

Transdiagnostic distortions in autobiographical memory recollection

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Abstract

Distortions in the recollection of autobiographical memories are a transdiagnostic feature of multiple mental health difficulties including mood, anxiety, stressor-related, eating and psychotic disorders. These distortions can be categorized into three broad domains: relatively increased accessibility, affective impact and degree of detail for memories of negatively valenced events with corollary reductions along these dimensions for positive memories; unwanted and distressing intrusive memories of salient past events such as traumas; and a marked relative difficulty in the voluntary retrieval of specific, emotive autobiographical episodes in favour of general themes aggregated across multiple episodes or across extended autobiographical periods. In this Review, we summarize basic science investigations that have carefully mapped the nature of these recollective distortions transdiagnostically across a range of syndromes, and elucidate their causal roles in the onset, maintenance and recovery from disorder. The amenability of these distortions to improvement through cognitive training has led to the translation of this basic science into a number of exciting memory-based interventions that target distortions to generate downstream improvements in clinical symptoms. We review and evaluate these interventions. Finally, we offer a theoretical framework that integrates the basic and clinical research across these three domains and suggest key future research directions.

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Introduction

Retrieving and reliving autobiographical memories (memories for past personal experiences) either as specific episodes ('my birthday last year') or as generalized summaries of event categories ('my childhood family holidays') or periods of time ('my time at university')¹ profoundly shapes human mental life. Autobiographical retrospection provides sustenance for social interactions², generates blueprints and solutions to help navigate future plans and problems^{3–5}, and sculpts affective experiences⁶. The interwoven store of autobiographical memories also scaffolds identity and supports dynamic and evolving self-models¹. These self-models combine autobiographical knowledge and memories with hierarchically nested long-, medium- and short-term personal goals, contextualized by ongoing perception of the world and its opportunities and contingencies in relation to those goals and one's capacity to realise them^{7–10}.

The ability to remember past experiences supports and enables myriad beneficial cognitive skills. However, dysfunctional influences on the recollection of past events are a transdiagnostic feature of many psychiatric conditions. Recollective autobiographical memory difficulties include disruptive intrusions of past traumas in post-traumatic stress disorder (PTSD)^{11,12}, painful yearning for lost loved ones in complicated grief¹³, and an increased focus on distressing autobiographical themes in disorders of mood and anxiety^{14–19}. These patterns of recollection define the mental lives of those with these syndromes and there is good evidence that these diverse problems are causally involved in disorder onset and maintenance^{20,21}. This putative causal role for disturbances in autobiographical memory recollection in diverse domains of poor mental health has led to a burgeoning interest in memory-based interventions (memory therapeutics). There is promising, albeit preliminary, evidence that treatments targeting these disturbances can reap therapeutic benefits.

In this Review, we first highlight key basic research findings and theoretical accounts in three domains of distorted autobiographical memory recollection that can have a transdiagnostic impact on mental health: recollective biases; involuntary recollection; and reduced memory specificity. Next, we consider the main pre-clinical and clinical interventions that seek to correct these distortions to ameliorate symptoms of mental ill-health. We then draw together the somewhat siloed research in these separate memory domains to propose an integrated transdiagnostic clinical framework, and conclude with an evaluation of the current status of the evidence and suggestions for future research.

We focus predominantly on autobiographical memory as a cognitive process, rather than its underlying neurobiology (for which there are already a number of excellent summaries)^{22,23}, as it is these cognitive insights that have had the most influence on the development of therapeutics. We also focus on distortions of memory recollection and the novel therapeutics that target these processes, because the difficulties and differences in the way that memories are originally encoded and/or processed have already been discussed in prior reviews²⁴.

Domains of recollective memory distortion

There are three key domains of distorted autobiographical memory recollection that can have a transdiagnostic impact on mental health: recollective biases that favour negatively valenced past experiences over positively valenced past experiences; the involuntary and intrusive recollection of distressing memories such as traumas; and difficulties with recollecting specific personal memories in favour of generalized summaries of past experience. There are already in-depth narrative

reviews of each of these domains^{24–26} and we do not seek to recapitulate those here. Rather, in this section we aim to highlight the key studies within each domain that have made the most substantial impact in advancing understanding; to evaluate for each domain the evidence that the recollective process under consideration has a causal role in the onset, maintenance or recovery from mental health problems; and evaluate the extent to which these recollective distortions are transdiagnostic indicators of prognosis and wellbeing. Our criteria for causality and transdiagnosticity are described in Box 1, and a summary of the status of this collective evidence for causality and transdiagnosticity is presented in Fig. 1.

Affective recollective biases

Three inter-related processes are proposed to underlie affective recollective biases during periods of poor mental health: enhanced access to negative (versus positive) autobiographical memories; impoverished experiential salience for recollected positive (versus negative) memories; and greater diversity of emotions allied to recollected negative (versus positive) memories (Fig. 2).

Biased recollection. There is good evidence that the preferential recollection of negative autobiographical information, assessed via laboratory tasks, where recollection is typically prompted by verbal or pictorial cues or with reference to autobiographical time periods, is a transdiagnostic phenomenon. Case-control studies have demonstrated the presence of negative memory bias in anxiety^{16,17}, mood²⁷, and trauma- and stressor-related^{28,29} disorders relative to healthy comparison groups. Correlations between degree of bias towards negative memories and symptom severity have also been reported in depression and anxiety^{30,31}, but this does not always replicate³².

Negative recollective biases persist into depressive remission^{33,34}, and are present in people at elevated risk who have never been depressed³⁵, suggesting that these biases are a vulnerability factor for depression (for meta-analysis, see ref. ³⁶). However, similar evidence has not been observed for other remitted disorders or at-risk samples. Furthermore, no studies so far have evaluated longitudinally whether negative memory biases predict the first onset of disorder. In the laboratory, inducing negative mood in healthy individuals increases the accessibility of negative memories³⁷, but evidence is mixed as to whether inducing anxiety produces biased retrieval of threat-related memories^{38,39}. Negative memory bias might therefore be considered a transdiagnostic feature of mental health problems, whereas evidence for its causal role is currently incomplete.

Impoverished positivity. Among mentally healthy participants, ratings of subjective affective intensity allied to positive events tend to decrease less between the time of the original event and when it is later recollected, relative to affective ratings for negative events⁴⁰. This so-called fading affect bias is postulated to maintain and enhance good mental health⁴⁰. Case-control studies have demonstrated that the fading affect bias is attenuated for individuals with elevated anxiety⁴¹ or depressive symptoms⁴².

Autobiographical memory imageability and detail are also diminished when recollecting positive memories in depression^{43,44}, PTSD⁴⁵ and social anxiety⁴⁶. In addition, attenuated affective experience for positive memories is associated with reductions in the capacity to lift transient low mood^{47,48}, and correlations have been observed between reduced positivity of memories and severity of depression, anxiety and stressor-related symptoms⁴⁹.

Box 1

Guidelines for evaluating causation and transdiagnosticity

In this Review, we apply established criteria to evaluate the status of the evidence for the extent to which each process under examination is causally implicated in mental ill-health, and the extent to which each processes can be considered transdiagnostic.

Guidelines for causation

In 1965, Sir Austin Bradford Hill proposed a set of guidelines for inferring causation between a variable of interest and a health outcome¹⁷⁶. Advances in epidemiology, research methodology and data science have prompted updates to Bradford Hill's original guidelines¹⁷⁶ that have meaningfully grouped them into three categories: direct evidence; mechanistic evidence; and parallel evidence¹⁷⁸.

Direct evidence comprises both experimental and observational studies showing that a probabilistic association between the variable of interest and the outcome is causal. Randomized experimental studies (including randomized controlled trials (RCTs)) are the gold standard and the guidelines indicate that the size of the relationship needs to exceed the combined effects of any residual risk-of-bias¹⁷⁸. Similarly, for observational studies the size of the effect should exceed the sum of the effects of plausible confounding variables. For observational research, there should also be appropriate temporal and spatial proximity between the variable and the outcome, along with dose responsiveness (a systematic relationship between changes in the variable of interest and the outcome) and/or reversibility

(where changes in the outcome lead to changes in the variable of interest).

Mechanistic evidence refers to how (rather than whether) the variable of interest leads to changes in the outcome. Mechanistic evidence covers investigations that explicitly focus on mechanisms either embedded within direct-evidence studies such as RCTs or as stand-alone studies that have identified a 'plausible mechanism'. Mechanistic evidence also includes a notion of coherence, that is, whether the mechanistic account coheres with other information about how the processes and mechanisms involved behave.

Finally, parallel evidence refers to the extent to which the findings have been replicated either directly or conceptually in similar studies and the quality of that aggregated evidence. Meta-analyses of multiple studies are the most compelling indicator of parallel evidence.

Transdiagnosticity

A transdiagnostic variable of interest or relationship between variables are ones that either pertain to more than one psychiatric diagnosis or that relate to broader mental ill-health constructs that cut across diagnostic boundaries such as symptoms or higher-order factors such as 'internalizing' and 'externalizing'¹⁷⁹. A process that is implicated across at least four or more disorders shows 'strong' evidence of transdiagnosticity, whereas a process that is present in only two or three disorders shows 'preliminary' evidence of transdiagnosticity¹⁷⁷.

There is sparse evidence for a causal role of impoverished positive memories in driving mental health problems. Some data are consistent with degradation of affective re-experiencing of positive memories in at-risk people, indicative of vulnerability. For example, young adults at familial risk of depression tend to experience positive memories from an external-observer perspective, rather than from a first-person perspective, which reduces the intensity of associated affect⁵⁰. However, prospective relationships between positive memory quality and mental health problems have not yet been evaluated.

Affective diversity. Reduced positive affect associated with recollected specific events is mirrored by a restricted range of positive emotions about the autobiographical past more generally. Life narratives (sometimes referred to as the 'life story') provide stability and consistency to the sense of self over time^{51,52}. These longer narratives contain substantially more negative than positive content for individuals with depression⁵³, post-traumatic stress⁵⁴, schizophrenia⁵⁵ and personality disorders⁵⁶. Individuals experiencing depression and post-traumatic stress also report a greater diversity (indexed as the number of different emotions reported) of negative emotions and a reduced diversity of positive emotions when describing their autobiographical past compared to healthy control participants^{53,54}. Such case-control studies dominate this literature. There are no studies that investigate differential granularity prior to first onset or remission of disorder nor longitudinal studies. Therefore, no conclusions can be drawn about the causal influence of affective diversity profiles on mental health problems.

Summary of recollective biases. Autobiographical recollection across a range of emotional disorders is characterized by systematic biases favouring negative over positive memories. Negative memories are accessed more easily, and the recollective experience is more emotionally intense, vivid, detailed and affectively diverse than for positive memories. Most research in this domain has focused on mood disorders, but negative memory biases have also been observed in anxiety, psychotic and trauma-related disorders, demonstrating strong evidence of transdiagnosticity. Much of the reviewed research applies case-control designs, with some evidence suggesting that affective biases have a role in maintaining symptoms. Retrospective or prospective cohort studies investigating mental health prognosis, relapse or recovery are lacking.

Theoretically, negative recollective biases have been conceptualized in terms of mood-congruent retrieval, whereby current mood facilitates recollection of memories matched in affective valence^{57,58}. More elaborate proposals, such as the schema-based account integral to cognitive therapy⁵⁹, or predictive processing instantiations of that account^{60,61}, postulate biased processing of memories that align with currently active mental models of the self⁶², rather than simply with current mood. Thus, these proposals offer an account of preferential access as well as increased vividness and salience of negative autobiographical memories. For those with mental health problems, these active self-models are constructed around themes of personal failure, threat and/or worthlessness. Consequently, autobiographical memories are processed as a function of their relevance: negative

		Negative memory bias	Reduced positivity	Differential granularity	Intrusions	Reduced specificity
Transdiagnosticity						
Causally implicated in onset/remission	Direct evidence: experimental					
	Direct evidence: observational					
	Parallel evidence: replicability					
	Mechanistic evidence: plausible					
	Mechanistic evidence: coherence					
Causally implicated in maintenance	Direct evidence: experimental					
	Direct evidence: observational					
	Parallel evidence: replicability					
	Mechanistic evidence: plausible					
	Mechanistic evidence: coherence					

Strong

Moderate

Preliminary

Absent

Fig. 1 | Summary evidence for causality and transdiagnosticity. Summary of the quality and extent of the evidence for causality and transdiagnosticity across the three domains of autobiographical recollection (see Box 1 for the evaluation criteria). The quality of the evidence supporting causality is categorized according to the following criteria (based on ref. 176): absent, no studies to date; preliminary, a small number of studies (fewer than four); moderate, a moderate number of studies (more than three but fewer than ten), ideally including a systematic or narrative review; and strong, a larger number of studies (more than ten), ideally including a meta-analytic review where at least two studies are large with low risk-of-bias. The quality of the evidence supporting transdiagnosticity is categorized according to the following criteria (based on ref. 177): absent, evidence for only one disorder; preliminary, present in two to three disorders; and strong, present in four or more disorders.

autobiographical memories that echo these representational themes receive enhanced processing and inconsistent positive memories receive diminished processing. By contrast, mentally well individuals experience facilitated access to, and augmented experience of, positive autobiographical memories⁶ that align with the putative positive models of the self that underpin good mental health.

Involuntary recollection

The intrusive and involuntary recollection of past autobiographical experiences ranging from affectively benign recollections to intrusive reliving of life-changing past traumas is a ubiquitous feature of human mental life⁶³. There is strong evidence from case-control studies that repeated involuntary recollection of highly emotive memories is a transdiagnostic phenomenon characterizing PTSD, mood, eating and anxiety disorders (reviewed previously^{26,64}). The evidence for a causal role of intrusive memories in mental health problems is less compelling. A small number of studies indicate that intrusions prospectively predict poorer prognosis for depression and anxiety^{65,66}. However, longitudinal studies exploring whether the presence and frequency of intrusive memories predate disorder onset, or remain evident as a vulnerability factor after remission, are sparse and inconclusive (see ref. 67 for a review and discussion in the context of PTSD). Establishing causality is complicated by the fact that intrusions are often measured as a symptom of disorder. Theoretical accounts of involuntary recollection emphasize that memories intrude because they are relevant to current concerns such as unresolved traumatic experience¹⁴ or to models (schemas) of the self (for example, schemas characterizing the ‘self-as-vulnerable’) and world (for example, schemas characterizing the ‘world-as-dangerous’) that

are either longstanding from a prior history of adversity or that have developed following a trauma. One proposed mechanism underlying this susceptibility to involuntary recollection is a reduced generalized ability to inhibit unwanted memories. That is, there is a reduced ability to prevent unwanted memories from entering conscious awareness when faced with relevant intrinsic or extrinsic cues^{11,26}. For example, someone experiencing symptoms of post-traumatic stress following a violent assault might find it difficult to inhibit intrusive memories of the assault in the face of reminders such as items of clothing similar to that worn by the assailant, or sounds that occurred at the time of the event (for example, running footsteps); consequently, this person might be more vulnerable to developing a disorder such as PTSD. Laboratory research seeking to elucidate such memory inhibition in the face of reminders has used experimental tasks to assay inhibitory ability and examine the degree to which it is compromised in clinical groups. For example, in the ‘think-no-think’ task participants first learn a series of word pairs (for example, ‘chair-tree’). They are then presented just with the cue (‘chair’) and instructed to try not to think about, or to suppress recollection of, the learned pair (‘-tree’)⁶⁸. After a period of such ‘no-think’ training, participants are presented with the original cues and are asked to recollect the pairs. A meta-analysis⁶⁹ found that healthy individuals successfully learn to suppress or inhibit their memory for the paired words, evidenced by poorer memory for word pairs subjected to no-think training relative to control word pairs (standardized mean difference 0.28, 95% CI 0.14–0.43). By contrast, this inhibition effect is smaller or absent for those experiencing depression (standardized mean difference 0.05, 95% CI –0.19 to 0.29) and anxiety (standardized mean difference –0.21, 95% CI –0.41 to –0.02)⁶⁹.

Similar results emerge using a retrieval-induced forgetting methodology⁷⁰. In the retrieval-induced forgetting paradigm, participants learn associations between cues and multiple targets (for example, 'chair–tree' and 'chair–light'). They are then presented with the cue ('chair') but instructed to repeatedly retrieve only one of the learned pairs (for example, '–light'). In the final test phase, participants are asked to retrieve all of the learned pairs associated with the cues. In healthy individuals, repeated retrieval of one of the pairs ('–light') in response to a cue ('chair') reduces the ability to retrieve the competing pair ('–tree'), purportedly owing to associative inhibition between the memory traces of competing pairs^{71,72}. The effect size for such retrieval-induced forgetting is moderated by anxiety⁷³ and depression^{74,75}, such that the experience of symptoms reduces the size of the effect, suggesting that the associative inhibitory mechanisms are compromised.

The retrieval-induced forgetting paradigm has also been used to investigate suppression of emotional memories of autobiographical experiences. For example, children completing a retrieval-induced forgetting task where they repeatedly practised retrieving positive associated details of a physically painful experience (for example, 'being brave'), but did not practice retrieval of negative associates (for example, 'crying a lot'), were less accurate at later recalling negative relative to positive details⁷⁶. Similarly, repeated retrieval practice of personal beliefs leads to reductions in the believability of un-practised competing beliefs regarding the same information^{77,78}.

This laboratory research on memory inhibition provides preliminary evidence that involuntary memory intrusions might be underpinned by a generally weakened capacity for mnemonic inhibition⁶⁹. Thus, cognitive training to strengthen this capacity might have therapeutic potential. However, studies directly examining inhibition of autobiographical memories or personal material are sparse relative to studies of memory for words or pictures. Furthermore, much of this proof-of-principle work has been conducted with healthy participants rather than those with mental health problems. Finally, although case-control studies have demonstrated suppression differences between those who do versus those who do not develop PTSD after trauma⁷⁹, longitudinal evidence of a causal role in symptom development has not been established.

Reduced memory specificity

A compromised ability to deliberately and intentionally recollect memories for individual past events – reduced memory specificity – is an established feature of mood^{20,80,81}, trauma- and stressor-related^{82,83}, and psychotic⁸⁴ disorders, with some evidence in eating^{85,86} and personality⁸⁷ disorders. Indeed, a transdiagnostic meta-analysis of 85 case-control studies provides strong evidence that those with a diagnosis of any mental health disorder experience poorer retrieval of specific memories (Hedges' $g = 0.86$, 95% CI -1.03 to -0.70) relative to those with no diagnosis⁸⁸.

Memory specificity is typically assessed using the autobiographical memory task⁸⁹. This is a cued-recall paradigm in which individuals are asked to retrieve a memory of a specific, individual event in response to positive, negative or emotionally neutral cue words (for example, recollecting 'handing in my final year psychology exam paper, believing I had done poorly' to the cue 'exam'). Reduced ability to successfully retrieve specific memories occurs for word cues of any valence across diagnoses (for meta-analysis, see ref. ⁸⁸). In place of the required specific memories, individuals with mental health problems tend to recall general memories about their past that summarize categories of events (for example, 'I never did well at exams') or relate to extended periods of time (for example, 'I felt like a failure all through university').

Meta-analytic evidence indicates a causal effect of reduced specificity on symptoms. Memory specificity predicts future depressive symptoms, over and above the effects of current symptoms, ($\beta = -0.16$, 95% CI -0.25 to -0.06)²⁰, and persists even when symptoms remit (reduced specificity relative to never-depressed controls, Hedges' $g = -0.31$, 95% CI -0.54 to -0.09)⁸¹, suggesting that reduced specificity is not simply a byproduct of acute disorder. There are also reports that reduced specificity predicts the primary onset of symptoms^{90–92}. These prospective relationships have been established for PTSD²¹, anxiety⁹¹ and depressive symptoms²⁰, but not for other symptom clusters. Meta-analysis supports longer-term effects of memory specificity on depression prognosis (up to 1 year later⁹³, although the effect does attenuate over time²⁰); related research demonstrates that recollection of specific, positive memories prospectively predicts fewer negative self-cognitions, lower morning cortisol and lower depressive symptoms

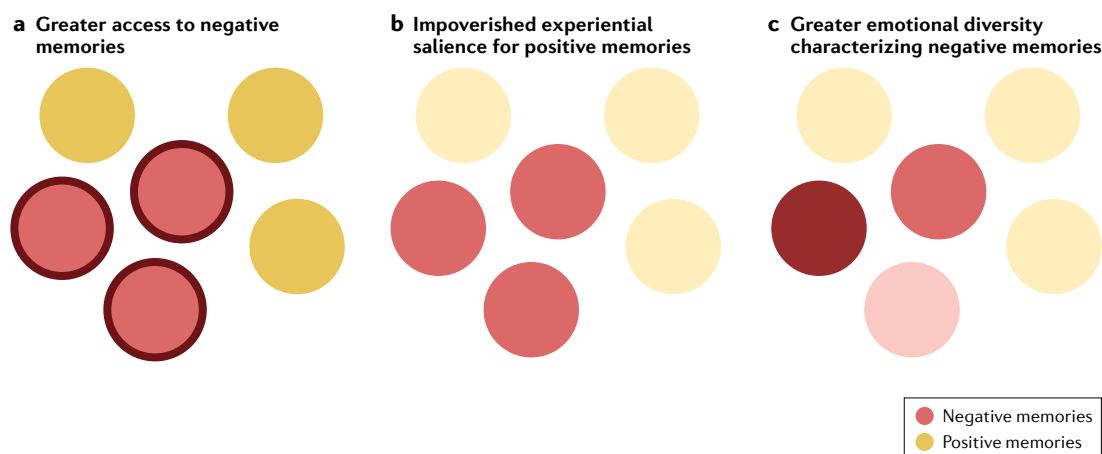


Fig. 2 | Affective recollective biases. Three interrelated processes underlie affective recollective biases for negative (red) versus positive (yellow) memories during periods of poor mental health. **a**, Greater access (denoted by outline thickness) to negative versus positive memories. **b**, Impoverished experiential

salience (denoted by lighter shading) for positive versus negative memories. **c**, Greater emotional diversity (denoted by variation in shading between memories) characterizing negative versus positive memories.

at 1-year follow-up in adolescents exposed to early life adversity⁹⁰. However, the effect of memory specificity on later symptoms does not always replicate, particularly in younger and/or nonclinical samples⁹¹. There is also experimental evidence that inducing negative mood in non-depressed participants leads to reduced memory specificity⁹⁴ suggesting that the causal relationship between low mood and specificity might be bidirectional. Moreover, because memory specificity has been primarily assessed using the autobiographical memory task, these results might be task-specific.

The CaRFAX model¹², which elaborates upon the self-memory system framework¹, is arguably the most influential theoretical model of reduced specificity. According to this model, the recollective process involves searching a hierarchical store of personal memories, typically starting from generalized memories at the top ('I never did well at exams') down to specific episodes ('handing in my final year Psychology exam paper, believing I had done poorly'). For individuals with mental health difficulties, the search is more likely to terminate at the level of generic recollection. This truncated memory search might occur because the general memory representations are more strongly activated than specific memory representations in those with mental health problems and thereby 'capture' the memory search. At the same time, the executive control capacity to resist such capture and maintain the memory search might be poorer in those with mental health difficulties. Alternatively, memories for specific highly distressing past events might be actively inhibited in those with mental health problems, making such memories relatively opaque to the search process¹².

Reduced memory specificity might affect mental health problems via two key mechanistic pathways¹². First, access to specific memories is important for everyday cognitive skills integral to successful psychological functioning, such as problem solving⁹⁵, planning for and imagining future events^{4,96}, and fostering intimacy in social relationships through reminiscence of shared experiences². Reduced memory specificity compromises these skills^{4,96}. One study provided support for a mediated effect of reduced specificity on general distress via poorer social support⁹⁷ but, in general, longitudinal studies evaluating these proposed mediation effects are lacking.

Second, retrieval of a specific autobiographical memory can set a boundary on generalized beliefs about the self or world that are inconsistent with that memory, thereby delimiting the breadth of impact of those beliefs on mental health. For example, in one study⁹⁸ individuals first rated how well a negative personality trait (such as 'boring') described them. They were then instructed to recollect a specific memory that was inconsistent with that trait. Healthy individuals were faster to recollect specific memories that were inconsistent with the negative traits (for example, 'I made a colleague laugh yesterday') compared to control trials where the trait word was not evaluated in a self-referential manner (participants simply provided the dictionary definition of the trait). These results suggest that evaluating the negative traits in relation to the self-primed faster recollection of a positive, specific memory as counter-evidence, thereby setting a boundary on the perceived pervasiveness of the negative trait. By contrast, faster retrieval of inconsistent specific positive memories following self-evaluation of negative traits (compared to the dictionary definition) was not observed in depressed individuals. This absence of primed access to specific counter-evidence that contradicts negative generalizations about the self is consistent with the relatively unbounded negative self-beliefs characterizing depression⁹⁸. Evidence for this delimiting role for specific memories is preliminary and replication alongside longitudinal investigation is now needed.

There is initial parallel evidence from literature on other cognitive biases that reduced memory specificity is associated with other forms of generalized cognition that characterize emotional disorders. Rumination and worry about distressing general autobiographical themes are transdiagnostic factors that maintain symptoms⁹⁹. Rumination, worry and reduced memory specificity all represent an abstracted mode of processing in which an individual fails to localize cognition to a specific situation (for example, an argument with a friend) and instead centralizes cognition within broader, more global contexts (for example, all relationships). Indeed, theoretical models, including the CaRFAX model, propose that rumination and reduced memory specificity feed into one another^{12,100}. This idea is supported by laboratory experiments demonstrating that inducing increases in rumination reduces memory specificity, and vice versa^{101,102}. Interestingly, however, a correlation between memory specificity and rumination is not well supported by meta-analysis combining clinical and non-clinical samples (pooled Cohen's *d* for the correlation -0.05 , $P = 0.09$)¹⁰³. One explanation for this small and non-significant correlation is that the relationship between memory specificity and rumination is predicated on the existence and activation of maladaptive models of the self in emotional disorders, and might therefore only be observed in clinical samples^{104–106}. Indeed, interventions that train individuals to focus on concrete, finely detailed cognition and that reduce generalized context-based cognition (such as mindfulness-based cognitive therapy) improve both memory specificity and rumination^{107,108}.

In summary, a reduced ability to retrieve specific, single-incident events characterizes a number of mood, anxiety, psychotic and stressor-related disorders. Compromised memory specificity independently both causally and prospectively predicts poorer clinical prognosis, and a number of potential mechanisms have been theorized to underlie this effect.

Memory-based interventions

Empirical research within the three key domains of recollective memory distortions outlined above has influenced the integration of memory intervention techniques into existing psychological therapies, and driven the development of novel memory-based interventions translated from basic science. These programmes seek to ameliorate one or more of the reviewed recollective distortions. The underlying assumption is that these distortions play a causal part in driving symptoms, and therefore correcting distortions will deliver improvements in mental health. However, as discussed above, the causal evidence is incomplete. Studies that evaluate memory-based interventions using experimental designs such as clinical trials, where the outcome is an index of mental health, also of course provide important information pertaining to underlying causal assumptions (Box 1).

In this section, we review this emerging body of clinical research for each of the three memory distortion domains. Some general words of caution are warranted. These techniques, mostly translated from basic science, are in almost all cases in the early stages of evaluation¹⁰⁹. As such, sample sizes are typically small, comparison to active treatment control groups (as opposed to wait-list controls or treatment as usual) is not widespread, long-term follow-ups are mostly absent, and mechanisms of action largely remain unestablished. Furthermore, despite the transdiagnostic nature of many recollective distortions, most of the evidence for the efficacy of the associated interventions is restricted to depression. Table 1 summarizes the current strength of evidence (including study design and type of control comparison) for each of the interventions described below.

Table 1 | Overview of novel autobiographical memory-based interventions

Memory bias targeted	Intervention	Description	Highest level of evidence	Symptoms targeted	Comparison group	Cohen's d ^a	95% CI
Affective biases	Method of Loci	Memory recollection technique that maps positive memories to a well known route to improve ease of retrieval Training typically completed on an individual basis for 1 week	RCT with active control ¹¹¹	Self-report ratings of mood repair during depressive remission	Memory rehearsal	1.03	0.19–1.87
	Imagery CBM	Computer-based intervention delivered via daily sessions that guide participants to practice imagining positive resolutions for ambiguous scenarios Training typically completed for 1 week	Meta-analysis ¹⁴⁰	Depression	Sham CBM	0.26	–0.06 to 0.58
			RCT with active control ¹⁶⁴	Depression	Sham CBM	–0.03	–0.36 to 0.29
			RCT with active control ¹⁶⁵	Depression	Sham CBM	0.66	–0.18 to 1.50
			RCT with active control ¹⁶⁶	Depression	Sham CBM	0.29	–0.18 to 0.76
			RCT with active control ¹⁶⁷	Depression	Sham CBM	0.91	0.05–1.77
Intrusive recollection	Imagery rescripting	Memory editing technique that directly targets the imagery within a distressing, specific memory Delivered in single or multiple sessions	Meta-analysis ¹²⁷	Mixed depression and anxiety	Wait-list or active control	0.90	0.46–1.35
	Tetris	Participant plays the video game Tetris on a smart phone for approximately 20 minutes while in hospital	RCT with active control ¹³⁵	PTSD	Podcast for matched time duration	0.86	0.11–1.61
Reduced specificity	Concreteness training	Aims to improve concreteness in recall of negative experiences through daily, verbal training exercises delivered online for 6 weeks	RCT with active intervention ¹¹⁶	Depression	Relaxation training	0.31	–0.15 to 0.77
				Depression	Non-specified TAU	0.96	0.49–1.43
	Life review/ reminiscence therapy	Discussion-based intervention that asks participants a series of questions designed to prompt specific memories Delivered as 6–12 sessions of in-person, group-based intervention	Meta-analysis ¹⁴⁰	Depression	All active interventions	–0.16	–0.67 to 0.07
			RCT with active intervention ¹⁶⁸	Depression	Supportive therapy	–0.12	–1.16 to 0.91
			RCT with active intervention ¹⁶⁹	Depression	Problem-solving therapy	–0.18	–0.79 to 0.43
	MeST	Provides practice in recalling and elaborating detail of specific positive, negative and neutral events from the past, in response to word cues Delivered via computer (text-based exercises) or in-person (verbal-based exercises); typically 5–8 sessions	Meta-analysis ¹³⁹	Depression	All control groups	0.29	–0.48 to –0.10
				Depression	Active control interventions	–0.17	–0.40 to 0.06
			RCT with active intervention ¹⁴¹	Depression	Psychoeducation and supportive counselling	–0.07	–0.59 to 0.44
Reduced specificity and affective biases	COMET	Increases activation frequency and emotional salience of positive memories using therapist-guided exercises Delivered via 7–8 in-person group-based sessions	Meta-analysis ¹⁴⁰	Depression	Specified TAU	0.62	0.28–0.94
			RCT with active intervention ¹⁷⁰	State anxiety in mixed anxiety disorders	EMDR	0.58	–0.05 to 1.20
			RCT with wait-list control ¹⁷¹	OCD	Wait-list control	0.11	–0.39 to 0.62
			RCT with active intervention ¹⁷²	Panic disorder	Applied relaxation	–0.23	–0.56 to 0.11
			RCT with active intervention ¹⁷³	Depression	Specified TAU	0.62	0.08–1.15
			RCT with active intervention ¹⁷⁴	Depression	Specified TAU	0.60	0.16–1.03
			RCT with active intervention ¹⁷⁵	PTSD	MeST	10.19	8.19–12.18

Table 1 (continued) | Overview of novel autobiographical memory-based interventions

Memory bias targeted	Intervention	Description	Highest level of evidence	Symptoms targeted	Comparison group	Cohen's d ^a	95% CI
Reduced specificity and affective biases (continued)	IMAGINE	Participants guided by therapist to complete memory rescripting exercises to improve specificity and imagery of past negative events and improve specificity, and to generate detail and imagery for positive future events Delivered as 4 in-person group sessions	RCT with active intervention ¹¹⁸	Anxiety	Non-directive supportive therapy	0.51	0.12–0.89
				Depression	Non-directive supportive therapy	1.34	0.80–1.87
				PTSD	Non-directive supportive therapy	0.35	0.12–0.82
	MemFlex	Workbook-based 8-session (two per week) intervention that provides written exercises guiding movement between specific and general memories, and elaboration of imagery and detail of positive specific event memories	RCT with active intervention ¹⁴⁵	Depression	Psychoeducation	0.22	–0.75 to 0.31
			RCT with wait-list control ¹⁴⁶	PTSD	Wait-list control	0.50	–0.15 to 1.15

Only randomized controlled trials (RCTs) with diagnosed samples are presented. Results from the highest-quality RCT are presented, determined in accordance with the Cochrane Risk of Bias guidance. CBM, cognitive bias modification; COMET, Competitive Memory Training; EMDR, eye movement desensitization and reprocessing therapy; MemFlex, Memory Flexibility Training; MeST, Memory Specificity Training; OCD, obsessive compulsive disorder; PTSD, post-traumatic stress disorder; TAU, treatment as usual. ^aCohen's d is for the between-group difference at post-intervention, adjusting for baseline values when possible, and is in favour of the memory intervention condition, except when the value is negative.

Ameliorating affective biases

The pervasive recollective bias in favour of negative autobiographical memories is one of a suite of 'thinking distortions' identified within cognitive behaviour therapy (CBT) approaches to mental ill-health²⁷. CBT helps recipients to identify when such distortions are operating in daily life and to understand their detrimental effect on affect and symptoms. These insights are then a prelude to learning and applying cognitive corrections to challenge and ameliorate the impact of cognitive distortions; for example, through selective emphasis on recollecting and savouring positive memories⁵⁹.

Helping recipients to savour positive emotions by focusing on those emotions is also an emerging feature of CBT¹¹⁰, and autobiographical memory represents a tangible cognitive system through which positive emotions can be evoked, experienced and enhanced¹¹¹. There are now promising interventions which therefore seek to utilize autobiographical memories to enhance positive affect and mental health. For instance, the Method of Loci is a mnemonic technique that has been successfully used to augment the ability to retrieve positive autobiographical memories, producing downstream improvements in the ability to repair low mood in everyday life¹¹¹. The Method of Loci involves matching a memory item to a location along a familiar geographical route (for example, the commute to work) and then mentally walking the route and recalling the matched memory 'stored' at each location. Individuals with chronic depression were trained to match a personal, positive memory to each locus of their chosen route and encouraged to recall the memories by mentally navigating the route in times of stress¹¹¹. This intervention led to both immediate and sustained (over three months) improvement in the ability to access positive memories and to use positive memories to regulate everyday downturns in mood¹¹¹ – a skill vital to resisting depression remission¹¹².

Other therapeutic approaches aim to augment the intensity of positive affect during the recollection of positive memories by manipulating the way that the recollected memories are processed¹¹³. In one experiment, participants were instructed either to focus on their feelings and physical state (experiential processing), to focus on the meaning and causes of an experience (analytic processing) or to use distraction. Following these manipulations, participants were asked to recollect and reflect on a memory of a positive event. Experiential processing led to

greater ratings of positive affect upon memory retrieval relative to the analytic and distraction conditions¹¹⁴. Concrete, experiential processing of autobiographical memories has subsequently been targeted in cognitive training programmes. Small trials demonstrate a beneficial impact of these programmes on depressive symptoms relative to an active control (but not to alternative treatment) conditions^{115,116}. These approaches are now being combined with CBT in an effort to boost treatment effects¹¹⁷.

Mental imagery enhancement techniques also target the recollective salience of positive memories. The four-session IMAGINE protocol combines imagery re-scripting elements with memory-specificity techniques to facilitate recollection of past positive events, and bolster positive imagery for recollected past events. IMAGINE has been shown to improve self-esteem and decrease depressive, post-traumatic stress, and anxiety symptoms in young people^{118,119}. A larger definitive trial with long-term follow-up is now needed.

In sum, a number of novel cognitive training interventions are emerging to improve the affective quality of positive memories. These techniques might have promise as stand-alone interventions or as augmentations of current gold-standard CBTs, but further evaluation in later-phase clinical trials, particularly for symptoms other than low mood, is needed.

Reducing memory intrusions

Therapeutic efforts to reduce memory intrusions often involve restructuring of intrusive, distressing memories. Such restructuring is a key technique within treatments such as trauma-focused CBT and Eye Movement Desensitization and Reprocessing (EMDR) that are recommended by the American Psychological Association and the UK National Institute for Health and Care Excellence as evidence-based psychological interventions for PTSD¹²⁰. Trauma-focused CBT for PTSD¹²¹ includes elements that restructure trauma memories to update or remove maladaptive cognitions known to drive disorder. During restructuring, the recipient provides a written or verbal account of the trauma memory containing as much detail as possible. The therapist then helps the recipient to identify and update maladaptive meanings embedded within the memory based on new information (for example, 'This is all my fault' might be updated to 'Now I know there was nothing I could

have done to stop this') and to reorganize the memory into a linear, cohesive narrative. The repeated exposure to the trauma memory as this process is iterated reduces associated emotional distress. In EMDR¹²² the recipient holds the trauma memory in mind while completing eye movement exercises in response to a moving visual cue. These eye movements act as a cognitive distractor from the trauma memory, although the precise mechanism of action remains unknown.

Meta-analysis supports the beneficial impact of trauma-focused CBT and EMDR on intrusions and broader PTSD symptoms¹²³, reflecting their international endorsement as gold-standard PTSD treatments. Because of their effectiveness in the treatment of PTSD, memory editing techniques have been extended to modify intrusions in the context of other disorders, (for example, anxiety and drug- or alcohol-use disorder^{18,24,124}) and as part of transdiagnostic therapy protocols¹²⁵, sometimes in combination with other behavioural and pharmacological treatment elements^{24,126}.

Imagery rescripting has also been used successfully to treat trauma-related intrusions, and intrusive memories associated with distress, elevated anxiety and cravings¹²⁷. Imagery rescripting aims to reduce intrusions by altering the imagery embedded within distressing memories (such as an image of oneself stumbling over words in the last team meeting) by, for example, inserting new imagery elements (such as smiling and nodding faces around the table) that change the meaning and reduce the negative affective impact of the intrusive memory. Meta-analysis indicates large pre-to-post transdiagnostic treatment effects of imagery rescripting, and large effects relative to passive treatment conditions, on symptoms of depression, social anxiety, health anxiety, and obsessions and compulsions¹²⁷. Individual trials also suggest significant treatment effects of imagery rescripting relative to active control interventions^{128,129} but it is important to note that these trials have recruited people on the basis of a single disorder diagnosis. In terms of mechanisms of action, imagery rescripting might help to update the core beliefs which drive disorder¹³⁰ and/or to strengthen more positive memory representations that compete for retrieval with the maladaptive, intrusive memory¹³¹.

In addition to these elements of established therapies, there are a number of potential new avenues for ameliorating intrusions translated from basic science. Meta-analysis of science-driven memory consolidation/reconsolidation interventions indicates that protocols that employ pharmacological or psychological techniques to update memories might be efficacious in reducing symptoms of PTSD¹³². One such approach¹³³ uses visuo-spatial cognitive distraction (for example, playing computer games with a high visuo-spatial load, such as Tetris)^{134–136} in the acute aftermath of a trauma. The rationale is that recurrent processing of benign visuo-spatial stimuli will recruit the limited visuo-spatial cognitive resources that are required for consolidation of the trauma memory. In early-phase RCTs, playing Tetris within hours of a traumatic event reduced post-traumatic intrusions up to one month later, relative to a verbal distraction control condition such as a quiz or listening to a podcast^{137,135}. An effect of Tetris has only been established against active control groups (not other treatments), long-term effects have yet to be established, and some have questioned the methodology of current studies¹³³.

A clinical limitation of the visuo-spatial cognitive distraction approach is that the proposed window for intervention is the acute aftermath of the traumatic event. This limits the situations in which it can be used. Some studies have therefore explored whether Tetris could be used to augment existing gold-standard PTSD treatments. In one study, participants played Tetris for 60 minutes each day during

the 6 weeks that they were receiving EMDR¹³⁸. Those who played Tetris showed a greater increase in the volume of the hippocampus – a brain region integral to autobiographical memory – post-therapy relative to a control group who only completed EMDR¹³⁸. The magnitude of increase in hippocampal volume correlated with a greater improvement in PTSD, depression and anxiety symptoms at the six-month follow-up assessment. These findings led the study authors to suggest that Tetris enhances the effect of EMDR by boosting hippocampal-based memory and visuo-spatial processing. This Tetris-based intervention is being further evaluated for potential treatment effects in larger, definitive clinical trials, and the concept is being applied to intrusive cognitions in other populations (for example, via smartphone delivery during everyday life for those experiencing alcohol, nicotine and gaming cravings¹³⁶).

In sum, many effective therapies for mental ill-health incorporate restructuring techniques that successfully reduce the experience of autobiographical memory intrusions. Novel protocols translated from basic science also have promise as stand-alone, low-intensity interventions for reducing intrusions. Larger-scale efficacy trials to determine whether there are longer-term treatment effects for psychiatric symptoms are now needed.

Enhancing memory specificity

Interventions to improve the recollection of specific memories are efficacious in improving symptoms of anxiety, post-traumatic stress and low mood (for meta-analysis, see refs. ^{139,140}). One of the more widely applied protocols is Memory Specificity Training (MeST), which involves repeated practice in retrieving specific memories in response to word or picture cues. RCTs demonstrate that MeST improves memory specificity for both positive and negative memories on the Autobiographical Memory Task relative to control conditions, and yields acute therapeutic effects on symptoms that are comparable to current frontline interventions, such as supportive counselling for depression¹⁴¹ and cognitive processing therapy for PTSD^{142,143}. However, a meta-analysis suggests that the benefits of MeST might not persist over the longer term¹³⁹. Indeed, a subsequent trial of computerized MeST only observed improvement in memory specificity at the one-month follow-up but not at the three- or six-months follow-ups¹⁴⁴. These findings suggest that previously reported treatment effects might be attributable to processes other than improved memory specificity (such as improved motivation or executive functioning). Thus, the jury remains out regarding the clinical utility of MeST as a stand-alone treatment.

Refinements of these memory interventions aim to simultaneously counteract the negative recollective bias and reduced memory specificity observed in affective disturbance, rather than targeting these memory distortions separately¹⁴⁰. One such programme is Memory Flexibility Training (MemFlex)¹⁴⁵, which trains the ability to flexibly search the hierarchically organized autobiographical knowledge base, and to select specific versus general memories, and memories with either a positive, negative or neutral affective meaning for the individual. This flexibility is achieved through exercises that promote recollection of both specific and general memories in response to the same word or picture cues, and through tasks that prompt the trainee to either recollect specific memories as exemplars of general memories or to recollect general memories that reflect regularities across sets of specific memories. MemFlex improves flexible retrieval of both specific and general memories on the Autobiographical Memory Task, with concomitant positive effects on symptoms for depression¹⁴⁵, PTSD¹⁴⁶ and psychosis¹⁴⁷. Efforts to simultaneously target reduced memory

specificity and affective biases have also been extended to children. Using age-adapted techniques (for example, drawing) to enhance mental imagery associated with positive specific memories yields both cognitive and emotional benefits^{118,119}. Extending such programmes to young people might be particularly important because meta-analyses suggest that reduced memory specificity might independently causally predict symptoms²⁰. Thus, interventions to enhance specificity have potential in preventative contexts.

To summarize, psychological interventions to improve memory specificity potentially offer a low-cost, accessible treatment alternative to more intensive, psychological interventions that require specialist therapists, for a number of mental health conditions. Larger effectiveness trials are now needed, with a particular focus on whether observed effects on symptoms persist over longer follow-up periods, outperform current treatment options, and whether such interventions should be used as stand-alone treatments or in combination with current treatment options. Elucidating links between autobiographical memory and other aspects of cognition such as episodic future thinking is also likely to produce novel therapeutic interventions (Box 2).

An integrated transdiagnostic framework

Taken together, the evidence reviewed thus far suggests that the three domains of autobiographical memory recollection perturbation are transdiagnostic and causally implicated to a greater or lesser extent in the maintenance, and potentially onset, of disorder. However, it is less clear how these different processes interrelate. Separately, each domain is characterized by careful and influential theorizing. Pervasive negative biases and corresponding attenuation in the processing of positive memories form part of a suite of cognitive distortions identified within cognitive therapy formulations of depression and anxiety^{15,59}. Theories of autobiographical memory intrusions have been most compellingly developed within the trauma literature¹¹ where disorders such as PTSD are paradigmatically defined by unwanted intrusive recollection of the original traumatic experience. Finally, within the domain of non-specific recall, the CaRFAX model¹² identifies multiple mechanistic routes to memory overgenerality (although these pathways are not always supported empirically) and dovetails with theoretical work on other aspects of cognitive generalization such as rumination and worry^{100,148}.

Box 2

Episodic future thinking

Reduced specificity in the recollection of prior experience is mirrored in the ability to simulate future events. Theories of episodic simulation stipulate that memories for episodes from the past provide a blueprint for imagining future events⁵, such that both engage the same cognitive skills and are underpinned by the same neural network^{3,180}. It is therefore no surprise that mental health problems are also associated with episodic future thinking difficulties, with reduced specificity, emotional vividness and detail for simulated future events observed across mood, anxiety, trauma-related and psychosis-related disorders (reviewed elsewhere¹⁸¹).

Interventions to improve specificity of event memories have been administered to enhance episodic future thinking. Meta-analysis¹⁴⁰ indicates that positive imagery cognitive bias modification produces moderate to large effects ($0.31 < d < 1.44$) on the ability to project future episodes, with a moderate pooled effect ($d = 0.46$, 95% CI 0.19–0.73) on symptoms, relative to control groups. There is limited evidence for effects of MeST and MemFlex on future thinking^{146,182}. These mixed findings motivated the development of interventions that solely target future thinking, such as future specificity training, which is an adaptation of MeST that involves repeated practice in projecting future events. Future specificity training produces large increases ($0.82 < d < 1.32$), in specificity, detail and imagery of future episodes in healthy individuals relative to wait-list controls¹⁸³. A preprint that has not yet been peer-reviewed demonstrated that relative to a wait-list control group, future specificity training led to a moderate improvement ($0.63 < d < 0.77$) in specificity of future thinking, anhedonia, and depressive symptoms in individuals with major depressive disorder¹⁸⁴. Efforts have also turned to embedding experimental manipulations that enhance vividness of simulated future events

into everyday life (for example, via online or smartphone delivery).

One experiment demonstrated small effects of episodic future thinking on anticipatory pleasure for maladaptive eating behaviour ($\eta_p^2 = 0.12$ – 0.20) relative to control¹⁸⁵, and a case series suggests that episodic future thinking can increase anticipatory pleasure in depressed individuals¹⁸⁶.

At the basic-science end of the translational trajectory is the development of a transient specificity induction^{4,96}, which aims to ‘switch on’ a specific processing style and temporarily alleviate difficulties, improving both future thinking specificity and memory specificity¹⁸⁷. This state-level induction has been shown to improve performance on problem solving, cognitive reappraisal, delay discounting and future planning tasks, and is being adapted for clinical populations such as those with dysfunctional patterns of eating or substance use^{185,187,188}.

Episodic inductions might also enhance performance on therapeutic tasks that require either retrieval of specific memories (such as cognitive restructuring tasks in CBT, whereby events are reframed through the inclusion of more positive or adaptive information⁵⁹, or imagery rescripting of adverse memories, whereby brought-to-mind imagery narratives of past distressing events are altered to introduce more functional components¹⁸⁹). Episodic inductions might also enhance performance on therapeutic tasks that require specific, detailed planning for future events (for example, creating activity schedules in behavioural activation interventions)¹⁹⁰. Similarly, transient inducement of specific processing (using, for example, concreteness training techniques) could help to counteract generalized cognitive processing styles such as worry and rumination¹¹⁶, which potentially interfere with the efficacy of existing gold-standard treatments.

The increased interest in transdiagnostic approaches to mental health¹⁴⁹ has coincided with broader theoretical frameworks that can sit above these more localized proposals to provide meta-theoretical accounts of multiple clinical conditions and the myriad psychological and behavioural features that characterize them. One such framework, grounded in the clinical domain, is the generic cognitive model of cognitive therapy⁶⁰, which builds on diagnosis-specific cognitive therapy theories to extract transdiagnostic and cross-process common principles. In this section, we use the generic cognitive model to outline an integrated framework for the three domains of autobiographical recollective memory disturbance and the interventions that seek to address them. The generic cognitive model is not the only candidate integrative framework. Comparable proposals could be derived from alternative cognitive architectures such as predictive processing approaches⁶¹. We have elected to use the generic cognitive model here because of its established clinical applicability¹⁵⁰.

The generic cognitive model

Central to the generic cognitive model is the theoretical notion of 'schemas'. Schemas are representations or 'models' of the self, world and others that encode generalizable knowledge extracted from regularities across past experience. Schemas become active when the individual encounters contexts or events for which the schemas are relevant, with a family of interrelated schemas active at any one time. This set of active schemas then directs mental processing to optimally navigate unfolding events based on lessons from the past. Schemas therefore represent the mind's 'best guess', based on prior experiences, of the broad nature of the individual's current and future reality in any given context. The suite of active schemas controls information processing: cognition and behaviour are biased in favour of schema-congruent information because, according to prior experience, this information is most important for ongoing adaptive functioning. As experiences relevant to a given context accumulate over the lifetime, the concordant schemas become more strongly consolidated. Furthermore, as similar experiences accrue across different contexts, schematic knowledge becomes increasingly abstracted and less granular to encompass this increased contextual diversity. It is therefore useful to think of hierarchies of schemas of the self and world, with schemas increasing in abstraction and generality as one ascends the hierarchy (Fig. 3a).

In the case of mental health problems, the argument is that information processing is guided by a family of active schemas that enshrine negative generalizable knowledge about the self, world and others compiled across previous life experiences. Unlike for mentally healthy individuals, for individuals with mental health problems schemas coding negative content tend to extend further up the schema hierarchy to encompass more abstracted negative information pertaining to a wider range of contexts. This reflects the fact that the negative schematic content has become increasingly abstracted over time as the individual encounters the same negative themes across a broader array of situations.

To illustrate, an individual with a history of mood problems might be characterized by an active higher-level schema representing an abstracted model of the self as 'unloveable'. This higher-level negative schema will have developed over time as a function of difficult lifetime experiences around a theme of 'unloveability' across multiple contexts (for example, dysfunctional romantic relationships, a difficult relationship with a parent throughout childhood, experiences of rejection at school). This higher-level schema will then be activated in diverse relationship contexts where, in terms of adaptive cognition, the schema's

content reflecting 'unloveability' arguably offers the best prediction of how that relationship will play out on the basis of what has happened in the past. The individual will then selectively process information and recollect instances from the past that are consistent with the schematic representation of 'self-as-unloveable', with unsurprising negative consequences for behaviour and mental health.

The schema hierarchy contains both the active 'online' schemas that are most relevant for the current context and latent schemas that are not currently active but can become activated when contextual circumstances change (Fig. 3a). At any one time, an individual's mental life is thereby driven by a family of active schemas, at different levels of abstraction within a schema hierarchy, that are constantly in flux as schemas transition from states of latency to activity as a function of context and circumstances. This provides an account of recovery and remission from mental ill-health: negative, maladaptive schemas become latent as a function of changes in current context, including through therapeutic interventions to reframe those contexts; the breadth and variety of contexts that can potentially re-activate these now latent negative schemas then represent the individual's degree of vulnerability to relapse or remission.

Importantly, this framework can be operationalized transdiagnostically, whereby differences in the nature of the negative content of active schematic knowledge differentiates different disorders. For example, schemas generically coding the self as 'worthless' or 'unloveable' would typically characterize depressive conditions¹⁵¹, whereas schemas of the world as 'dangerous' and 'unpredictable' typically characterize anxiety, psychotic and post-trauma disorders¹⁵².

Applying the generic cognitive model to domains of memory distortion

The generic cognitive model can be used to theoretically integrate the three domains of memory distortion. There are two central notions. First, mental health problems are characterized by a suite of hierarchically organized active schemas that drive mental life (Fig. 3a). These active schemas are negative in content and extend upwards to encompass higher levels of the hierarchy in mental ill-health, thus representing increasingly broad and generalized negative summaries of the past that pertain to a wider range of current contexts. Second, information that is schema-consistent, including autobiographical memories, will be preferentially processed and processed more deeply. By contrast, schema-inconsistent information will receive more shallow processing and is more likely to be discounted in terms of ongoing goals and plans.

For individuals with mental health problems, there will thus be preferential access to schema-congruent negative personal memories. This preferential access will extend to negative memories with higher levels of generality (referencing repeated events or extended lifetime periods)¹ (Fig. 3b) compared to individuals without current mental health problems. There will be a corresponding reduction in access to positive memories. Each of these proposals is supported by the literature reviewed above. Furthermore, accessed negative memories will be experienced as more intense, detailed, intrusive and with a greater diversity of affect, relative to the relatively impoverished recollective experience of positive memories. This accounts for the high correlations between lack of episodic detail and reduced specificity¹⁵³.

This preferential access to negative memories includes both voluntary recollection and memory intrusions. Intrusive memories of specific experiences that are prototypical exemplars of the active schema content provide important past information of potential relevance to

current circumstances (Fig. 3b) and serve as indicators that there is significant relevant information in the current context that competing latent schemas are unable to account for⁹⁸. Such intrusions are particularly likely when active schemas represent aspects of threat or personal safety and therefore maximize chances of survival. These involuntary recollections of specific salient negative past events are accompanied by intrusions of generalized past knowledge, reflecting active schemas from higher in the schema hierarchy, and fuelling perseverative generalized ruminations and worries.

This framework concordantly proposes that interventions targeting autobiographical memory operate via one or more of three inter-related mechanisms of action (Fig. 4). First, interventions that, all or in part, seek to train access to specific memories (MeST, MemFlex and

the Method of Loci) shift emphasis away from a mental life (worries, thoughts, ruminations or memories) dominated by abstract, higher-level active negative schemas ('I am unlovable') towards a psychology driven by lower-level, more localized schemas fuelled by event-specific information. Second, interventions that seek to enhance the salience, vividness and richness of specific positive memories (MemFlex, the Method of Loci and positive imagery training) all increase the power of those memories to provide schema-incongruent information to counteract and eventually weaken highly consolidated active negative schemas. Finally, interventions that seek to restructure either specific negative memories (imagery rescripting and CBT) or negative schemas (CBT) or to build competing less-negative or positive schemas (CBT and mindfulness-based CBT) also weaken the grip of negative

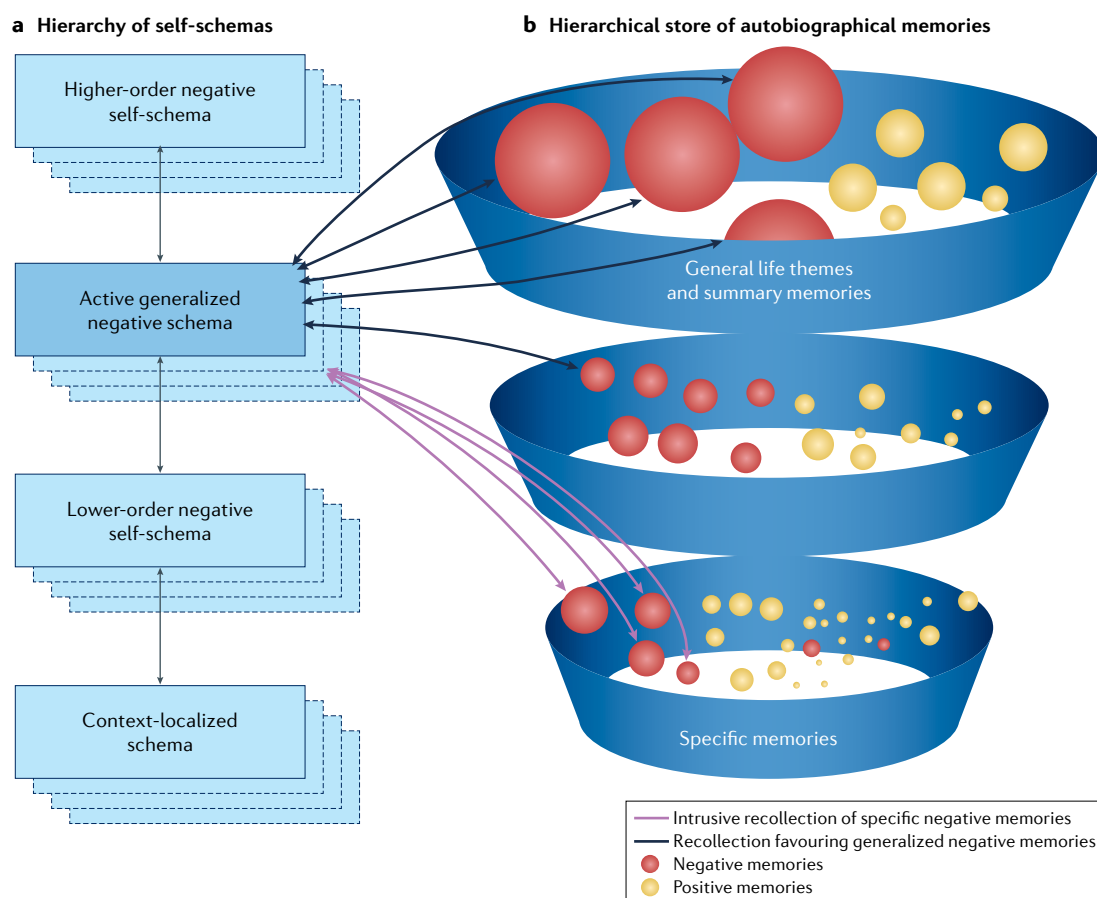


Fig. 3 | An integrative transdiagnostic framework. a, Self-schemas are organized hierarchically (boxes with solid lines) ranging from lifelong, existential, identity-defining self-schemas at the top to localized self-schemas pertaining to specific contexts at the bottom. In this illustration, processing is driven by active generalized negative self-schemas that reflect relatively abstracted conceptualizations of the self that pertain to multiple life contexts. Competing models in probability space at the same level of abstraction, including more positive, functional models, are represented by partially occluded boxes with dashed lines. Less active models at other levels in the hierarchy are presented in a lighter shade. **b,** Hierarchical autobiographical memory store (based on ref. ¹). Summary memories reflect lifetime periods and autobiographical themes at the higher levels, down to specific episodic records of individual events at the lowest level. Red circles represent negatively valenced

memories. Yellow circles represent positively valenced memories. Circle size reflects the accessibility of the memory in the recollective context, that is, the weighting of the memory in terms of its relevance to active self-schemas. Black arrows indicate 'self-evidencing' of the active generalized self-schema via facilitated access to more heavily weighted (indicated by larger circle size) generalized negative autobiographical mnemonic content at the top of the hierarchical memory store relative to diminished accessibility of more specific autobiographical memories lower in the hierarchy. Purple arrows indicate intrusive, involuntary memories of specific events that are prototypical with respect to the active negative self-schema and that, as a corollary, set boundaries on the applicability of competing models (boxes with dashed lines) within the same probability space, thereby maintaining the active model as the driver of cognition and behaviour.

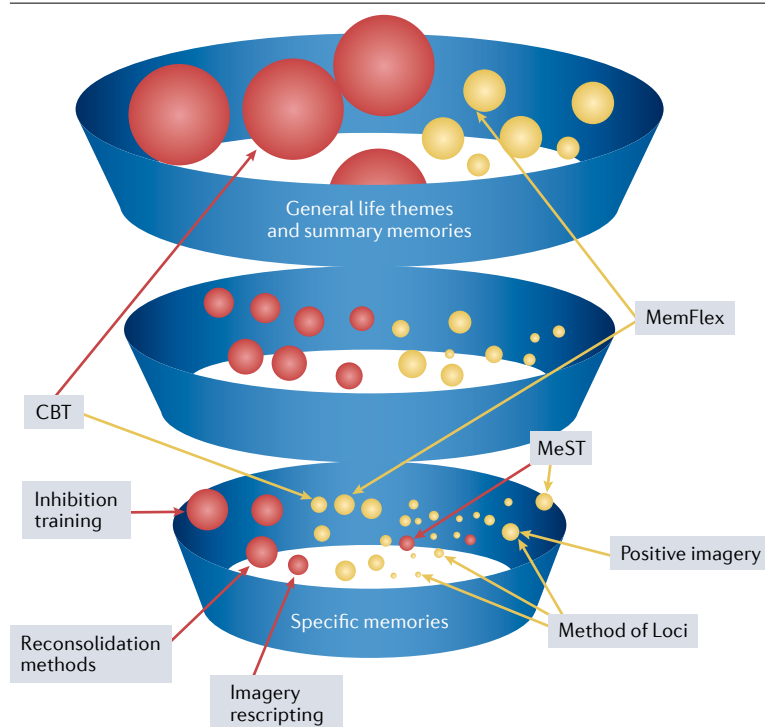


Fig. 4 | Links between the integrative framework and therapeutic interventions. Different memory therapeutic protocols target memories of differing valence and level of generality in the memory hierarchy (based on ref. ¹). Red circles represent negatively valenced memories. Yellow circles represent positively valenced memories. Circle size reflects the accessibility of the memory in the recollective context, that is, the weighting of the memory in terms of its relevance to active self-schemas. Red arrows indicate that the intervention reduces access to, or weakens, the memory. Yellow arrows indicate that the intervention facilitates access to or strengthens the memory. CBT, cognitive behaviour therapy; MemFlex, Memory Flexibility Training; MeST, Memory Specificity Training.

schemas over mental life and enhance the probability that more functional positive schemas will replace them. Further exploration of these theorized mechanisms of action may help to refine the efficacy of science-driven, memory-based interventions, and illustrate how the active components of higher-intensity interventions such as CBT can be disseminated into lower-intensity, more accessible interventions.

Summary and future directions

The recollection and processing of autobiographical memories, in particular of emotive past events, is disrupted in multiple ways across psychiatric conditions. These disruptions fall within three domains. First, autobiographical recollection is negatively biased such that memories for negative events are preferentially accessed, retain their emotional impact, and are more detailed relative to more benign memories. By contrast, positive personal memories are more difficult to access, emotionally blunted and impoverished. Second, there is disruptive and distressing intrusive recollection of self-defining, often upsetting, past events. Third, deliberate recall of the personal past is characterized by difficulty accessing specific events in favour of generalized 'summary memories' that reflect regularities across multiple past experiences and that are associated with other modes of generalized cognition such as rumination and worry. Overall, there is good evidence that these three domains of recollective distortions are both transdiagnostic and causally implicated in the onset and/or maintenance of difficulties (Fig. 1).

Nevertheless, there remain important gaps in mapping the different components of the argument that these domains have a transdiagnostic causal role in mental health difficulties and studies targeting these gaps are indicated. The integrated account of the three domains that we proposed based on the generic cognitive model⁶⁰ provides a platform for future studies. The framework predicts that the presence of memory distortions should be closely coupled to the existence

of active negative self-referent schemas. This is consistent with the reviewed research linking the distortions to the presence of emotional disorders. However, one would also expect to find evidence of such distortions in those who are currently mentally well but vulnerable to disorder, in contexts where proposed latent negative schemas are activated. There is some support for this proposal in the case of negative memory biases, which can be induced in individuals vulnerable to depression by activating putative latent negative schemas³⁶. Similar patterns of findings would be predicted for the other memory distortions.

Induction techniques would also provide a means of evaluating how effective therapeutic interventions are in changing maladaptive schemas and resolving biases. Schema activation protocols (such as a negative mood induction) delivered post-therapy could reveal to what extent biases remain present even when symptoms have remitted, potentially providing an assay of the depth of therapeutic impact. Relatedly, the reversed patterns of memory distortions – positive memory biases, richly recollected positive memories, unbidden positive recollections, and overgeneral positive memories – should characterize individuals who are flourishing and should predict good mental health prognostically, as they are cognitive markers of consolidated and active positive self-referent schemas.

Within these broad proposals, one would also expect evidence of context-specificity. For example, if the presenting clinical pattern indicates deeply held negative self-schemas in the domain of intimate relationships but not in other domains, the hypothesis would be that the presence and content of memory distortions would be similarly context-bound even if the symptoms of emotional disorder were generalized across contexts. Finally, the framework predicts that the relationship between active generalized negative self-schemas and overgenerality of autobiographical recollection should be mirrored by

over-generality in other cognitive domains such as attention, reasoning, social processing, thinking (for example, rumination and worry), as well as behaviour.

In addition to these empirical predictions, further theoretical integration, both at the functional level of analysis incorporating other domains of affect, cognition and behaviour, and bridging to the neural level of analysis, is now warranted. Theoretical architectures such as predictive processing^{154,155} offer a powerful set of explanatory tools (hierarchical prediction models, prediction error signals, and the precision of those models and errors, operationalized within a Bayesian computational framework) for such within- and across-level advances and map isomorphically to the integrated transdiagnostic framework outlined above⁶¹. The broader field faces challenges in mapping clinically oriented cognitive constructs with these methods¹⁵⁶. Thus, an important next step will be to operationalize the reviewed memory processes computationally to enable quantification of their role in predictive processing.

Contextualizing memory distortions within these broader frameworks that link to biological and neurological processes also generates new research questions, particularly regarding the integration or augmentation of the cognitive behavioural memory interventions described here with pharmacological or neurofeedback methods. For example, a low dose of D-cycloserine (a drug that increases glutamatergic activity) enhances recollection of specific autobiographical memories up to 24 hours later in healthy individuals¹⁵⁷. Drug enhancements might therefore potentiate the effects of the reviewed memory techniques. Similarly, autobiographical memory may represent one system through which novel antidepressants that target glutamatergic systems¹⁵⁸ operate. Multiple studies have also demonstrated that biofeedback training improves memory specificity and vividness^{159,160}. A subsequent early-phase trial that delivered neurofeedback training in conjunction with CBT demonstrated that depressed individuals who received neurofeedback training when retrieving positive memories prior to CBT experienced greater symptom improvement than those who received sham training prior to CBT¹⁶¹. This is an exciting avenue for further research to improve the impact of current gold-standard treatments, as the synthesis of psychological, neural and biological indices of memory offers rich opportunities for multidisciplinary treatment of mental health problems.

Memory-based interventions have emerged based on the rationale that amelioration of the underlying autobiographical memory disturbance will reap therapeutic benefits in terms of clinical symptoms and improved prognosis (Table 1). Initial meta-analyses of these interventions suggest promising effects on symptoms; however, development is ongoing and large, later-phase trials are now urgently needed. The integrative transdiagnostic framework we outline provides a structure for thinking about the different domains of memory distortion collectively, and how they relate to the mental architecture underpinning a broad range of therapy elements within CBT. This will facilitate the integration of memory therapeutics into the broader CBT paradigm, as well as the further development and extension of memory-based interventions. In particular, our framework predicts that interventions targeting multiple memory distortions are likely to have a larger effect on symptoms than interventions that target a single distortion.

To date, memory therapeutics have focused mostly on treatment¹⁴⁰. There is further potential to adapt protocols for use as preventative interventions. Population-based research showing that memory distortions predict poorer mental health prognosis^{90,162} suggest opportunities to develop prevention tools for use with younger people who have yet to develop mental health problems and populations with

a history of mental health problems who are currently well¹⁶³. Memory protocols have also typically been evaluated as stand-alone interventions. However, they will probably have greater potency as augmentations of existing evidence-based interventions such as CBT, either delivered in advance, in parallel, or subsequently, when acute symptoms are diminished. Translation of this basic science towards preventative and improved therapeutic interventions is integral to harnessing the omnipresent influence of autobiographical memory on mental and emotional life.

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