Research Paper

Major depressive disorder and schizophrenia are associated with a disturbed experience of temporal memory

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ABSTRACT

Background: Disturbances in 'psychological time' are frequently reported in major depressive disorder (MDD) and schizophrenia. If one accepts the suggestion that the experience of the dimensions of time, past-present-future, are not inseparable then a disturbance in episodic memory is implicated. Episodic memory allows us to make sense of the world and our place within it by constructing a temporal context and temporal flow between events. These temporal representations are disordered in schizophrenia, but whether this is reflected in MDD is not known. Temporal-order memory deficits can be explained by two hypotheses. The prefrontal-organisational hypothesis suggests that deficits result from a breakdown in processes involved in encoding, retrieval, monitoring and decision-making. Whereas the hippocampal-mnemonic theory suggests that item-encoding, and inter-item associative encoding contribute to temporal-order memory.

Methods: New learning, recency judgments and executive function were investigated in 14 MDD patients, 15 schizophrenia patients and 10 healthy volunteers (HVs).

Results: Relative to HVs, both MDD and schizophrenia made more temporal errors despite achieving 100% learning. Deficits in executive function and item-recognition were present in both psychiatric groups, but executive function correlated to temporal errors in MDD only, and item-recognition to new learning in schizophrenia only.

Limitations: MDD and schizophrenia patients were taking medication

Conclusions: Temporal-ordering deficits are evident in both MDD and schizophrenia, and whilst the disruption of organisational and mnemonic processes appears to be ubiquitous, preliminary evidence from the correlational analysis suggests prefrontal problems are implicated in MDD temporal-order deficits, whereas hippocampal are more associated to temporal-order memory deficits in schizophrenia.

1. Introduction

Psychological time is constructed by the mind and reflects the conscious experience of time. Although psychological time is experienced in physical time, and both can be represented in terms of duration, pace, and the order of perceived and internal events, they do not have a one to one relationship. The basic measurements that mark the passage of time are accurately scaled in identical units (milliseconds, seconds, days, years, and so on) which remain stable and immutable worldwide (Wearden et al., 2014). Psychological time on the other hand is constructed by the mind and is a defining feature of episodic memory. Episodic memory allows us to make sense of the world and our place within it by creating life stories around events and episodes in which

we are both actor and narrator. It provides that sense of continuity and coherence to the self across time, and is fundamental to the interconnectedness of the self and memory Conway (2005).

Each act or episode opens with a scene, a series of events then occur, until a final scene brings about an end to that particular episode, and then a new scene begins. To make sense of these episodes the constituent events are chronologically sequenced, allowing us to establish cause-effect relationships between events and players. It is then the very act of reliving these past experiences from a first-person perspective that establishes personal identity and a sense of continuity of the lived experience over time. The episodic memory provides the temporal context or dimension to our life stories. It locates events within a time-frame - when they occurred, how long they lasted, the sequence

in which events occurred, enabling us to establish cause-effect relations between events and antecedents, as well as between events and their consequence, which will inform our current and future oriented decisions. From a more experiential perspective, episodic memory enables us to consciously travel back in time, to project ourselves into the future, or place ourselves in counterfactual situations (i.e. what would have happened if I had reacted in 'this' way rather than in 'that' way?), to reflect on these experiences or thoughts and make causal inferences between seemingly unrelated temporal events Tulving (2002).

One approach to exploring episodic memory in schizophrenia (SCZ) and depressive disorders is to apply thematic or content analysis to their personal life-story narratives. Life-story narratives yield much richer empirical data than autobiographical questions which are structured to focus on specific stages of the life course, as they require individuals to place events within a temporal context and to integrate cause-effect relationships such as "I've always been a shy person and had problems to make friends"(Allé et al., 2015). Individuals diagnosed with SCZ (Allé et al., 2015; Ben Malek et al., 2019; Holm et al., 2016) or depression (Habermas et al., 2008; Vogel et al., 2018) produce life stories showing a significantly reduced linear temporal order coherence and cause-effect relationships relative to age- and gender-matched non-psychiatric controls. Linear temporal order was assessed through the proportion of anachronies present in narratives. Every deviation from the linear temporal order encompassing at least four propositions was counted as an anachrony. On the other hand, cultural knowledge of key events and an understanding of the fundamental structure of time as it relates to past – present – future were both spared in SCZ (Allé et al., 2015; Ben Malek et al., 2019) and depression (Vogel et al., 2018).

The two main experimental paradigms used to study memory for temporal information in cognitive psychology measure recency judgements and temporal order judgements. Recency judgements assess the relative timing of events. Here, a list of items is studied, and participants must decide which of a pair of items was encountered more recently. Temporal order memory tasks present participants with a sequence of items, usually numbering between 3 and 5, the items are then jumbled up, and the task is to re-order the items in the sequence they were originally presented in.

Both recency judgements (Rizzo et al., 1996; Schwartz et al., 1991) and temporal order judgements (Brébion et al., 2020, 2007; Elvevåg et al., 2000; Sullivan, 1997; Waters et al., 2004) are impaired in SCZ, and these impairments are independent of modality (visual or auditory) and stimulus domain (pictorial or verbal memoranda). As far as we are aware, there are no studies investigating recency judgements or temporal order memory in major depressive disorder (MDD). However, we anticipated MDD would be marked by difficulties on these kinds of paradigms given the disordered temporal coherence evident in their life-story narratives. A second point of significance addressed in this study is the inclusion of a comparator group of individuals with SCZ, which provides a transdiagnostic framework in temporal order memory in SCZ and MDD that can be directly equated and putative neurocognitive mechanisms explored. For example, successful completion of the temporal order memory tasks are likely to enlist prefrontal-dependent executive functions involved in the organisation of material at encoding, maintaining information about the temporal order of events or items for upcoming actions, post retrieval monitoring, and decision-making. Hippocampal-dependent mnemonic processes have also been considered critical to bind individual events or items to their temporal context in episodic memory (Downes et al., 2002; DuBrow and Davachi, 2014; Ekstrom et al., 2011; Howard et al., 2015; Jenkins and Ranganath, 2016; Naya et al., 2017; Wang and Diana, 2017).

Accordingly, our study was designed to examine three aims: the first aim was to characterise temporal order memory in MDD. The second aim was to examine the extent to which the neuropsychological profile of the MDD group cut across traditional diagnostic boundaries. Our final aim was to assess the contribution of prefrontal-dependent organi-

sational processes and hippocampal –dependent mnemonic processes to temporal-order memory.

To address our first aim, estimates of new learning, hit rate, forgetting rate, false alarms and temporal errors were obtained from a recency judgement test. Our second aim was addressed by comparing MDD with a group of individuals diagnosed with SCZ. Finally, measures of executive function and item recognition provided proxy measures of prefrontal-dependent organisational processes and hippocampal-dependent mnemonic processes.

Both the prefrontal and the hippocampal accounts allow for:

1. New learning to be impaired.
2. A gradual reduction in new learning performance across trials due to increased demand on either disorganised or fragile encoding processes.
3. Once 100% learning criterion is achieved hit rate will decline due to disorganised or fragile encoding ('forgetting rate').
4. Elevated levels of temporal errors.

But only the prefrontal-organisational hypothesis predict a deficit in executive function and false alarms, and for these measures to correlate to the dependent variables listed above; whilst only the hippocampal hypothesis allows for a deficit in item-recognition and for item-recognition to correlate to the dependent variables listed above.

2. Methods

2.1. Participants

Fourteen MDD patients (2 males, 12 females) and fifteen SCZ patients (9 males, 6 females) were recruited from the National Centre for Mental Health, Birmingham, UK. Diagnoses were determined from clinical interviews in line with the Diagnostic and Statistical Manual of Mental Disorders version IV criteria (DSM IV; American Psychiatric Association, 1994). No additional diagnostic instruments were used. This was a sample from general outpatient clinics, and they did not have any comorbidities. This is not unusual in a UK sample. The current level of psychopathology was assessed in each patient using the 19-item Brief Psychiatric Rating Scale (BPRS; Overall and Gorham (1962). Patient performance was compared to ten (3 males, 7 females) healthy volunteers (HVs).

2.1.1. Inclusion/exclusion criteria

All participants were community dwelling, had normal or corrected-to-normal vision, were right-handed and English was their first language. General exclusion criteria for the study included: a history of substance abuse (including alcohol), dyslexia, neurological illness or trauma, or any physical incapacity likely to make participants incapable of undertaking the test investigations. Patients were also excluded if they had ever received electroconvulsive therapy. HVs were excluded if they had a psychiatric history or a first-degree relative diagnosed with a psychiatric illness. Exclusion criteria was verified from medical records in patients and through self-report.in HVs.

The study had local National Health Service research ethics approval and all participants provided written informed consent.

2.1.2. Medication

At the time of testing, four MDD patients were medication free and ten MDD patients were receiving psychotropic medication. Of these ten patients, eight were receiving antidepressant medication, which included: venlafaxine ($n = 5$), mirtazapine ($n = 2$), and nefazodone ($n = 1$), and two patients were taking benzodiazepines together with paroxetine ($n = 1$), and dothiepin ($n = 1$).

All SCZ patients, except one, were taking psychotropic medication. Five were taking typical antipsychotics, which included: sulpiride ($n = 1$), fluphenazine decanoate ($n = 1$) and clopixol ($n = 3$) and nine were taking atypical antipsychotics which included: risperidone ($n = 1$),

quetiapine ($n = 2$), olanzapine ($n = 4$) and clozapine ($n = 2$). Of the five patients receiving typical antipsychotics, three were also taking anticholinergic agents (procyclidine) and one was taking antidepressant medication (cipramil). Of the nine patients receiving atypical antipsychotic medication, one was also taking antidepressant medication (fluoxetine) together with an anticholineric agent (procyclidine) and one was taking an antidepressant (venlafaxine).

2.2. Design

The study was divided into two stages. A clinical interview (patients only) and the research sessions (all participants). The clinical interview was performed by one of three psychiatrists (SS, WRC or TM) and took approximately 30-60 minutes. Patients were given a research diagnosis according to DSM-IV criteria (American Psychiatric Association, 1994) and assessed for current levels of psychopathology using the BPRS Overall and Gorham (1962). There was a good level of agreement between the three psychiatrists for determining severity and range of symptoms using the BPRS (Intra-class correlation coefficient = 0.94, 95% CI 0.92–0.96; McGraw and Wong, 1996). The first research session commenced either on the same day as the clinical interview or within two weeks. The order of test administration was counterbalanced across all participants.

2.3. Experimental memory tests

2.3.1. Item recognition
Item recognition was measured using a single yes-no verbal recognition memory test.

Stimuli: A mixture of 100 single syllable high- and low-frequency words (high frequency words are commonly used in daily speech, whereas low frequency words are not commonly used in every day speech) were used in the verbal recognition memory test (mean frequency = 137, range 2-2035; Friendly et al., 1982). Fifty words served as targets and fifty served as distractors. The words were presented in a program written in Microsoft Visual C++ using Microsoft Foundation Classes on a laptop computer running in Windows 98.

Procedure: The format of the yes-no verbal recognition memory test involved a study phase that was immediately followed by a test phase. During the study phase, participants viewed 50 targets presented individually at a rate of one every 3000 ms with an inter-stimulus interval of 3000 ms. To aid concentration, participants were instructed to state whether the target was pleasant or not. During the test phase, targets were randomly intermixed with 50 distractors (i.e., new words). Participants were instructed to identify targets and reject distractors by pressing handheld response buttons. Participants had a 3000 ms window in which to respond before the next item was presented.

Performance Measures: The correct identification of a target item was recorded as a hit, and the incorrect endorsement of a distractor was recorded as a false alarm. A correction was made to the data to eliminate extreme scores (corrected probability score = $[Y+0.5]/N+1\}$, where Y is the raw score and N is the total number of target items or distractors) in accordance with Snodgrass and Corwin's (1988) recommendation. A measure of memory strength i.e., discrimination sensitivity (d') was calculated using signal detection theory.

2.3.2. Recency judgement test
Temporal order memory was measured using the recency judgement test. The recency judgement test used in our study was a modified version of the recency judgement test used by Rizzo et al., (1996).

Stimuli: Two separate versions of the recency judgement test were constructed for words and abstract paintings. One hundred nouns and adjectives with a mean frequency of 4.20 (SD = 1.18) were used in the word version and 100 black and white abstract paintings were used in the abstract painting version. The stimuli for each version of the recency judgement test were divided into 10 lists, with each list containing 10 items. Lists 1–5 served as items for the recency judgement test. Lists 6–10 served as distractors for the recognition memory tests used during the learning phase of the recency judgement test.

Procedure: The recency judgement tests comprised of 5 trials, with each trial involving: a learning phase, a 3 min filler task, and a recency judgement test. The procedure is illustrated and described in Fig. 1.

Performance Measures: The number of times the learning phase was repeated to achieve 100% learning was recorded as new learning for each trial. The number of correctly identified targets for each trial was recorded as hit rate, together with the number of errors. In trial 1, participants could only make one error: a false alarm (incorrect endorsement of an item not previously presented as a target). In trials 2–4, participants could make two errors: a false alarm or a temporal error (incorrect endorsement of an item which had served as a target in a previous trial i.e., an error in remembering *when* an item had been previously presented). In trial 5, participants could only make temporal errors. Thus, recency judgement measures included: new learning, hit rate, forgetting rate (number of targets missed), false alarms, and temporal errors.

2.3.3. Tests of executive function
Executive function was measured using two tests. The WCST (Heaton, et al, 1989) was used to provide a measure of executive function and the letter number sequencing (LNS) subtest of the Wechsler Memory Scales Wechsler (1997) was used to provide a measure of verbal working memory.

Executive function refers to a variety of skills such as abstract thinking, planning, problem solving, cognitive flexibility and concept formation (Lezak et al., 2004). Although there is no single neuropsychological measure of executive function, the WCST is commonly used to measure executive function in terms of concept formation, problem solving and cognitive flexibility (Heaton, et al, 1989). The WCST requires participants to sort cards according to shape (crosses, circles, triangles or stars), colour (red, blue, yellow or green) or number (one, two, three or four figures) to one of four key cards (one red triangle, two green stars, three yellow crosses and four blue circles). The first sorting category is 'colour'. Participants are given a 'correct' response each time they sort to colour and an 'incorrect' response when they sort to a different category. This process continues until the participant produces 10 consecutive correct 'colour' responses. Then, without telling the participant, the sorting category is changed to 'shape' and the process continues until 10 consecutive correct 'shape' responses have been made. The sorting category is then changed to 'number' without telling the participant and the process continues until 10 consecutive 'number' responses have been made. The sorting category then switches back to 'colour' and then 'shape' and then 'number' until all six categories have been matched or until all cards have been used, whichever occurs first.

Performance measures: The WCST produced the following measures: number of categories (i.e., each sequence of 10 consecutive correct matches to 'colour', 'shape' or 'number') completed; failure to maintain a set (i.e., 5 or more consecutive correct matches but the participant makes an error before successfully completing a category); perseverative errors (i.e., participant continues to sort cards according to the previous sorting principle) and conceptual level responses (i.e., consecutive correct responses occurring in runs of three or more).

In the LNS, participants are verbally given strings of letters and numbers (e.g., 9, C, 3, A), which they are required to re-order and repeat verbally by giving the numbers first in ascending order followed by the letters in alphabetical order (e.g., 3, 9, A, C). The letter and number groups increase as participants progress through the test (Wechsler, 1997).

Performance measures: Accuracy data is reported for the LNS.

3. Results

Between group differences in demographic features were investigated using a series of one-way ANOVAs. Sex ratios between groups were investigated using chi-square analysis and differences in clinical
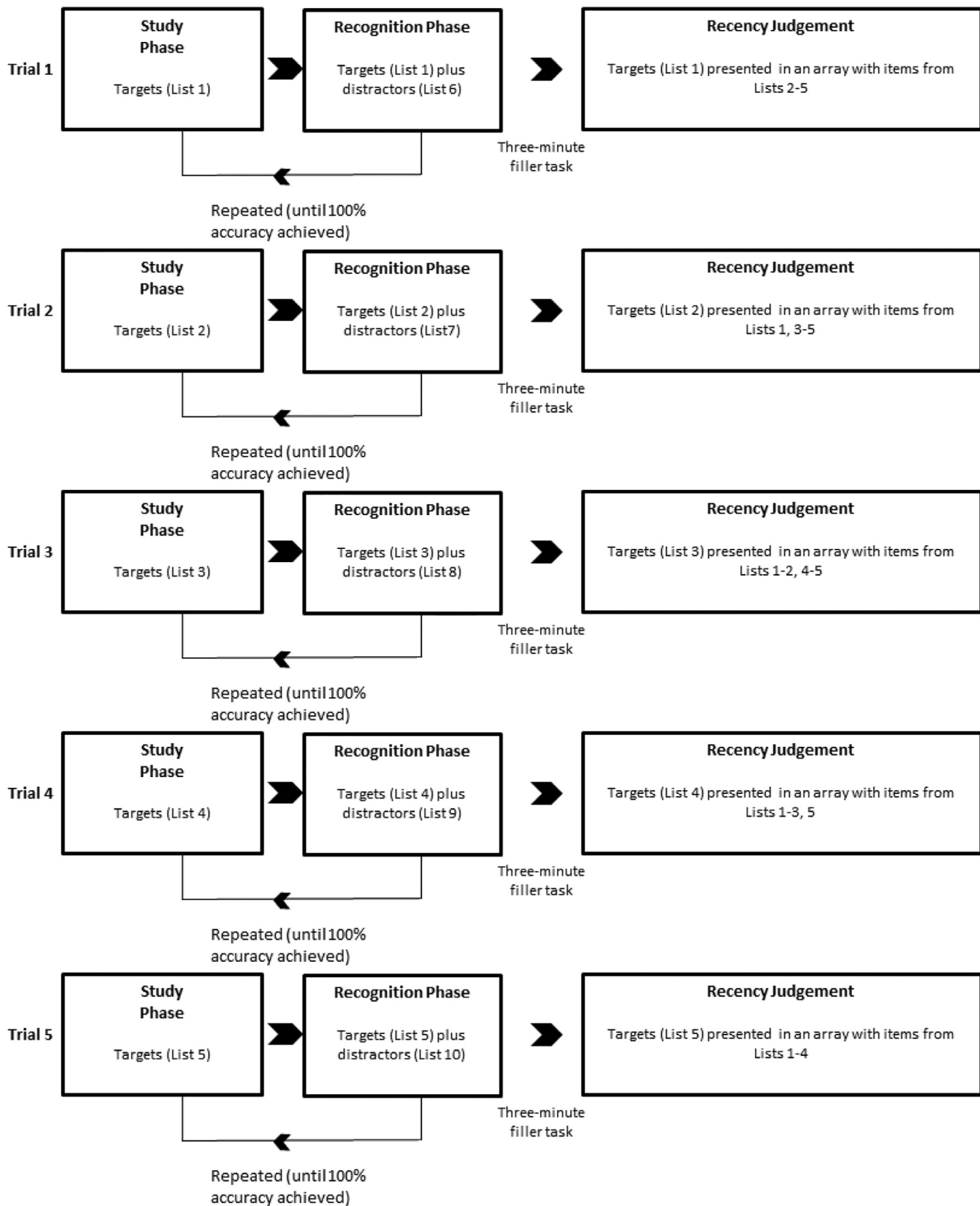
Fig. 1. The recency judgement paradigm comprised of 5 trials, with each trial involving a learning phase, a 3-minute filler task, and a recency judgement paradigm. Trial 1: During the learning phase, participants studied 10 targets from List 1. Each target item was presented for 3000msec. Learning was measured using a recognition memory test in which the 10 previously studied targets (List 1) had to be identified from 10 distractors (List 6). The learning phase was repeated until participants achieved 100% learning (i.e. achieved 10 hits and 0 false alarms on the recognition memory test). The number of presentations required to achieve 100% learning was used to provide a measure of new learning. Participants who achieved 100% learning were then given a 3-minute filler task (word search), followed by the recency judgement test. During the recency judgement test, participants were presented with a random array of 50 items, the 10 target items (List 1) and 40 distractor items from Lists 2-5 and asked to identify the 10 target items (i.e., the most recently presented targets) and reject the unstudied items. In trial 2, the items from List 2 served as targets and the items from Lists 1, 3, 4 and 5 served as distractors. In trial 3, the items from List 3 served as targets and the items from Lists 1, 2, 4 and 5 served as distractors. In trial 4, the items from List 4 served as targets and the items from Lists 1, 2, 3, and 5 served as distractors. In trial 5, the items from List 5 served as targets and the items from Lists 1-4 served as distractors.

Table 1
Participant demographics, clinical background (patients only) and statistical analyses.

	MDD (N=14) Mean (SD)	SCZ (N=15) Mean (SD)	HVs (N=10) Mean (SD)	Statistic
Age (years)	51.64 (7.11)	43.33 (11.79)	41.30 (14.80)	$F(2, 36) = 3.036$, $p = .06$, $\eta^2 = .144$
Sex: male/female	2/12	9/6*	3/7	$\chi^2(2) = 6.78$, $p = .04$, Cramer's $\phi = .417$
Premorbid IQ (NART)	118.07 (6.69)	107.93 (6.41)*	113.80 (4.29)	$F(2, 36) = 10.234$, $p < .001$, $\eta^2 = .362$ [a]
Age at onset	36.86 (10.93)	27.20 (8.43)*	n/a	$t(27) = -2.675$, $p = .013$, $d = -0.96$
Duration of illness	16.21 (13.03)	16.13 (8.72)	n/a	$t(27) = -0.020$, $p = .984$, $d = -0.01$
Number of previous episodes	2.79 (3.79)	1.87 (1.92)	n/a	$t(27) = -0.833$, $p = .412$, $d = -0.30$
Psychopathology (BPRS)	5.64 (5.11)	13.27 (9.11)*	n/a	$t(27) = 2.752$, $p < .05$, $d = 0.99$

Notes and abbreviations: Significant at * $p<.05$. MDD, Major depressive disorder remitted; SCZ, schizophrenia; HV, healthy volunteers. SD, standard deviation; NART, National Adult Reading Test; BPRS, Brief Psychiatric Rating Scale.

[a] Tukey's HSD showed that SCZ patients had significantly lower premorbid IQ levels than MDD patients ($p <.001$, $d = 1.55$), but they did not differ significantly from HVs, ($p =.059$, $d = -1.08$). MDD patients and HVs did not differ significantly in premorbid IQ, although the effect size was just below what Cohen considered a large effect ($p = .22$, $d = 0.76$).

Table 2
The means, standard deviations (SD) and ANCOVAs (with IQ entered as a covariate) for executive function and verbal working memory.

	MDD (n=14) Mean (SD)	SCZ (n=15) Mean (SD)	HVs (n=10) Mean (SD)	ANCOVAs
Executive Function				
Wisconsin Card Sort Test:				
Categories completed	4.17 (2.09)*	4.33 (1.91)	6.00(0.00)	$F(2, 35) = 4.520$, $p = .018$, $\eta^2 = .205$ [a]
Failure to maintain set	1.25 (1.71)	0.60 (0.74)	0.40 (0.70)	$F(2, 35) = 1.408$, $p =.259$, $\eta^2 = .079$
Percent perseverative errors	14.57 (11.57)	22.93 (18.31)	10.40 (4.88)	$F(2, 35) = 1.373$, $p = .267$, $\eta^2 = .073$
Percent conceptual level responses	60.29 (26.30)*	49.07 (22.59)*	77.70 (9.41)	$F(2, 35) = 4.957$, $p = .013$, $\eta^2 = .221$ [b]
Verbal working memory Letter-Number sequencing	11.07 (2.81)	9.53 (2.39)	11.80 (1.87)	$F(2, 35) = 1.327$, $p =.278$, $\eta^2 = .070$

* $p<.05$

[a] Pairwise comparisons showed that MDD patients completed fewer categories than HVs ($t = -3.00$, $p <.05$, $d = -1.24$) but did not differ from SCZ ($t = 1.66$, $p > .05$, $d = 0.62$). SCZ and HVs did not differ significantly in the number of categories completed ($t = -1.19$, $p >.05$, $d = -0.49$).

[b] Pairwise comparisons showed that MDD ($t = -2.98$, $p < .05$, $d = -1.24$) and SCZ ($t = -2.19$, $p < .05$, $d = -0.89$) made fewer conceptual level responses than HVs. There were no significant differences in conceptual level responses between MDD and SCZ ($t = 0.69$, $p > 0.05$, $d = 0.26$).

characteristics were investigated using independent t-tests. Significant findings were investigated further by using post hoc pair-wise comparisons.

Each analysis was checked for homogeneity of regression slope. Where heterogeneity of regression slope was detected, ANCOHET was conducted Maxwell and Delaney (2004). For each significant ANCOVA unplanned paired contrasts were conducted using the Bryant-Paulson basis for finding the critical value of t. When an ANCOHET was significant the appropriate procedure was used to calculate the paired contrasts Maxwell and Delaney (2004).

3.1. Demographic and clinical characteristics

The demographic, clinical (patients only) characteristics and statistical analyses are presented in Table 1. The three groups did not differ significantly in age, although the effect size was large. However, there was a significantly higher proportion of males in the SCZ group compared to MDD patients and HVs. Premorbid IQ (NART; Nelson, 1982) also differed between the groups with SCZ patients displaying a significantly lower premorbid IQ than MDD patients but they did not differ significantly from HVs. MDD patients and HVs did not differ significantly in premorbid IQ. MDD patients also had a later age of onset and lower levels of psychopathology than SCZ, but MDD and SCZ patients did not differ significantly in duration of illness or in number of previous episodes.

3.2. Executive function and verbal working memory

The means, standard deviations (SD) and ANCOVAs, with IQ entered as a covariate, are presented in Table 2 for executive function and verbal working memory. MDD patients completed significantly fewer categories than HVs but did not differ significantly from SCZ patients. There

Table 3
The means and standard deviations (SD) for recency judgement performance and item recognition.

	MDD (N=14) Mean (SD)	SCZ (N=15) Mean (SD)	HVs (N=10) Mean (SD)
Words			
New learning	15.00 (6.75)*	16.07 (6.16)*	7.60 (0.97)
Hit rate	36.07 (5.99)*	36.07 (4.53)*	46.70 (0.82)
Forgetting rate	13.93 (5.99)*	13.93 (4.53)*	3.30 (0.82)
False alarms	1.86 (1.83)	2.27 (1.75)	1.70 (0.68)
Temporal errors	11.57 (4.45)*	11.67 (3.87)*	1.60 (0.52)
Abstract Paintings			
New learning	9.36 (4.01)	12.67 (5.98)*	6.30 (1.25)
Hit rate	39.29 (6.72)*	38.13 (7.02)*	46.60 (0.84)
Forgetting rate	10.00 (6.87)*	11.87 (7.02)*	3.40 (0.84)
False alarms	1.36 (1.50)	2.40 (3.20)	1.90 (0.57)
Temporal errors	9.43 (5.81)*	9.47 (5.17)*	1.60 (0.52)
Item recognition	2.08 (0.46)*	2.14 (0.58)*	2.77 (0.51)

* $p\leq.05$

were no significant differences in the number of categories completed between SCZ patients and HVs. Both MDD and SCZ patients made significantly fewer conceptual level responses relative to HVs. There were no significant differences in conceptual level responses between MDD and SCZ.

There were no significant between group differences for failure to maintain a set, perseverative errors, or verbal working memory.

3.3. Recency judgement and item recognition

The means and standard deviations (SD) for recency judgement test measures and item recognition are presented in Table 3. Between group differences in recency judgement performance were investigated using

Table 4
The results of the ANCOVAs for recency judgement performance and item recognition, showing contrasts, 95% CI, t and d.

	F (df), p and partial η^2	Contrast	Mean difference	95% CI for mean difference	t	d
Words						
Learning trials	$F(2,35) = 7.150$, $p = .002$, $\eta^2 = .290$	SCZ MDD	0.117	-6.43, 6.66	0.04	0.02
		SCZ HVs	7.917	1.73, 14.10	3.19*	1.30
		MDD HVs	7.800	1.74, 13.86	3.20*	1.33
Hit rate	$F(2, 35) = 19.741$, $p <.001$, $\eta^2 = .530$	SCZ MDD	1.295	-4.02, 6.61	0.61	0.23
		SCZ HVs	-9.881	-14.90, -4.86	-4.90*	-2.00
		MDD HVs	-11.176	-16.10, -6.25	-5.65*	-2.34
Forgetting rate	$F(2, 35) = 19.741$, $p <.001$, $\eta^2 = .530$	SCZ HVs	-1.295	-6.61, 4.02	-0.61	-0.23
		SCZ HVs	9.881	4.86, 14.90	4.90*	2.00
		MD HVs	11.176	6.25, 16.10	5.65*	2.34
False alarm rate[H]	$F(2,33) = 4.214$, $p = .023$, $\eta^2 = .203$	SCZ MDD	0.785	-0.57, 2.14	1.44	0.54
		SCZ HVs	1.115	-0.38, 2.61	1.86	0.76
		MDD HVs	0.330	-1.18, 1.84	0.54	0.23
Temporal errors	$F(2, 35)=30.972$, $p <.001$, $\eta^2 =.639$	SCZ MDD	-1.874	-5.88, 2.13	-1.17	-0.43
		SCZ HVs	8.927	5.14, 12.71	5.88*	2.40
		MDD HVs	10.801	7.09, 14.51	7.25*	3.00
Abstract Paintings						
Learning trials	$F(2,35) = 4.151$, $p = .024$, $\eta^2 = .192$	SCZ MDD	1.153	-3.89, 6.20	0.57	0.21
		SCZ HVs	5.119	0.35, 9.88	2.68*	1.09
		MDD HVs	3.966	-0.70, 8.64	2.11	0.88
Hit rate	$F(2,35) = 7.817$, $p = .002$, $\eta^2 = .309$	SCZ MDD	3.037	-3.32, 9.40	1.19	0.44
		SCZ HVs	-6.042	-12.05, -0.03	-2.50*	-1.02
		MDD HVs	-9.079	-14.97, -3.19	-3.84*	-1.59
Forgetting rate	$F(2,35) = 6.478$, $p <.05$, $\eta^2 = .270$	SCZ MDD	-2.087	-8.60, 4.43	-0.80	-.30
		SCZ HVs	6.179	0.03, 12.33	2.50*	1.02
		MDD HVs	8.266	2.23, 14.30	3.41*	1.41
False alarm rate	$F(2,35) = 0.036$, $p = .965$, $\eta^2 = .002$	SCZ MDD	-0.217	-2.65, 2.22	-0.22	-0.08
		SCZ HVs	-0.229	-2.53, 2.07	-0.25	-0.10
		MDD HVs	-0.012	-2.27, 2.25	-0.01	-0.01
Temporal errors	$F(2, 35)=11.626$, $p <.001$, $\eta^2 =.399$	SCZ MDD	-2.806	-8.02, 2.41	-1.34	-0.50
		SCZ HVs	6.221	1.29, 11.15	3.14*	1.28
		MDD HVs	9.027	4.20, 13.86	4.65*	1.93
Item recognition	$F(2, 29) = 6.142$, $p = .006$, $\eta^2 =.298$	SCZ MDD	0.327	-0.33, 0.98	1.26	.53
		SCZ HVs	-0.475	-1.05, 0.10	-2.07*	-.87
		MDD HVs	-0.802	-1.40, -.21	-3.40*	-1.52

[H] denotes ANCOHET

* $p \leq .05$

a series of one-way between subjects ANCOVAs with IQ entered as a covariate. One participant – in the SCZ group – was signalled as a multivariate outlier by markedly high leverage and in some cases Cook's distance. Removing this person and re-running the analyses had no effect on the pattern of contrasts.

The results of the ANCOVAs for recency judgement performance and item recognition are presented in Table 4. Relative to HVs, MDD patients exhibited new learning deficits for words only, whereas SCZ patients exhibited new learning deficits for both words and abstract paintings. Despite achieving 100% learning criterion, both MDD and SCZ patients exhibited a significantly reduced hit rate, a significantly increased forgetting rate, and made significantly more temporal errors for both words and abstract paintings compared to HVs.

MDD and SCZ patients also exhibited reduced item recognition compared to HVs. There was no significant difference between MDD and SCZ in item recognition.

3.4. Trend analysis

To test performance across trials, groups were tested separately. The performance across trials was entered into a one-way within-subjects ANOVA which was followed by a trend test to see whether there was evidence of a gradual reduction in performance. Adjustments for lack of sphericity did not affect whether any result would be considered significant. There was no consistent pattern for the trends, with MDD patients having a linear trend for abstract paintings ($F(1,13) = 11.92$, $p = .004$, $\eta^2 = .478$), while HVs had large effect sizes for the linear trends for words ($F(1,9) = 4.73$, $p = .058$, $\eta^2 = .345$) and abstract paintings ($F(1,9) = 3.18$, $p = .11$, $\eta^2 = .261$). Nonetheless, SCZ patients had large

effect sizes for the linear trends for abstract paintings ($F(1,14) = 2.51$, $p = .14$, $\eta^2 = .152$).

3.5. Correlational analysis

For each patient group, scatter grams were created for executive function (WCST measures: categories completed and conceptual level responses) with item recognition and recency judgement measures, and for item recognition with recency judgement measures. There was no indication of non-linear relationships but there were isolated values which may have created artificially high correlation coefficients. To counter this, Spearman's *rho*, which is based on ranks, was used.

The Spearman's *rho* correlations are presented in Table 5. The number of categories completed in MDD correlated positively to hit rate for abstract paintings and negatively to false alarms and temporal errors for abstract paintings. In addition, there was a borderline positive correlation between conceptual level responses and hit rate for abstract paintings and a negative correlation between conceptual level responses and false alarms for abstract paintings. However, MDD item recognition failed to correlate with any of the recency judgement measures. SCZ item recognition correlated negatively to new learning for words but failed to correlate with any other measure on the recency judgement tests. SCZ categories completed and conceptual level responses also failed to correlate with any of the recency judgement measures.

4. Discussion

This study examined temporal order memory for words and abstract paintings using the recency judgement test in MDD patients and com-

Table 5

Spearman's *rho* correlations for executive function with item recognition and recency judgement performance, and for item recognition with recency judgement performance in MDD and SCZ patients.

	MDD (*n* =14)						SCZ (*n* = 15)					
	Item recognition		Executive Function: WCST				Item recognition		Executive Function: WCST			
			Categories Completed		Conceptual Level Responses				Categories Completed		Conceptual Level Responses	
	rho	p	rho	p	rho	p	rho	p	rho	p	rho	p
Item recognition	–	–	.28	.44	-.09	.80	–	–	.11	.72	-.06	.84
Recency Judgement Tests:												
Words												
New learning	-.37	.30	-.19	.51	.16	.58	-.61	.027*	-.10	.74	-.11	.71
Hit rate	.36	.31	.34	.24	.20	.50	.31	.31	.13	.63	.22	.42
False alarms	-.47	.17	-.25	.39	-.16	.59	.20	.52	.30	.28	.28	.32
Forgetting rate	-.36	.31	-.34	.24	-.20	.50	-.31	.31	-.13	.63	-.22	.42
Temporal errors	-.28	.44	-.36	.20	.34	.23	-.38	.20	-.35	.21	-.46	.09
Abstract paintings												
New learning	-.62	.058	.44	.12	-.15	.61	.25	.40	.27	.33	-.42	.12
Hit rate	.41	.24	.63	.02*	.53	.051	.20	.52	.35	.20	.35	.20
False alarms	.04	.92	-.67	.009**	-.79	.001**	-.28	.36	-.18	.52	-.21	.46
Forgetting rate	-.41	.24	-.44	.11	-.39	.17	-.20	.52	-.35	.20	-.35	.20
Temporal errors	-.42	.23	-.60	.023*	-.47	.09	.035	.91	-.26	.35	-.31	.26

* $p < .05$,
** $p \leq .01$

pared their performance to SCZ patients and HVs. Relative to HVs, MDD patients exhibited new learning deficits for words only, whereas SCZ patients exhibited new learning deficits for both words and abstract paintings. Furthermore, despite achieving 100% learning criterion, both MDD and SCZ patients displayed reduced hit rate, increased forgetting rate, and made significantly more temporal errors for both words and abstract paintings. We also found MDD executive dysfunction was related to hit rate and temporal errors for abstract paintings only, whereas executive dysfunction in SCZ patients failed to correlate with any measure on the recency judgement tests. Finally, both MDD and SCZ patients were impaired on item recognition memory. These findings are not only consistent with previous studies reporting deficits for episodic content memory in MDD (Drakeford et al., 2010; Hartlage et al., 1993; Hertel and Milan, 1994; Jermann et al., 2005) but they also show that MDD patients, like SCZ patients, have impairments for the temporal aspects of episodic memory i.e., both psychiatric groups have problems remembering the temporal order of events.

Both MDD and SCZ patients experienced new learning deficits, but we did not find a gradual deterioration in learning performance across trials, which is what we would have expected to see given the increased demand on prefrontal organisational strategies and/or hippocampal-dependent mnemonic processes. Instead, we found a gradual improvement across trials for abstract paintings in MDD patients which was not evident in SCZ. One possible explanation is that MDD patients were able to recruit some organisational strategy which was not available to SCZ patients. However, fewer categories completed and lower conceptual level responses on the WCST failed to correlate with new learning in MDD. The absence of an association does not necessarily imply that executive function was not related to new learning in MDD, only that no association was found in our group of MDD patients.

Despite reaching learning criterion, MDD patients exhibited impaired hit rate for both words and abstract paintings. A positive correlation between the number of categories completed on the WCST and hit rate for abstract paintings suggests that higher levels of executive functioning in MDD was associated with improved hit rate. In addition, MDD patients made significantly more temporal errors for both words and abstract paintings and the number of temporal errors made were inversely correlated with the number of categories completed on the WCST. On the other hand, the SCZ patients showed a correlation between new learning for words and item recognition, but not with execu-

tive function which implies a greater hippocampal rather than prefrontal involvement.

Both patient groups also showed stimuli nonspecific impairments for hit rate, forgetting rate and temporal errors. However, despite both MDD and SCZ patients showing similar levels of difficulty with new learning, hit rate, forgetting rate and temporal errors, associated prefrontal-dependent processes do not overlap. For the MDD group, WCST categories completed and conceptual level responses are associated only to hit rate and temporal errors for abstract paintings, which was not the case for SCZ patients. On the other hand, item recognition was associated with new learning for words only in SCZ. These findings, however, do not necessarily rule out the involvement of other executive and/or mnemonic processes that may be shared across both groups but not assessed in this study.

The MDD pattern of results is broadly consistent with a number of studies reporting that MDD patients have memory abnormalities that are linked to disorganised strategic memory processes (Behnken et al., 2010; Corrêa et al., 2012; Taconnat et al., 2010) that rely on the integrity of the prefrontal cortex (Dobbins et al., 2002; Moscovitch, 1992; Preston and Eichenbaum, 2013; Postle, 2006; Szczepanski and Knight, 2014). Surprisingly, we did not find any correlation with our measure of hippocampal function in MDD despite previous research showing reduced hippocampal activity in depressed individuals (Bremner et al., 2000; Koolschijn et al., 2009). Furthermore, if it occurs, the extent of medial temporal lobe contribution is likely to vary across different MDD patients, although the factors underlying this remain to be fully clarified, so a significant effect may not always be found except within a very large groups of patients.

This interpretation of our findings is consistent with morphometric and functional imaging studies, that report prefrontal impairments in MDD. A systematic review of volumetric magnetic resonance imaging (MRI) studies showed that patients with MDD in relation to healthy controls had large volume reductions in frontal regions, especially in the anterior cingulate and orbitofrontal cortex with smaller reductions in the prefrontal cortex (Koolschijn et al., 2009). Furthermore, MRI (Coffey et al., 1993, 1990; Soares and Mann, 1997), post-mortem (Thomas et al., 2002), and diffusion tensor imaging studies (Alexopoulos et al., 2002; Bae et al., 2006; Li et al., 2007; Nobuhara et al., 2006, 2004; Taylor et al., 2004) show deep white matter hyperintensities and microstructural abnormalities at the level of the prefrontal cortex in late-life depression. Functional imaging studies

have also demonstrated lower glucose metabolism and cerebral blood flow in the prefrontal cortex in depressed patients (Baxter et al., 1989; Mayberg et al., 1999; Nobler et al., 2000). White-matter integrity has also been shown to predict executive function, assessed by the Stroop task, in older adults with depression (Murphy et al., 2007).

Disruption to the ordering of events in MDD may be down to the fact that negative valence determines what is recalled and thereby disrupting the actual ordering of events. In contrast, the mechanism implicated in SCZ may be attributed to abnormal salience linked to dopamine function and impaired reward error prediction Howes and Nour (2016).

The finding that both MDD and SCZ patients have problems ordering events has clinical implications for these patients. For instance, MDD temporal ordering impairments may be linked to problems with goal directed behaviours, self-worth, and identity. Both MDD and SCZ patients have problems remembering the temporal order of events i.e., they have problems organising their experiences into temporally distinctive units which makes it difficult for them to discriminate among experiences with respect to time.

Impaired frontal function may underlie clinical features such as formal thought disorder. The putative mechanism might simply be that as the patient is speaking, they lose track of the focus or purpose of their speech such that the listener finds it difficult to follow. As for temporal order impairment, this might mean that the order of events is disrupted, and this may be related to the fact that items or events stand out without reference to their relevance or importance and therefore jeopardise the temporal order in which events occur. Research has shown that formal thought disorder in SCZ is linked to poor spatiotemporal integration Izawa and Yamamoto (2002).

A limitation that warrants mention is the effects of medication on memory performance. Two of our MDD patients were taking benzodiazepines at the time of testing which does have implications for memory related impairments (Valerie Curran, 1991). Similarly, three of our SCZ patients were treated with anticholinergic agents which have also been linked to memory related impairments (Joshi et al., 2019). However, when we conducted the same analysis with these MDD and SCZ patients removed, the main group effect remained significant. Therefore, we do not believe that the effects of benzodiazepines or anticholinergic agents can be entirely responsible for our findings. Furthermore, four of our MDD patients were medication free which implies that these individuals were in remission and so any abnormalities in these individuals suggests the structural changes underpinning these findings are stable and reflect trait markers. However, caution must be taken here as the sample is small and it may be that residual depressive symptoms contribute to the findings in all MDD cases. Thus, we cannot be certain whether these findings are features of an episode of illness or are trait markers of MDD.

In so far as depression contributes to both prefrontal and hippocampal dysfunction in MDD and SCZ, resolution would require a much larger sample size to control for sampling bias and Type II errors, and regression analysis or the use of structural and possibly functional MRI to discover how strongly each structural region relates to episodic memory deficits.

Declaration of Competing Interest

None.

References

Alexopoulos, G.S., Kiosses, D.N., Choi, S.J., Murphy, C.F., Lim, K.O., 2002. Frontal white matter microstructure and treatment response of late-life depression: a preliminary study. Am. J. Psychiatry 159, 1929–1932. doi:10.1176/appi.ajp.159.11.1929.

Allé, M.C., Potheegadoo, J., Köber, C., Schneider, P., Coutelle, R., Habermas, T., Danion, J.M., Berna, F., 2015. Impaired coherence of life narratives of patients with schizophrenia. Sci. Rep doi:10.1038/srep12934.

American Psychiatric Association, 1994. Diagnostic and statistical manual of mental disorders: DSM-IV, 4th ed. American Psychiatric Association, Washington (DC).

Bae, J.N., MacFall, J.R., Krishnan, K.R.R., Payne, M.E., Steffens, D.C., Taylor, W.D., 2006. Dorsolateral prefrontal cortex and anterior cingulate cortex white

matter alterations in late-life depression. Biol. Psychiatry 60, 1356–1363. doi:10.1016/j.biopsych.2006.03.052.

Baxter, L.R., Schwartz, J.M., Phelps, M.E., Mazziotta, J.C., Guze, B.H., Selin, C.E., Gerner, R.H., Sumida, R.M., 1989. Reduction of prefrontal cortex glucose metabolism common to three types of depression. Arch. Gen. Psychiatry 46, 243–250. doi:10.1001/archpsyc.1989.01810030049007.

Behnken, A., Schöning, S., Gerß, J., Konrad, C., de Jong-Meyer, R., Zwanzger, P., Arolt, V., 2010. Persistent non-verbal memory impairment in remitted major depression - Caused by encoding deficits? J. Affect. Disord. 122, 144–148. doi:10.1016/j.jad.2009.07.010.

Ben Malek, H., D'Argembeau, A., Allé, M.C., Meyer, N., Danion, J.M., Berna, F., 2019. Temporal processing of past and future autobiographical events in patients with schizophrenia. Sci. Rep doi:10.1038/s41598-019-50447-y.

Brébion, G., David, A.S., Jones, H.M., Ohlsen, R., Pilowsky, L.S., 2007. Temporal context discrimination in patients with schizophrenia: associations with auditory hallucinations and negative symptoms. Neuropsychologia. doi:10.1016/j.neuropsychologia.2006.08.009.

Brébion, G., Stephan-Otto, C., Cuevas-Esteban, J., Usall, J., Ochoa, S., 2020. Impaired memory for temporal context in schizophrenia patients with hallucinations and thought disorganisation. Schizophr. Res doi:10.1016/j.schres.2020.03.014.

Bremner, J.D., Narayan, M., Anderson, E.R., Staib, L.H., Miller, H.L., Charney, D.S., 2000. Hippocampal volume reduction in major depression. Am. J. Psychiatry 157, 115–118. doi:10.1176/ajp.157.1.115.

Coffey, C.E., Figiel, G.S., Djang, W.T., Weiner, R.D., 1990. Subcortical hyperintensity on magnetic resonance imaging: a comparison of normal and depressed elderly subjects. Am. J. Psychiatry 147, 187–189. doi:10.1176/ajp.147.2.187.

Coffey, C.E., Wilkinson, W.E., Weiner, R.D., Parashos, L.A., Djang, W.T., Webb, M.C., Figiel, G.S., Spritzer, C.E., 1993. Quantitative cerebral anatomy in depression: a controlled magnetic resonance imaging study. Arch. Gen. Psychiatry 50, 7–16. doi:10.1001/archpsyc.1993.01820130009002.

Conway, M.A., 2005. Memory and the self. J. Mem. Lang doi:10.1016/j.jml.2005.08.005.

Corrêa, M.S., Balardin, J.B., Caldieraro, M.A.K., Fleck, M.P., Argimon, I., Luz, C., Bromberg, E., 2012. Contextual recognition memory deficits in major depression are suppressed by cognitive support at encoding. Biol. Psychol. 89, 293–299. doi:10.1016/j.biopsycho.2011.11.001.

Dobbins, I.G., Foley, H., Schacter, D.L., Wagner, A.D., 2002. Executive control during episodic retrieval: Multiple prefrontal processes subserve source memory. Neuron.

Downes, J.J., Mayes, A.R., MacDonald, C., Hunkin, N.M., 2002. Temporal order memory in patients with Korsakoff's syndrome and medial temporal amnesia. Neuropsychologia. doi:10.1016/S0028-3932(01)00172-5.

Drakeford, J.L., Edelstyn, N.M.J., Oyebode, F., Srivastava, S., Calthorpe, W.R., Mukherjee, T., 2010. Recollection deficiencies in patients with major depressive disorder. Psychiatry Res. 175. doi:10.1016/j.psychres.2008.08.010.

DuBrow, S., Davachi, L., 2014. Temporal memory is shaped by encoding stability and intervening item reactivation. J. Neurosci doi:10.1523/JNEUROSCI.2535-14.2014.

Ekstrom, A.D., Copara, M.S., Isham, E.A., Wang, W.chun, Yonelinas, A.P., 2011. Dissociable networks involved in spatial and temporal order source retrieval. Neuroimage. doi:10.1016/j.neuroimage.2011.02.033.

Elvevåg, B., Egan, M.F., Goldberg, T.E., 2000. Memory for temporal order in patients with schizophrenia. Schizophr. Res. 46, 187–193. doi:10.1016/S0920-9964(00)00014-1.

Friendly, M., Franklin, P.E., Hoffman, D., Rubin, D.C., 1982. The Toronto word pool: norms for imagery, concreteness, orthographic variables, and grammatical usage for 1,080 words. Behav. Res. Methods Instrum. 14, 375–399. doi:10.3758/BF03203275.

Habermas, T., Ott, L.-M., Schubert, M., Schneider, B., Pate, A., 2008. Stuck in the past: negative bias, explanatory style, temporal order, and evaluative perspectives in life narratives of clinically depressed individuals. Depress. Anxiety doi:10.1002/da.20389.

Heaton, R.K.K., Chelune, G.J., Talley, J.L., Kay, G.G., Curtiss, G., 1989. Wisconsin Card Sorting Test. Psychological Assessment Resources Inc, Odessa, FL.

Hartlage, S., Alloy, L.B., Vázquez, C., Dykman, B., 1993. Automatic and effortful processing in depression. Psychol. Bull doi:10.1037/0033-2909.113.2.247.

Hertel, P.T., Milan, S., 1994. Depressive deficits in recognition: dissociation of recollection and familiarity. J. Abnorm. Psychol. 103, 736–742. doi:10.1037/0021-843X.103.4.736.

Holm, T., Thomsen, D.K., Bliksted, V., 2016. Life story chapters and narrative self-continuity in patients with schizophrenia. Conscious. Cogn doi:10.1016/j.concog.2016.08.009.

Howard, M.W., Shankar, K.H., Aue, W.R., Criss, A.H., 2015. A distributed representation of internal time. Psychol. Rev doi:10.1037/a0037840.

Howes, O.D., Nour, M.M., 2016. Dopamine and the aberrant salience hypothesis of schizophrenia. World Psychiatry. doi:10.1002/wps.20276.

Izawa, R., Yamamoto, S., 2002. Spatio-temporal disintegration of visual perception in schizophrenia as revealed by a novel cognitive task, the Searchlight Test. Schizophr. Res. doi:10.1016/S0920-9964(00)00116-X.

Jenkins, L.J., Ranganath, C., 2016. Distinct neural mechanisms for remembering when an event occurred. Hippocampus. doi:10.1002/hipo.22571.

Jermann, F., Van Der Linden, M., Adam, S., Ceschi, G., Perroud, A., 2005. Controlled and automatic uses of memory in depressed patients: effect of retention interval lengths. Behav. Res. Ther. 43, 681–690. doi:10.1016/j.brat.2004.07.009.

Joshi, Y.B., Thomas, M.L., Hochberger, W.C., Bismark, A.W., Treichler, E.B.H., Molina, J., Nungaray, J., Cardoso, L., Sprock, J., Swerdlow, N.R., Light, G.A., 2019. Verbal learning deficits associated with increased anticholinergic burden are attenuated with targeted cognitive training in treatment refractory schizophrenia patients. Schizophr. Res. doi:10.1016/j.schres.2019.01.016.

Koolschijn, P.C.M.P., Van Haren, N.E.M., Lensvelt-Mulders, G.J.L.M., Hulshoff Pol, H.E., Kahn, R.S., 2009. Brain volume abnormalities in major depressive disorder: a meta-

analysis of magnetic resonance imaging studies. Hum. Brain Mapp. 30, 3719–3735. doi:10.1002/hbm.20801.

Lezak, M.D., Howieson, D.B., Loring, D.W., Hannay, H.J., Fischer, J.S., 2004. Neuropsychological assessment, 4th ed. Oxford University Press.

Li, L., Ma, N., Li, Z., Tan, L., Liu, J., Gong, G., Shu, N., He, Z., Jiang, T., Xu, L., 2007. Prefrontal white matter abnormalities in young adult with major depressive disorder: a diffusion tensor imaging study. Brain Res 1168, 124–128. doi:10.1016/j.brainres.2007.06.034.

Maxwell, S.E., Delaney, H., 2004. Designing experiments and analyzing data: a model comparison perspective. Chapter 15. mixed models. Designing Experiments and Analyzing Data: A Model Comparison Perspective.

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, 675–682. doi:10.1176/ajp.156.5.675.

McGraw, K.O., Wong, S.P., 1996. Forming inferences about some intraclass correlation coefficients. Psychol. Methods doi:10.1037/1082-989X.1.1.30.

Moscovitch, M., 1992. Memory and working-with-memory: A component process model based on modules and central systems. J. Cogn. Neurosci.

Murphy, C.F., Gunning-Dixon, F.M., Hoptman, M.J., Lim, K.O., Ardekani, B., Shields, J.K., Hrabe, J., Kanellopoulos, D., Shanmugham, B.R., Alexopoulos, G.S., 2007. White-matter integrity predicts stroop performance in patients with geriatric depression. Biol. Psychiatry 61, 1007–1010. doi:10.1016/j.biopsych.2006.07.028.

Naya, Y., Chen, H., Yang, C., Suzuki, W.A., Squire, L.R., 2017. Contributions of primate prefrontal cortex and medial temporal lobe to temporal-order memory. Proc. Natl. Acad. Sci. U. S. A. doi:10.1073/pnas.1712711114.

Nelson, H.E., 1982. The National Adult Reading Test (NART): Test Manual. NFER-Nelson, Wind. UK.

Nobler, M.S., Roose, S.P., Prohovnik, I., Moeller, J.R., Louie, J., Van Heertum, R.L., Sackeim, H.A., 2000. Regional cerebral blood flow in mood disorders, V.: Effects of antidepressant medication in late-life depression. Am. J. Geriatr. Psychiatry 8, 289–296.

Nobuhara, K., Okugawa, G., Minami, T., Takase, K., Yoshida, T., Yagyu, T., Tajika, A., Sugimoto, T., Tamagaki, C., Ikeda, K., Sawada, S., Kinoshita, T., 2004. Effects of electroconvulsive therapy on frontal white matter in late-life depression: a diffusion tensor imaging study. Neuropsychobiology 50, 48–53. doi:10.1159/000077941.

Nobuhara, K., Okugawa, G., Sugimoto, T., Minami, T., Tamagaki, C., Takase, K., Saito, Y., Sawada, S., Kinoshita, T., 2006. Frontal white matter anisotropy and symptom severity of late-life depression: a magnetic resonance diffusion tensor imaging study. J. Neurol. Neurosurg. Psychiatry 77, 120–122. doi:10.1136/jnnp.2004.055129.

Overall, J.E., Gorham, D.R., 1962. The brief psychiatric rating scale. Psychol. Rep 10, 799–812. doi:10.2466/pr0.1962.10.3.799.

Preston, A.R., Eichenbaum, H., 2013. Interplay of hippocampus and prefrontal cortex in memory. Curr. Biol. doi:10.1016/j.cub.2013.05.041.

Postle, B.R., 2006. Working memory as an emergent property of the mind and brain. Neuroscience. doi:10.1016/j.neuroscience.2005.06.005.

Rizzo, L., Danion, J.M., Van Der Linden, M., Grangé, D., 1996. Patients with schizophrenia remember that an event has occurred, but not when. Br. J. Psychiatry 168, 427–431. doi:10.1192/bjp.168.4.427.

Schwartz, B.L., Deutsch, L.H., Cohen, C., Warden, D., Deutsch, S.I., 1991. Memory for temporal order in Schizophrenia. Biol. Psychiatry doi:10.1016/0006-3223(91)90218-B.

Snodgrass, J.G., Corwin, J., 1988. Pragmatics of measuring recognition memory: applications to dementia and amnesia. J. Exp. Psychol. Gen. 117, 34–50. doi:10.1037/0096-3445.117.1.34.

Soares, J.C., Mann, J.J., 1997. The anatomy of mood disorders—review of structural neuroimaging studies. Biol. Psychiatry 41, 86–106. doi:10.1016/S0006-3223(96)00006-6.

Sullivan, E.V., 1997. Patterns of content, contextual, and working memory impairments in schizophrenia and nonamnesic alcoholism. Neuropsychology. doi:10.1037/0894-4105.11.2.195.

Szczepanski, S.M., Knight, R.T., 2014. Insights into Human Behavior from Lesions to the Prefrontal Cortex. Neuron. doi:10.1016/j.neuron.2014.08.011.

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, 719–727. doi:10.1080/13803390903512645.

Taylor, W.D., MacFall, J.R., Payne, M.E., McQuoid, D.R., Provenzale, J.M., Steffens, D.C., Krishnan, R.R., 2004. Late-life depression and microstructural abnormalities in dorsolateral prefrontal cortex white matter. Am. J. Psychiatry 161, 1293–1296. doi:10.1176/appi.ajp.161.7.1293.

Thomas, A.J., O'Brien, J.T., Davis, S., Ballard, C., Barber, R., Kalaria, R.N., Perry, R.H., 2002. Ischemic basis for deep white matter hyperintensities in major depression: a neuropathological study. Arch. Gen. Psychiatry 59, 785–792. doi:10.1001/archpsyc.59.9.785.

Tulving, E., 2002. Episodic memory: from mind to brain. Ann. Rev. Psychol doi:10.1146/annurev.psych.53.100901.135114.

Valerie Curran, H., 1991. Benzodiazepines, memory and mood: a review. Psychopharmacology (Berl). doi:10.1007/BF02316856.

Vogel, D.H.V., Krämer, K., Schoofs, T., Kupke, C., Vogeley, K., 2018. Disturbed experience of time in depression—evidence from content analysis. Front. Hum. Neurosci doi:10.3389/fnhum.2018.00066.

Wang, F., Diana, R.A., 2017. Temporal context in human fMRI. Curr. Opin. Behav. Sci doi:10.1016/j.cobeha.2017.06.004.

Waters, F.A.V., Maybery, M.T., Badcock, J.C., Michie, P.T., 2004. Context memory and binding in schizophrenia. Schizophr. Res doi:10.1016/S0920-9964(03)00221-4.

Wearden, J., O'Donoghue, A., Ogden, R., Montgomery, C., 2014. Subjective duration in the laboratory and the world outside, in: subjective time: the philosophy. Psychol., Neurosci. Temporality doi:10.7551/mitpress/8516.003.0022.

Wechsler, D., 1997. Wechsler Memory Scale, Third Ed. Psychol. Corp.