean performance of major depressive disorder (MDD) subjects on subscales of the Buschke Selective Reminding Task (SRT), expressed as *z*-scores. (*−1): denotes variables, where errors are originally positively scaled, multiplied here by −1 for consistency with the other variables, worse performance depicted as more negative. Dotted lines are 0.5 of a standard deviation from the mean; error bars depict the standard error of the mean.

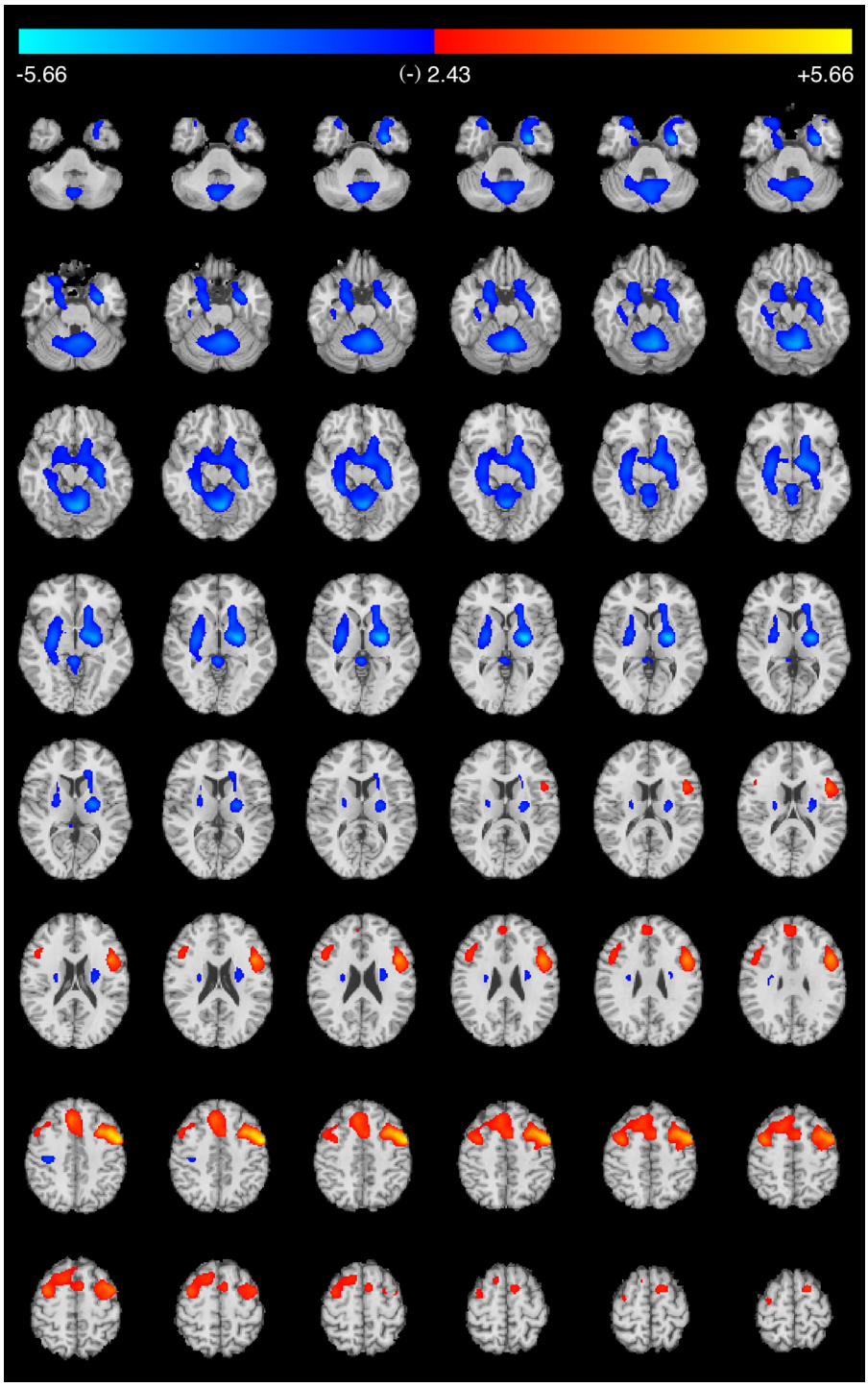

Fig. 2. A map of correlations between relative regional cerebral metabolic rate for glucose (rCMRglu) in major depressive disorder (MDD) subjects at rest, measured using positron emission tomography (PET), and Buschke Selective Reminding Task (SRT) Total Recall score (TR), computed as *z*-scores, or the rate of verbal list-learning. The color scales in the figure indicate the strength (*t* score) of the correlation (*t* score maps are overlaid on a series of transaxial slices (2 mm apart) of a coregistered MRI scan from 38 mm below to 72 mm above the line connecting the anterior and posterior commissure). Red to yellow regions are uniquely positively correlated with SRT TR; blue to light blue regions are uniquely negatively correlated with SRT TR. *t* score maps were thresholded at $p = 0.05$, after Family Wise Error (FWE) correction. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Mesiotemporal/subcortical correlations of TR and rCMRglu survive the removal of the variance of TR explained by HDRS from TR, but not the removal of the variance explained by BDI.

3.4. Metabolic inter-correlations between an a priori selection of ROIs in MDD (N = 60, 29 inclusive) and in healthy controls (N = 43)

In the healthy comparison group, rCMRglu in the right amygdala correlates negatively with rCMRglu in left and right dlPFC (top-down control; see Discussion) ($r = -0.41$, $df = 40$, $p < 0.01$; $r = -0.40$, $df = 40$, $p < 0.01$, respectively). In our MDD sample, these correlations cannot be found (a loss of top-down control) ($r = -0.23$, $df = 57$, $p = 0.08$; $r = -0.07$, $df = 57$, $p = 0.59$, respectively).

4. Discussion

We have previously reported that higher depression severity predicts lower resting rCMRglu in dorsal prefrontal cortex, and predicts higher rCMRglu in subcortical regions (Milak et al., 2010, 2005). Here we report that depression severity-related decreases in resting rCMRglu of prefrontal cortical regions predict worse performance on the SRT. Our findings are consistent with studies suggesting that a deficit in memory performance in depression is related to those components of verbal learning that are thought to be subserved by prefrontal cortical

regions (Takeda et al., 2013), for example the demands on working memory made by these tasks (George et al., 1994), and/or the initiation of recall strategies (Nitschke et al., 2004; Taconnat et al., 2010).

We find that depression severity-related increases in resting rCMRglu in mesiotemporal and subcortical regions also predict poorer performance on the SRT in these unmedicated depressed MDD patients. This is in contrast with positive correlations reported in resting state studies of memory performance in other disease states (Keilp et al., 1996; Teipel et al., 2006) or in task-based fMRI studies (Buckner et al., 2000; Wagner et al., 1998). One possible explanation for this difference is that higher relative mesiotemporal and subcortical (as well as lower relative prefrontal cortical) resting activity are results of the pathophysiology of MDD and interfere with learning and memory processes in these parts of the brain (Buckner et al., 2000; Wagner et al., 1998).

4.1. Prefrontal cortical correlations

The SRT is a list learning task that relies on working memory (Jacobsen, 1935; Jacobson et al., 1935), mnemonic storage and rehearsal processes (Awh et al., 1996; Awh et al., 1995) and extra-mnemonic ``executive control" processes (D'Esposito et al., 2002; Postle et al., 1999) including: shifting attention (Garavan, 1998), gating irrelevant stimuli (Chao and Knight, 1995), suppressing inappropriate responses (Diamond, 1988; Roberts et al., 1994), resolving interference between competing stimuli (May et al., 1999; Postle et al., 1999), selecting among competing responses (Thompson-Schill et al., 1997), and maintaining and refreshing information (D'Esposito et al., 2002; Johnson, 1992). Left mid-ventrolateral prefrontal cortex (Badre et al., 2005) also has a role in learning, especially semantic retrieval, and in selecting from competing items stored in working memory. All of these operations are involved in the performance of the SRT. Resting brain activity in dlPFC correlates with depression severity and likely contributes to the functional deficits of depressed patients on various aspects of the SRT, insomuch as this difference in resting state activity could be detracting from task-relevant processes conducted by the dlPFC and other brain regions involved in the performance of the SRT.

4.2. Mesiotemporal cortical correlations

Resting rCMRglu in structures in the left and right mesiotemporal cortices (i.e., amygdala, hippocampus and parahippocampal gyrus) correlates negatively with TR in this sample. SRT performance is known to be affected by temporal lobe abnormalities (Dietsche et al., 2014; Lee et al., 1989; Lee et al., 1990; Lencz et al., 1992; Levin et al., 1982; Martin et al., 1988; Snow et al., 1992). Most studies (cited above) of the neural correlates of memory find that activity (recorded *during* task performance) in mesiotemporal regions is positively correlated with performance of verbal learning tasks in healthy individuals. Taken together, these findings suggest that the correlation pattern found in *resting* brain activity of MDD patients is a product of depressive pathophysiology and likely contributes to the reduced adaptive and functional capacity of these brain regions leading to lower SRT scores.

4.3. Subcortical correlations

We find that higher resting rCMRglu in subcortical regions correlates with lower TR. ``Basal ganglia" disorders are associated with deficits in recall and decreased use of clustering strategies in recall (Butters et al., 1986; Taylor et al., 1990). It is known that disease of the basal ganglia and associated nuclei impairs performance on implicit sequence learning tasks (Doyon et al., 1997; Ferraro et al., 1993; Helmuth et al., 2000; Jackson et al., 1995; Knopman and Nissen, 1991; Pascual-Leone et al., 1993; Sommer et al., 1999; Willingham and Koroshetz, 1993). Human (Poldrack et al., 1999) and animal experimental work (Packard and McGaugh, 1996), as well as theoretical computational models (Ashby et al., 1998), indicate that there is competition between the implicit and declarative learning systems (medial temporal cortex and neostriatum) (Knowlton et al., 2002). Heightened activation in subcortical nuclei may reflect competition between these memory systems, which could be detrimental to memory processes.

4.4. Cerebellum correlations

We find that higher activity in the cerebellar region correlates with lower TR but the basis for this relationship is unclear. Increased activity in the cerebellum is reported during verbal learning and memory tasks (Andreasen et al., 1995; Chein and Fiez, 2001; De Smet et al., 2013; Fu et al., 2003; Li et al., 2004; Neau et al., 2000; Raichle et al., 1994). A small cohort of patients with cerebellar damage had worse verbal working memory symptoms than spatial memory ones (Ravizza et al., 2006). PFC and/or global neocortical function impairment (Block et al., 2002; Crespo-Facorro et al., 2001) increases activation in the cerebellum during list-learning tasks. Higher resting activity in the cerebellum could reflect differential recruitment of certain brain areas in depression, perhaps to mitigate the effect of MDD (a compensatory mechanism) (Guo et al., 2013).

4.5. Relationship between verbal learning and depression severity

We find that there is only a modest shared variance (16%) between verbal learning deficit and depression severity as measured by BDI, but not by HDRS, consistent with the literature on neurocognitive deficits in depression (Lee et al., 2012; Parlar et al., 2017; Rock et al., 2014). Even though the shared variance between TR and rCMRglu (54%, 37%, 51%) reaches much higher values, at least at local maximas, than that between verbal learning deficit and depression severity, the correlations between TR and rCMRglu do not survive corrections for the variance shared with BDI, which suggests that depression-related changes present in rCMRglu measured resting brain activity are central to the memory deficit found in MDD (please see Supplementary Fig. 2).

4.6. Metabolic correlations reflecting loss of top-down control in depression

This study finds negative correlations between resting rCMRglu in right amygdala *versus* rCMRglu in both right and left dlPFC in healthy comparison subjects but not in MDD subjects.

Few studies have examined cross-correlations of brain activity in psychiatric patients (Benson et al., 2008; Horwitz et al., 1988; Horwitz et al., 1991) or healthy subjects (Horwitz et al., 1984; Lee et al., 2008; Willis et al., 2008; Yakushev et al., 2013; Zouet al., 2015). These studies examined small samples, and none studied unmedicated depressed individuals.

Prior publications of similar finding in eight subjects (Mayberg et al., 1999) are consistent with our findings. The bottom-up model of depression (Mayberg, 1997) proposes that depression symptomatology is characterized by lower activity in dorsal neortical regions and higher activity in ventral paralimbic regions and implicates dlPFC in impaired cognitive functions requiring selective attention. We find evidence that part of MDD pathology is the loss of top-down control whereby phylogenetically newer structures lose their ability to control or suppress the undesired activity of a phylogenetically more archaic part of the brain.

4.6.1. Limitations

Control subjects were on average slightly younger than our MDD population. In order to avoid effect of age on the results we repeated analyses involving control subjects after removing the variance associated with age from rCMRglu. Clusters of voxels where brain activity predicted performance on the SRT in MDD patients extended beyond the brain structures associated with execution of this verbal learning task. It is important to note, however, that we are using a 'voxel-by-

Table 1
Demographic and clinical variables, presented as Mean ± Standard Deviation, of a cohort of major depressive disorder (MDD) patients and healthy controls (HC). The Buschke Selective Reminding Task (SRT) was administered to a subgroup (MDD SRT Subgroup) of the MDD (Total). One-way analysis of variance (ANOVA) was used to compare continuous variables across groups. *p*-values for the comparisons between MDD Total and MDD SRT are presented in the third column. *p*-values for the comparisons between MDD Total and HC are presented in the last column.

	MDD Total	MDD SRT Subgroup	*p*	Controls	*p*
N	60	29		43	
Sex (female %)	61%	59%		61%	
Age (years)	37.3 ± 12.3	38.9 ± 13.3	***0.275***	31.0 ± 9.80	***0.011***
Education (years)	15.5 ± 2.70	16.1 ± 2.50	***0.100***	15.9 ± 3.30	***0.642***
Age at first MDE (years)	24.3 ± 13.7	22.0 ± 13.9	***0.186***	N/A	
Number of MDEs	5.10 ± 13.0	4.40 ± 3.90	***0.666***	N/A	
GAF	47.9 ± 11.4	44.4 ± 11.5	***0.001***	92.1 ± 4.80	***0.000***
HDRS-24 score	28.3 ± 6.40	29.1 ± 6.20	***0.252***	1.40 ± 2.00	***0.000***
BDI score	28.2 ± 11.0	30.9 ± 10.1	***0.038***	0.90 ± 1.60	***0.000***
Melancholic[a] (%)	10%	14%		N/A	
Atypical[b] (%)	8%	14%		N/A	

[a] Melancholic depression was defined as marked anhedonia (HDRS item 7 ≥ 3) with at least three of the following: excessive or inappropriate guilt (item 2 ≥ 3), severe late insomnia or diurnal variation (HDRS items 6 and 18, respectively), significant motor retardation (item 8 ≥ 2), frequent agitation or restlessness (item 9), severe loss of appetite (item 12), or obvious weight loss per history or weight measurement (item 16).

[b] Atypical depression was defined by a score of ≥3 in the `atypical items' of the HDRS (hypersomnia, hyperphagia and weight gain) in patients who that did not present melancholic depression.

voxel' analysis. These large, contiguous clusters of voxels were found despite rigorous correction for multiple comparisons in SPM12.

We examined resting brain activity only, and activation patterns during memory-related tasks were not assessed. Resting state studies are particularly useful for identifying areas of the brain that are pathologically overactive. Future studies should explore differences in learning and memory between MDD subjects and healthy volunteers as well as the impact of remission on memory (Table 1).

4.7. Summary

We identified correlations between resting brain activity in a number of brain structures and deficits in performance on a verbal list-learning task in MDD subjects. In the prefrontal cortex, the association between resting brain activity and memory performance is consistent with the role of this region in rehearsal and organization of verbal memory. In mesiotemporal cortical regions, higher resting brain activity reflects a lower capacity to process information effectively. In the cerebellum, negative correlation between recall and neuronal activity is not well understood. It may be just an extension of the depression-related abnormalities seen elsewhere in the brain. Alternatively it may reflect a compensatory mechanism trying to restore homeostasis. Future studies should combine imaging technologies to determine how the above-described patterns of resting activity in specific brain regions are related to depressive mood states and how they may predict treatment outcome for depression as a whole and cognitive deficits specifically.

Acknowledgments

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Conflicts of interest

Dr. Milak; Dr. Potter; Dr. Pantazatos; Dr. Keilp; Dr. Zanderigo; Dr. Schain; Dr. Sublette; Dr. Oquendo; Dr. Malone; Dr. Parsey and Dr. Mann report no competing interests. Dr. Oquendo receives royalties for use of the C-SSRS and her family owns stock in Bristol Myers Squibb. Dr. Mann receives royalties for commercial use of the C-SSRS from the Research Foundation for Mental Hygiene.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.pscychresns.2018.12.006.

References

Anderson, A.D., Oquendo, M.A., Parsey, R.V., Milak, M.S., Campbell, C., Mann, J.J., 2004. Regional brain responses to serotonin in major depressive disorder. J. Affect. Disord. 82 (3), 411–417.

Andreasen, N.C., O'Leary, D.S., Cizadlo, T., Arndt, S., Rezai, K., Watkins, G.L., Ponto, L.L., Hichwa, R.D., 1995. II. PET studies of memory: novel versus practiced free recall of word lists. Neuroimage 2 (4), 296–305.

Ardekani, B.A., Guckemus, S., Bachman, A., Hoptman, M.J., Wojtaszek, M., Nierenberg, J., 2005. Quantitative comparison of algorithms for inter-subject registration of 3D volumetric brain MRI scans. J. Neurosci. Methods 142 (1), 67–76.

Ashby, F.G., Alfonso-Reese, L.A., Turken, A.U., Waldron, E.M., 1998. A neuropsychological theory of multiple systems in category learning. Psychol. Rev. 105 (3), 442–481.

Austin, M.P., Ross, M., Murray, C., O'Carroll, R.E., Ebmeier, K.P., Goodwin, G.M., 1992. Cognitive function in major depression. J. Affect. Disord. 25 (1), 21–29.

Awh, E., Jonides, J., Smith, E.E., Schumacher, E.H., Koeppe, R.A., Katz, S., 1996. Dissociation of storage and rehearsal in verbal working memory: evidence from positron emission tomography. Psychological Science 7, 25–31 SRC - GoogleScholar.

Awh, E., Smith, E.E., Jonides, J., 1995. Human rehearsal processes and the frontal lobes: PET evidence. Ann. N. Y. Acad. Sci. 769, 97–117.

Badre, D., Poldrack, R.A., Pare-Blagoev, E.J., Insler, R.Z., Wagner, A.D., 2005. Dissociable controlled retrieval and generalized selection mechanisms in ventrolateral prefrontal cortex. Neuron 47 (6), 907–918.

Baune, B.T., Miller, R., McAfoose, J., Johnson, M., Quirk, F., Mitchell, D., 2010. The role of cognitive impairment in general functioning in major depression. Psychiatry Res. 176 (2-3), 183–189.

Bellani, M., Dusi, N., Yeh, P.-H., Soares, J.C., Brambilla, P., 2011. The effects of antidepressants on human brain as detected by imaging studies. Focus on major depression. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 35 (7), 1544–1552.

Benson, B.E., Willis, M.W., Ketter, T.A., Speer, A., Kimbrell, T.A., George, M.S., Herscovitch, P., Post, R.M., 2008. Interregional cerebral metabolic associativity during a continuous performance task (Part II): differential alterations in bipolar and unipolar disorders. Psychiatry Res. 164 (1), 30–47.

Block, R.I., O'Leary, D.S., Hichwa, R.D., Augustinack, J.C., Boles Ponto, L.L., Ghoneim, M.M., Arndt, S., Hurtig, R.R., Watkins, G.L., Hall, J.A., Nathan, P.E., Andreasen, N.C., 2002. Effects of frequent marijuana use on memory-related regional cerebral blood flow. Pharmacol. Biochem. Behav. 72 (1-2), 237–250.

Boeker, H., Schulze, J., Richter, A., Nikisch, G., Schuepbach, D., Grimm, S., 2012. Sustained cognitive impairments after clinical recovery of severe depression. J. Nerv. Ment. Dis. 200 (9), 773–776.

Brett, M., Persey, M.R., Reilly, M.M., Revesz, T., Booth, D.R., Booth, S.E., Hawkins, P.N., Pepys, M.B., Morgan-Hughes, J.A., 1999. Transthyretin Leu12Pro is associated with systemic, neuropathic and leptomeningeal amyloidosis. Brain 122 (Pt 2), 183–190.

Buckner, R.L., Logan, J., Donaldson, D.I., Wheeler, M.E., 2000. Cognitive neuroscience of episodic memory encoding. Acta Psychol. 105 (2-3), 127–139.

Buschke, H., 1973. Selective reminding for analysis of learning and memory. J. Verb.

Learn. Verb. Behav. 12, 543–550.
Buschke, H., Fuld, P., 1974. Evaluating storage, retention, and retrieval in disordered memory and learning. Neurology 24, 1019–1025.
Butters, N., Wolfe, J., Granholm, E., Martone, M., 1986. An assessment of verbal recall, recognition and fluency abilities in patients with Huntington's disease. Cortex 22 (1), 11–32.
Calder, A.J., Lawrence, A.D., Young, A.W., 2001. Neuropsychology of fear and loathing. Nat. Rev. Neurosci. 2 (5), 352–363.
Chao, L.L., Knight, R.T., 1995. Human prefrontal lesions increase distractibility to irrelevant sensory inputs. Neuroreport 6 (12), 1605–1610.
Chein, J.M., Fiez, J.A., 2001. Dissociation of verbal working memory system components using a delayed serial recall task. Cereb. Cortex 11 (11), 1003–1014.
Christensen, H., Griffiths, K., Mackinnon, A., Jacomb, P., 1997. A quantitative review of cognitive deficits in depression and Alzheimer-type dementia. J. Int. Neuropsychol. Soc. 3 (6), 631–651.
Crespo-Facorro, B., Wiser, A.K., Andreasen, N.C., O'Leary, D.S., Watkins, G.L., Boles Ponto, L.L., Hichwa, R.D., 2001. Neural basis of novel and well-learned recognition memory in schizophrenia: a positron emission tomography study. Hum. Brain Mapp. 12 (4), 219–231.
D'Esposito, M., Postle, B.R., Squire, L.R., Schacter, D.L., New, P., 2002. The neural basis of working memory storage, rehearsal, and control processes. Neuropsychology of Memory, third ed. .
De Smet, H.J., Paquier, P., Verhoeven, J., Marien, P., 2013. The cerebellum: its role in language and related cognitive and affective functions. Brain Lang. 127 (3), 334–342.
Diamond, A., 1988. Abilities and neural mechanisms underlying AB performance. Child Dev. 59 (2), 523–527.
Diener, C., Kuehner, C., Brusniak, W., Ubl, B., Wessa, M., Flor, H., 2012. A meta-analysis of neurofunctional imaging studies of emotion and cognition in major depression. Neuroimage 61 (3), 677–685.
Dietsche, B., Backes, H., Stratmann, M., Konrad, C., Kircher, T., Krug, A., 2014. Altered neural function during episodic memory encoding and retrieval in major depression. Hum. Brain Mapp. 35 (9), 4293–4302.
Doyon, J., Gaudreau, D., Laforce Jr., R., Castonguay, M., Bedard, P.J., Bedard, F., Bouchard, J.P., 1997. Role of the striatum, cerebellum, and frontal lobes in the learning of a visuomotor sequence. Brain Cogn. 34 (2), 218–245.
Duncan, J., Seitz, R.J., Kolodny, J., Bor, D., Herzog, H., Ahmed, A., Newell, F.N., Emslie, H., 2000. A neural basis for general intelligence. Science 289 (5478), 457–460.
Dutta, A., McKie, S., Deakin, J.F., 2014. Resting state networks in major depressive disorder. Psychiatry Res. 224 (3), 139–151.
Duvernoy, O., Malm, T., Thuomas, K.A., Larsson, S.G., Hansson, H.E., 1991. CT and MR evaluation of pericardial and retrosternal adhesions after cardiac surgery. J. Comput. Assist. Tomogr. 15 (4), 555–560.
Ferraro, F.R., Balota, D.A., Connor, L.T., 1993. Implicit memory and the formation of new associations in nondemented Parkinson's disease individuals and individuals with senile dementia of the Alzheimer type: a serial reaction time (SRT) investigation. Brain Cogn. 21 (2), 163–180.
Friston, K.J., Robert, W., et al., 1994. Statistical parametric mapping, *thatcher*. In: Hallett, M. (Ed.), Functional Neuroimaging: Technical Foundations, pp. 303.
Fu, F.Y., Zhan, H., Zhang, Z., Li, T., Xin, Y.M., Wei, S.H., 2003. [Effects of low-G preconditioning on contractive ability of left ventricle and contents of endothelin and prostacycline in myocardium of rats after repeated +10 Gz stress]. Space Med. Med. Eng. 16 (6), 414–417.
Garavan, H., 1998. Serial attention within working memory. Memory Cognit. 26 (2), 263–276.
George, M.S., Ketter, T.A., Parekh, P., Gill, D.S., 1994. Spatial ability in affective illness: differences in regional brain activation during a spatial matching task (H-sub–5O PET). Neuropsychiatry Neuropsychol. Behav. Neurol. 7, 143–153 SRC - GoogleScholar, 2-1.
Gourovitch, M.L., Torrey, E.F., Gold, J.M., Randolph, C., Weinberger, D.R., Goldberg, T.E., 1999. Neuropsychological performance of monozygotic twins discordant for bipolar disorder. Biol. Psychiatry 45 (5), 639–646.
Gruber, O., Zilles, D., Kennel, J., Gruber, E., Falkai, P., 2011. A systematic experimental neuropsychological investigation of the functional integrity of working memory circuits in major depression. Eur. Arch. Psychiatry Clin. Neurosci. 261 (3), 179–184.
Guo, W., Liu, F., Liu, J., Yu, L., Zhang, Z., Zhang, J., Chen, H., Xiao, C., 2013. Is there a cerebellar compensatory effort in first-episode, treatment-naive major depressive disorder at rest? Prog. Neuro-Psychopharmacol. Biol. Psychiatry 46, 13–18.
Hamilton, M., 1960. A rating scale for depression. J. Neurol. Neurosurg. Psychiatry 23, 56–62.
Hamilton, M., 1967. Development of a rating scale for primary depressive illness. Br. J. Soc. Clin. Psychol. 6 (4), 278–296.
Harper, D.G., Jensen, J.E., Ravichandran, C., Perlis, R.H., Fava, M., Renshaw, P.F., Iosifescu, D.V., 2017. Tissue type-specific bioenergetic abnormalities in adults with major depression. Neuropsychopharmacology 42 (4), 876–885.
Helmuth, L.L., Mayr, U., Daum, I., 2000. Sequence learning in Parkinson's disease: a comparison of spatial-attention and number-response sequences. Neuropsychologia 38 (11), 1443–1451.
Hermens, D.F., Naismith, S.L., Redoblado Hodge, M.A., Scott, E.M., Hickie, I.B., 2010. Impaired verbal memory in young adults with unipolar and bipolar depression. Early Interv. Psychiatry 4 (3), 227–233.
Horwitz, B., Duara, R., Rapoport, S.I., 1984. Intercorrelations of glucose metabolic rates between brain regions: application to healthy males in a state of reduced sensory input. J. Cereb. Blood Flow Metabolism 4 (4), 484–499.
Horwitz, B., Rumsey, J.M., Grady, C.L., Rapoport, S.I., 1988. The cerebral metabolic landscape in autism. Intercorrelations of regional glucose utilization. Arch. Neurol. 45 (7), 749–755.
Horwitz, B., Swedo, S.E., Grady, C.L., Pietrini, P., Schapiro, M.B., Rapoport, J.L., Rapoport, S.I., 1991. Cerebral metabolic pattern in obsessive-compulsive disorder: altered intercorrelations between regional rates of glucose utilization. Psychiatry Res. 40 (4), 221–237.
Ilsley, J.E., Moffoot, A.P., O'Carroll, R.E., 1995. An analysis of memory dysfunction in major depression. J. Affect. Disord. 35 (1-2), 1–9.
Jackson, G.M., Jackson, S.R., Harrison, J., Henderson, L., Kennard, C., 1995. Serial reaction time learning and Parkinson's disease: evidence for a procedural learning deficit. Neuropsychologia 33 (5), 577–593.
Jacobsen, C.F., 1935. Functions of frontal association areas in primates. Arch. Neurol. Psychiatry 33, 558–569.
Jacobson, C., Wolfe, J., Jackson, T., 1935. An experimental analysis of the functions of the frontal association areas in primates. J. Nerv. Mental Dis. 82, 1–14 SRC - GoogleScholar.
Johnson, M.K., 1992. MEM: mechanisms of recollection. J. Cogn. Neurosci. 4 (3), 268–280.
Kaneda, Y., 2009. Verbal working memory impairment in patients with current episode of unipolar major depressive disorder and in remission. Clin. Neuropharmacol. 32 (6), 346–347.
Kates, W.R., Abrams, M.T., Kaufmann, W.E., Breiter, S.N., Reiss, A.L., 1997. Reliability and validity of MRI measurement of the amygdala and hippocampus in children with fragile X syndrome. Psychiatry Res. 75 (1), 31–48.
Kegeles, L.S., Malone, K.M., Slifstein, M., Ellis, S.P., Xanthopoulos, E., Keilp, J.G., Campbell, C., Oquendo, M., Van Heertum, R.L., Mann, J.J., 2003. Response of cortical metabolic deficits to serotonergic challenge in familial mood disorders. Am. J. Psychiatry 160 (1), 76–82.
Keilp, J.G., Alexander, G.E., Stern, Y., Prohovnik, I., 1996. Inferior parietal perfusion, lateralization, and neuropsychological dysfunction in Alzheimer's disease. Brain Cogn. 32 (3), 365–383.
Keilp, J.G., Sackeim, H.A., Brodsky, B., Oquendo, M.A., Malone, K.M., Mann, J.J., 2001. Neuropsychological dysfunction in depressed suicide attempters. Am. J. Psychiatry. 158, 735–741.
Killiany, R.J., Moss, M.B., Nicholson, T., Jolesz, F., Sandor, T., 1997. An interactive procedure for extracting features of the brain from magnetic resonance images: the lobes. Hum. Brain Mapp. 5 (5), 355–363.
Kindermann, S.S., Brown, G.G., 1997. Depression and memory in the elderly: a meta-analysis. J. Clin. Exp. Neuropsychol. 19 (5), 625–642.
Klein, A., Andersson, J., Ardekani, B.A., Ashburner, J., Avants, B., Chiang, M.C., Christensen, G.E., Collins, D.L., Gee, J., Hellier, P., Song, J.H., Jenkinson, M., Lepage, C., Rueckert, D., Thompson, P., Vercauteren, T., Woods, R.P., Mann, J.J., Parsey, R.V., 2009. Evaluation of 14 nonlinear deformation algorithms applied to human brain MRI registration. Neuroimage 46 (3), 786–802.
Knopman, D., Nissen, M.J., 1991. Procedural learning is impaired in Huntington's disease: evidence from the serial reaction time task. Neuropsychologia 29 (3), 245–254.
Knowlton, B.J., Squire, L.R., Schacter, D.L., New, P., 2002. The *role* of the Basal Ganglia in *learning and memory*. Neuropsychology of Memory, third ed. .
Korgaonkar, M.S., Cooper, N.J., Williams, L.M., Grieve, S.M., 2012. Mapping inter-regional connectivity of the entire cortex to characterize major depressive disorder: a whole-brain diffusion tensor imaging tractography study. Neuroreport 23 (9), 566–571.
Lee, D.S., Kang, H., Kim, H., Park, H., Oh, J.S., Lee, J.S., Lee, M.C., 2008. Metabolic connectivity by interregional correlation analysis using statistical parametric mapping (SPM) and FDG brain PET; methodological development and patterns of metabolic connectivity in adults. Eur. J. Nuclear Med. Mol. Imaging 35 (9), 1681–1691.
Lee, G.P., Loring, D.W., Thompson, J.L., 1989. Construct validity of material-specific memory measures following unilateral temporal lobe ablations. Psychol. Assess. 1, 192–197.
Lee, G.P., Meador, K.J., Loring, D.W., Smith, J., 1990. Behavioral activation of human hippocampal EEG: Relationship to recent memory. J. Epilepsy 3, 137–142 SRC - GoogleScholar.
Lee, R.S., Hermens, D.F., Porter, M.A., Redoblado-Hodge, M.A., 2012. A meta-analysis of cognitive deficits in first-episode Major Depressive Disorder. J. Affect. Disord. 140 (2), 113–124.
Lencz, T., McCarthy, G., Bronen, R.A., Scott, T.M., Inserni, J.A., Sass, K.J., Novelly, R.A., Kim, J.H., Spencer, D.D., 1992. Quantitative magnetic resonance imaging in temporal lobe epilepsy: relationship to neuropathology and neuropsychological function. Ann. Neurol. 31 (6), 629–637.
Levin, H.S., Benton, A.L., Grossman, R.G., New, P., 1982. Neurobehavioral Consequences of Closed Head Injury.
Li, X., Wong, D., Gandour, J., Dzemidzic, M., Tong, Y., Talavage, T., Lowe, M., 2004. Neural network for encoding immediate memory in phonological processing. Neuroreport 15 (16), 2459–2462.
Maldjian, J.A., Laurienti, P.J., Burdette, J.H., 2004. Precentral gyrus discrepancy in electronic versions of the Talairach atlas. Neuroimage 21 (1), 450–455.
Maldjian, J.A., Laurienti, P.J., Kraft, R.A., Burdette, J.H., 2003. An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. Neuroimage 19 (3), 1233–1239.
Martin, R.C., Loring, D.W., Meador, K.J., Lee, G.P., 1988. Differential forgetting in patients with temporal lobe dysfunction. Arch. Clin. Neuropsychol. 3 (4), 351–358.
Marvel, C.L., Paradiso, S., 2004. Cognitive and neurological impairment in mood disorders. Psychiatr. Clin. North Am. 27 (1), 19–36 vii-viii.
May, C.P., Hasher, L., Kane, M.J., 1999. The role of interference in memory span. Mem. Cognit. 27 (5), 759–767.
Mayberg, H.S., 1997. Limbic-cortical dysregulation: a proposed model of depression. J. Neuropsychiatry Clin. Neurosci. 9 (3), 471–481.
Mayberg, H.S., Liotti, M., Brannan, S.K., McGinnis, S., Mahurin, R.K., Jerabek, P.A., Silva,

J.A., Tekell, J.L., Martin, C.C., Lancaster, J.L., Fox, P.T., 1999. Reciprocal limbic-cortical function and negative mood: converging PET findings in depression and normal sadness. Am. J. Psychiatry 156 (5), 675–682.
Milak, M.S., Keilp, J., Parsey, R.V., Oquendo, M.A., Malone, K.M., Mann, J.J., 2010. Regional brain metabolic correlates of self-reported depression severity contrasted with clinician ratings. J. Affect. Disord. 126 (1-2), 113–124.
Milak, M.S., Parsey, R.V., Keilp, J., Oquendo, M.A., Malone, K.M., Mann, J.J., 2005. Neuroanatomic correlates of psychopathologic components of major depressive disorder. Arch. Gen. Psychiatry 62 (4), 397–408.
Murray, E.A., Wise, S.P., Drevets, W.C., 2011. Localization of dysfunction in major depressive disorder: prefrontal cortex and amygdala. Biol. Psychiatry 69 (12), e43–e54.
Neau, J.P., Arroyo-Anllo, E., Bonnaud, V., Ingrand, P., Gil, R., 2000. Neuropsychological disturbances in cerebellar infarcts. Acta Neurol. Scand. 102 (6), 363–370.
Nitschke, J.B., Heller, W., Etienne, M.A., Miller, G.A., 2004. Prefrontal cortex activity differentiates processes affecting memory in depression. Biol. Psychol. 67 (1-2), 125–143.
Nobler, M.S., Oquendo, M.A., Kegeles, L.S., Malone, K.M., Campbell, C.C., Sackeim, H.A., Mann, J.J., 2001. Decreased regional brain metabolism after ect. Am. J. Psychiatry 158 (2), 305–308.
Oquendo, M.A., Krunic, A., Parsey, R.V., Milak, M., Malone, K.M., Anderson, A., van Heertum, R.L., John Mann, J., 2005. Positron emission tomography of regional brain metabolic responses to a serotonergic challenge in major depressive disorder with and without borderline personality disorder. Neuropsychopharmacology 30 (6), 1163–1172.
Oquendo, M.A., Placidi, G.P., Malone, K.M., Campbell, C., Keilp, J., Brodsky, B., Kegeles, L.S., Cooper, T.B., Parsey, R.V., van Heertum, R.L., Mann, J.J., 2003. Positron emission tomography of regional brain metabolic responses to a serotonergic challenge and lethality of suicide attempts in major depression. Arch. Gen. Psychiatry 60 (1), 14–22.
Ottowitz, W.E., Deckersbach, T., Savage, C.R., Lindquist, M.A., Dougherty, D.D., 2010. Neural correlates of strategic processes underlying episodic memory in women with major depression: a 15O-PET study. J. Neuropsychiatry Clin. Neurosci. 22 (2), 218–230.
Packard, M.G., McGaugh, J.L., 1996. Inactivation of hippocampus or caudate nucleus with lidocaine differentially affects expression of place and response learning. Neurobiol. Learn. Mem. 65 (1), 65–72.
Palmer, S.M., Crewther, S.G., Carey, L.M., Team, S.P., 2014. A meta-analysis of changes in brain activity in clinical depression. Front. Hum. Neurosci. 8 (1045), 1045.
Paradiso, S., Lamberty, G.J., Garvey, M.J., Robinson, R.G., 1997. Cognitive impairment in the euthymic phase of chronic unipolar depression. J. Nerv. Ment. Dis. 185 (12), 748–754.
Parlar, M., Densmore, M., Hall, G.B., Frewen, P.A., Lanius, R.A., McKinnon, M.C., 2017. Relation between patterns of intrinsic network connectivity, cognitive functioning, and symptom presentation in trauma-exposed patients with major depressive disorder. Brain Behav. 7 (5), e00664.
Pascual-Leone, A., Grafman, J., Clark, K., Stewart, M., Massaquoi, S., Lou, J.S., Hallett, M., 1993. Procedural learning in Parkinson's disease and cerebellar degeneration. Ann. Neurol. 34 (4), 594–602.
Poldrack, R.A., Prabhakaran, V., Seger, C.A., Gabrieli, J.D., 1999. Striatal activation during acquisition of a cognitive skill. Neuropsychology 13 (4), 564–574.
Postle, B.R., Berger, J.S., D'Esposito, M., 1999. Functional neuroanatomical double dissociation of mnemonic and executive control processes contributing to working memory performance. Proc. Natl. Acad. Sci. U. S. A 96 (22), 12959–12964.
Raichle, M.E., Fiez, J.A., Videen, T.O., MacLeod, A.M., Pardo, J.V., Fox, P.T., Petersen, S.E., 1994. Practice-related changes in human brain functional anatomy during nonmotor learning. Cereb. Cortex 4 (1), 8–26.
Ravizza, S.M., McCormick, C.A., Schlerf, J.E., Justus, T., Ivry, R.B., Fiez, J.A., 2006. Cerebellar damage produces selective deficits in verbal working memory. Brain 129 (2), 306–320.
Roberts, R.J., Hager, L.D., Heron, C., 1994. Prefrontal cognitive processes: working memory and inhibition in the antisaccade task. J. Exp. Psychol. Gen. 123, 374–393 SRC - GoogleScholar.
Rock, P.L., Roiser, J.P., Riedel, W.J., Blackwell, A.D., 2014. Cognitive impairment in depression: a systematic review and meta-analysis. Psychol. Med. 44 (10), 2029–2040.
Shan, Y., Jia, Y., Zhong, S., Li, X., Zhao, H., Chen, J., Lu, Q., Zhang, L., Li, Z., Lai, S., 2017. Correlations between working memory impairment and neurometabolites of prefrontal cortex and lenticular nucleus in patients with major depressive disorder. J. Affect. Disord. 227, 236–242.
Snow, J.H., English, R., Lange, B., 1992. Clinical utility of the Selective Reminding Test-children's version. J. Psychoeduc. Assess. 10, 153–160 SRC - GoogleScholar.
Snyder, H.R., 2013. Major depressive disorder is associated with broad impairments on neuropsychological measures of executive function: a meta-analysis and review. Psychol. Bull. 139 (1), 81–132.
Sommer, M., Grafman, J., Clark, K., Hallett, M., 1999. Learning in Parkinson's disease: eyeblink conditioning, declarative learning, and procedural learning. J. Neurol. Neurosurg. Psychiatry 67 (1), 27–34.
Spreen, O., Strauss, E., New, P., 1998. A compendium of Neuropsychological Tests: Administration, Norms, and Commentary, second ed. .
Strauss, E., Sherman, E.M.S., Spreen, O., 2006. A compendium of Neuropsychological Tests: Administration, Norms, and Commentary, third ed. .
Taconnat, L., Baudouin, A., Fay, S., Raz, N., Bouazzaoui, B., El-Hage, W., Isingrini, M., Ergis, A.-M., 2010. Episodic memory and organizational strategy in free recall in unipolar depression: The role of cognitive support and executive functions. J. Clin. Exp. Neuropsychol. 32 (7), 719–727.
Takeda, K., Meguro, K., Tanaka, N., Nakatsuka, M., 2013. Difficulty with learning of exercise instructions associated with 'working memory'dysfunction and frontal glucose hypometabolism in a patient with very mild subcortical vascular dementia with knee osteoarthritis. BMJ Case Rep. 2013 bcr2013008577.
Talairach, J., Tournoux, P., Medical, N.Y., New, P., 1988. Co-planar Stereotaxic Atlas of the Human Brain: 3-Dimensional Proportional System-an Approach to Cerebral Imaging.
Taylor, A.E., Saint-Cyr, J.A., Lang, A.E., 1990. Memory and learning in early Parkinson's disease: evidence for a "frontal lobe syndrome". Brain Cognit. 13 (2), 211–232.
Teipel, S.J., Willoch, F., Ishii, K., Burger, K., Drzezga, A., Engel, R., Bartenstein, P., Moller, H.J., Schwaiger, M., Hampel, H., 2006. Resting state glucose utilization and the CERAD cognitive battery in patients with Alzheimer's disease. Neurobiol. Aging 27 (5), 681–690.
Thompson-Schill, S.L., D'Esposito, M., Aguirre, G.K., Farah, M.J., 1997. Role of left inferior prefrontal cortex in retrieval of semantic knowledge: a reevaluation. Proc. Natl. Acad. Sci. U. S. A. 94 (26), 14792–14797.
van Gorp, W.G., Altshuler, L., Theberge, D.C., Mintz, J., 1999. Declarative and procedural memory in bipolar disorder. Biol. Psychiatry 46 (4), 525–531.
Wagner, A.D., Schacter, D.L., Rotte, M., Koutstaal, W., Maril, A., Dale, A.M., Rosen, B.R., Buckner, R.L., 1998. Building memories: remembering and forgetting of verbal experiences as predicted by brain activity. Science 281 (5380), 1188–1191.
Westerveld, M., Sass, K.J., Sass, A., Henry, H.G., 1994. Assessment of verbal memory in temporal lobe epilepsy using the Selective Reminding Test: Equivalence and reliability of alternate forms. J. Epilepsy 7, 57–63 SRC - GoogleScholar.
Williams, K.G., 1992. Pharmacists' duty to warn of drug interactions. Dooley v. Everett. Am. J. Hosp. Pharm. 49 (11), 2787–2789.
Willingham, D.B., Koroshetz, W.J., 1993. Evidence for dissociable motor skills in Huntington's disease patients. Psychobiol. 21 (3), 173–182 SRC - GoogleScholar.
Willis, M.W., Benson, B.E., Ketter, T.A., Kimbrell, T.A., George, M.S., Speer, A.M., Herscovitch, P., Post, R.M., 2008. Interregional cerebral metabolic associativity during a continuous performance task (Part I): healthy adults. Psychiatry Res. 164 (1), 16–29.
Woods, R.P., Grafton, S.T., Watson, J.D., Sicotte, N.L., Mazziotta, J.C., 1998. Automated image registration: II. Intersubject validation of linear and nonlinear models. J. Comput. Assist. Tomogr. 22 (1), 153–165.
Worsley, K.J., Poline, J.B., Vandal, A.C., Friston, K.J., 1995. Tests for distributed, non-focal brain activations. Neuroimage 2 (3), 183–194.
Yakushev, I., Chételat, G., Fischer, F.U., Landeau, B., Bastin, C., Scheurich, A., Perrotin, A., Bahri, M.A., Drzezga, A., Eustache, F., Schreckenberger, M., Fellgiebel, A., Salmon, E., 2013. Metabolic and structural connectivity within the default mode network relates to working memory performance in young healthy adults. Neuroimage 79, 184–190.
Zakzanis, K.K., Leach, L., Kaplan, E., 1998. On the nature and pattern of neurocognitive function in major depressive disorder. Neuropsychiatry Neuropsychol Behav Neurol. 11 (3), 111–119.
Zou, N., Chetelat, G., Baydogan, M.G., Li, J., Fischer, F.U., Titov, D., Dukart, J., Fellgiebel, A., Schreckenberger, M., Yakushev, I., 2015. Metabolic connectivity as index of verbal working memory. J. Cereb. Blood Flow Metabolism 35 (7), 1122–1126.
Zubieta, J.K., Huguelet, P., Lajiness-O'Neill, R., Giordani, B.J., 2001. Cognitive function in euthymic bipolar I disorder. Psychiatry Res. 102 (1), 9–20.