Memory Specificity in Tic Disorders

Reduced Specificity of Autobiographical Memories in Young People with Tic Disorders

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Short title: Memory Specificity in Tic Disorders
Abstract

Objective: Depression is common in Tourette syndrome and Chronic Tic Disorders (TS/CTD) and contributes to significant impairment. The specificity of autobiographical memories is implicated in an individual’s sense of self and their daily functioning but also in the onset and development of depression in the general population. Here, we examined whether memory specificity is reduced in young people with TS/CTD, relative to control participants, and whether memory specificity is associated with depression. Method: Thirty young people with TS/CTD (14 females; age: \( \bar{x} = 11.31 \); SD=1.66; 87% White British) and twenty-six (12 females; age: \( \bar{x} = 11.23 \); SD=2.43; 77% White British) control participants completed the study. Participants completed the Autobiographical Memory Task, which asks participants to respond with a specific memory to cue words, and a questionnaire measure of depressive symptoms. Results: There was no significant difference between the two groups in terms of age, gender, ethnicity, IQ and depressive symptomatology. Young people with TS/CTD had less specific autobiographical memories than their peers (\( p < .001, r = 0.49 \)). Across both groups, increased memory specificity for positive cue words was associated with reduced depressive symptomatology (\( p < 0.001, R^2 = .51 \)). Conclusions: Our findings indicate that autobiographical memory in young people with TS is characterised by a lack of specificity and, as with neurotypical peers, reduced memory specificity for positive words is associated with depressive symptoms. Autobiographical memory specificity could be an important factor in understanding mood symptoms that characterise young people with TS/CTD and may be an important cognitive target to reduce the development of depression in young people with TS/CTD.

Keywords: Tourette syndrome, tic disorders, autobiographical memory, memory specificity, depression
1. Introduction

Tourette syndrome and Chronic Tic Disorders (TS/CTD), defined by the presence of tics, are heritable neuropsychiatric disorders with an onset in early childhood. TS features both motor and vocal tics, whereas CTD involves the presence of motor or vocal tics but not both [1]. In addition to having tics, as many as 90% of individuals with TS/CTD have a co-morbid psychiatric disorder [2,3]. In particular, individuals with TS/CTD are at higher risk of developing depression [4], with data estimating that 13% of adult patients with TS meet diagnostic criteria for depression (compared to 3% of the general population [5]) and many more experiencing sub-clinical symptoms [4]. Furthermore, the risk of developing depression across youth appears to be much higher in those with TS compared to general-population samples [6], and also, in one study, to a control cohort of patients (though the diagnoses of these patients was not reported) [7]. The presence of depression is associated with lower quality of life as well as being a risk factor for suicide [4,8,9].

Research suggests that whilst tics tend to diminish before age 18 (90% of individuals with TS/CTD will have mild tics or none at all by age 18 [10]), co-occurring anxiety and depression persist and contribute to the disability experienced by individuals with TS/CTD [11,12]. Given that depression is well known to complicate neurological disorders [4] and that young people with TS/CTD are at increased risk of depression, the paucity of research investigating cognitive factors that make young people with TS/CTD vulnerable to developing depression is surprising. A valuable direction for current psychological research is to identify factors that a) may contribute to risk of depression and its associated impairment in individuals with TS/CTD and, b) are amendable to psychological intervention. Autobiographical memory specificity is one cognitive factor strongly implicated in the development of depression in the general population [13,14]. In this present study, we investigate whether autobiographical memory specificity characterises individuals with
TS/CTD, given they are at-risk for developing depression, and if this cognitive factor contributes to depressive symptoms. These data could inform whether autobiographical memory specificity is an appropriate target for treatments aiming to prevent later disability and improve functioning.

Autobiographical memory relates to the ability to recollect facts and personal events from one’s life [15] and is important for the individual’s sense of self and daily functioning, even in psychiatrically-healthy individuals. Indeed, our sense of self across time is defined by our collection of autobiographical memories and the fluent processing of these memories is key for social discourse [15]. The specificity of this recollection is variable across people.

Specific memories identify unique events, occurring at a particular time and place, and are in contrast with memories that are of repeated events (categorical memories) or events that last longer than a day (extended memories). For example, when asked to recall a specific event in response to a cue word (e.g. grass), one might recall a specific memory (e.g. we had a picnic on the grass last weekend); a categorical memory (e.g. I cut the lawn every two weeks); an extended memory (e.g. I developed hay fever last summer); [16]; or a semantic associate which is not a true autobiographical memory (e.g. my garden). Overgeneral memory (OGM) is a phenomenon where individuals have difficulty retrieving specific autobiographical memories and instead generate categorical or extended memories. Difficulties in accessing and processing specific autobiographical memories impacts on daily cognitive functioning, including planning, problem-solving and social interaction [13].

Reduced memory specificity (or OGM), has been strongly implicated in depression [17], being not only associated with current symptoms but also with the onset and course of depression. It is predictive of developing depression [18] and of later depression severity, even when one is not currently depressed [19]. Importantly, research with adults has demonstrated that OGM is specific to depression (rather than anxiety or general distress);
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does not reflect a general defect of memory functioning [16]; and is not purely a correlate of current low mood state [20]. Given that people with TS/CTD are at higher risk for developing depression [4], it seems important to investigate OGM in TS/CTD. Furthermore, as autobiographical memory is important for our sense of self and our ability to understand and respond to social situations, impairments in related domains of social cognition and difficulties making self-other distinctions amongst people with TS/CTD [21–23] provides another reason for studying the specificity of memories in this sample. Relatedly, children and adults with other neurodevelopmental disorders that are also characterised by poor social cognition (e.g. Autism Spectrum Disorders [ASD] [24,25]), have also been found to have higher OGM compared to controls.

Finally, Williams et al. (1996) affect-regulation hypothesis identifies that a function of OGM is to minimise negative affect associated with negative memories. Experimental studies demonstrate that a negative event leads to more subjective stress in high compared to low (memory) specific adults [27]. Compared to peers, young people with TS/CTD experience more environmental stress, for example young people with TS/CTD are at enhanced risk of peer victimisation [1], as well as more distress in response to emotional social situations [28,29]. Reducing specificity of autobiographical memories could, therefore, be a coping mechanism employed by young people with TS/CTD to manage negative affect from past memories (this is consistent with previous suggestions that people with TS may reduce social perspective taking to cope with negative affect [29]). However, whilst reduced memory specificity may function in the short term to reduce negative affect, it is a dysfunctional longer term coping strategy as it leads to reduced specificity for all memories (i.e. OGM). This has implications for increasing vulnerability to depression and reducing successful daily cognitive functioning (e.g. planning, problem solving and social interaction) [13].
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Given its association with psychopathology and everyday functioning, memory specificity offers a credible cognitive candidate to understand why adolescents and adults with TS/CTD have increased levels of depression, despite decreased tic severity. Here we investigate OGM as an underlying cognitive feature in young people with TS/CTD, who are the age when tic frequency is likely to peak. Firstly, as they are more vulnerable to developing depression, we predict that young people with TS/CTD will have less specific autobiographical memories than controls (matched for current depressive symptoms). Secondly, we hypothesise that lower memory specificity will be associated with more symptoms of depression in both groups. We also explore whether this relationship will be stronger in the TS/CTD group or similar in magnitude to neurotypical peers. As it is important to identify whether OGM is uniquely associated with depression, rather than symptoms of anxiety, anxiety will also be measured and included as a covariate in the second analysis.

2. Methods

2.1. Participants

Thirty young people with TS/CTD (14 females; age: \( \bar{x} = 11.31; \) SD=1.66) and twenty-seven control participants completed the tasks. One control participant was excluded as tics were noted by the researcher during the testing session. The parent of this participant did not report a diagnosis of TS/CTD during the initial interview but did acknowledge concerns about the young person’s movements. No other control participants showed any tics during testing or were reported to have a history of tics by their parent. Therefore, there were twenty-six control participants (12 females; age: \( \bar{x} = 11.23; \) SD=2.43). All participants were fluent in English. Participants were recruited via advertisements on Tourette’s Action volunteer webpage and King’s College London volunteer webpage, from the Tics and
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Neurodevelopmental Movements Disorder Service (TANDeM) at Evelina London Children Hospital and from schools in London. Ethical approval was obtained from the Psychiatry, Nursing and Midwifery Research Ethics Committee at Kings College London and from National Research Ethics Service Committee South Central – Oxford C. All participants provided written consent prior to their participation in the study. Participants completed this study as part of a larger experimental battery, which included two other experimental cognitive tasks (unrelated to the present study).

Inclusion criteria for the TS/CTD group were a young person aged 8 to 19 with a diagnosis of TS or CTD. For both groups, participants were only invited to take part if one family member was also willing to take part. Exclusion criteria included participants who, either by their own or their family member’s judgment, could not understand and complete the consent form and measures; participants with any other diagnosed neurological condition or diagnosed learning disability. In the control group, participants were also excluded if they had a diagnosis of TS/CTD or if they displayed tics during the testing session. In an initial interview with the first author of the study (who is also a trained clinician), parents were asked brief screening questions to list any medical (including psychiatric and neurological) diagnoses that the young person had received. Due to the well-established high rates of comorbidity in TS/CTD, participants with comorbid neurodevelopmental (providing that they were able to understand the consent process and measures) or psychiatric diagnoses were not excluded. A formal diagnostic assessment for depression was not conducted due to time constraints. Some participants were also excluded due to performance requirements on the task.

Diagnoses were recorded based on parental report and clinical records. In the final sample (TS/CTD group, n=26; control, n=24), twenty-one participants had a diagnosis of Tourette’s syndrome and five a diagnosis of a Chronic Tic Disorder in the TS/CTD group. No
participants had a comorbid diagnosis of depression. Eight participants in the TS/CTD group had additional diagnoses, including Autism Spectrum Disorder (n=3); Attention Deficit Hyperactivity Disorder (ADHD) (n=5); Obsessive Compulsive Disorder only (n=3). These figures include two participants who had diagnoses of both ADHD and ASD and one participant diagnosed with ASD, ADHD and OCD. In terms of medication at the time of completing the study, three participants were prescribed clonidine and two prescribed aripiprazole.

2.2 Measures

2.2.1. Autobiographical memory task. Williams & Broadbent (1986) procedure and coding scheme was followed in administering the Autobiographical Memory Task (AMT). Participants were asked to give a specific memory to each cue word and were provided with one example of a specific memory in the instructions. Participants were informed that the memory they recalled could have happened recently or a long time ago, and could be of an important or trivial event. Before beginning, participants were asked to practise with two cue words (beach and egg) and were given feedback on their responses. Further instructions and examples were given here, if necessary. All participants had to generate a specific memory to at least one example before continuing with the task. No participants required more than two practise words to generate a specific memory.

Similar to previous studies with children [14,31], five positive (happy, excited, hopeful, proud, loved); five negative (lonely, frightened, sad, ashamed, angry); and five neutral (grass, book, purchase, carrot, music) cues were presented in a randomised order. Words were presented orally and in writing (printed on index cards) to the participants. Participants were given 60 seconds to respond to each cue word. Each memory was coded as either (1) ‘specific’ if the memory was of an event occurring at a particular place and time
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and lasting less than a day; (2) ‘general categorical’ if the memory was of a repeated event; (3) ‘general extended’ if the memory referred to an event that lasted longer than a day; (4) ‘semantic associate’ if the response was not a true autobiographical memory; or (5) ‘no response’. All responses were audio recorded and co-rated to ensure accuracy. Internal reliability for the total specificity score was acceptable (Cronbach’s alpha = .74) as was inter-rater consistency ($\kappa = .664, p < .001; \%$ agreement = 80.75).

Following the AMT, participants rated each of their memories for how pleasant they were on Likert scale ranging from 1 (very unpleasant) to 7 (very pleasant). This was completed as a manipulation check to ensure that the memories that participants provided for positive, negative and neutral cue words corresponded to the respective valence.

2.2.2. Revised child anxiety and depression scale (RCADS) – self report. The RCADS is a 47 item questionnaire, measuring depression and anxiety. Items are scored on a 4-point Likert-scale from 0 (“never”) to 3 (“always”). Scores are converted into standardised T-scores for the young person’s age. In terms of clinical cut-offs, the recommended interpretation for all subscales is that scores above 65 indicate scores at borderline clinical threshold and scores of 70 or higher indicate scores above the clinical threshold. Investigations have demonstrated a factor structure consistent with depression and anxiety disorders in the DSM-IV[32,33]. The measure demonstrates high internal consistency and convergent validity, and has been shown to accurately assess anxiety and depression symptoms in youth [33,34]. The RCADS is a recommended tool for assessing depression and anxiety in child mental health services in the UK[35]. In the current study, the internal consistency for the depression scale was questionable (Cronbach’s alpha = .61) and was excellent for the anxiety scale (Cronbach’s alpha = .92).
2.2.3. Wechsler Abbreviated Scale of Intelligence – Second UK Edition (WASI-II<sup>UK</sup>). The WASI-II<sup>UK</sup> [36] is a brief measure of IQ that is suitable for children from age six. Due to time constraints, the two subtest version (Matrix Reasoning and Vocabulary) was used in the current study.

2.2.4 Tic-Specific Measures. The Yale Global Tic Severity Scale (YGTSS [37]) was administered to participants with TS/CTD only. The YGTSS is a clinician rated interview used to assess tic severity, which shows good internal consistency and inter-rater reliability as well as good convergent, divergent and discriminant validity [9]. This measure was rated by the first author (VP, a Clinical Psychologist with experience of working with young people with TS/CTD) and co-rated for a subsample of participants (n=14) showing high inter-rater agreement (94%).

2.3. Data Analysis

The number of specific memories, overgeneral memories and semantic associates given in response to positive, negative and neutral cue words was recorded. Six participants were excluded due to minimum performance requirements on the AMT (defined as providing a response to more than ten of fifteen cue words), resulting in twenty-six participants in the TS/CTD group and twenty-four participants in the control group. No participants in this final sample took longer than 60 seconds to respond to the cue words and so no responses were categorised as “no response” due to time. Independent t-tests were used to check for any differences between the groups for demographic variables, IQ, depression and anxiety. A repeated measures ANOVA was used to compare the pleasantness ratings for the three cue word Valences (positive; negative; neutral) and whether these ratings varied by group. This was included as a manipulation check to ensure that the predicted valence of the cue words elicited corresponding memories, i.e. negative cue words generated negative memories.
To test hypothesis 1 - that young people with TS/CTD generate fewer specific memories than controls - a 3x2 mixed design ANOVA was conducted. The number of specific memories to the three valences of cue word, Valence (positive; negative; neutral), was entered as the within subject variable and Group (TS/CTD; control) as the between subject variable. Memory specificity data were not normally distributed so, as there is no non-parametric equivalent to the mixed design ANOVA, non-parametric tests were used to follow up significant results. We also repeated this analysis with response time as the dependent variable to check whether having a diagnosis of TS/CTD impacted on the time that young people took to provide a memory and investigated whether tic severity correlated with memory specificity.

To test hypothesis 2 – that lower memory specificity is associated with more symptoms of depression – depression was first included in the above mixed design ANOVA to identify whether there was a significant interaction between depression and Valence. Regression analyses were then conducted to further investigate this interaction, and to control for anxiety. Depression was entered as the dependent variable and group, anxiety and memory specificity as the predictor variables in step one. In step 2, we investigated whether the relationship between depression and memory specificity was moderated by Group. Continuous variables were mean-centred and the product of the two predictor variables entered into the second step of the model to represent their interaction. For data that did not meet distributional assumptions, bootstrapping\(^1\) was used for inference. Given association between OGM and ASD [38], analyses were also re-run excluding participants with ASD. Whilst our hypotheses were directional, given the exploratory and novel nature of this study, a two-tailed significance level of $\alpha=0.05$ was used throughout the analysis.

\(^1\)Bootstrapping is a computer-intensive, non-parametric approach to statistical inference that provides valid standard errors, confidence intervals and $p$ values for hypothesis tests. It only assumes that the sampled data provide a reasonable representation of the population from which they came and therefore do not have to meet distributional assumptions (Davison & Hinkley, 2006).
3. Results

The groups did not significantly differ in terms of gender, age, ethnicity and IQ. There was also no significant difference between the groups on self-reported depression and anxiety scores (see Table 1). Two participants in the TS/CTD group had depression scores that were at borderline clinical threshold and one participant in the control group had a depression score that was above the clinical threshold. In terms of tic-specific measures, the sample means were consistent with previous studies in similar populations [39,40] (see Table 1).

3.1. Pleasantness Ratings

A repeated-measures ANOVA compared the pleasantness ratings given to the cue words for the different valences and whether the ratings of valence varied by group. There was a significant main effect of Valence ($F(2,47) = 151.60, p<.01, \eta_p^2 = .87$) but the group by valence interaction was not significant ($F(2,47) = 3.148, p>.05$) and there was no main effect of group ($F(1,48) = 2.65, p>.05$). Across groups, participants rated memories to negative cue words as the least pleasant ($\bar{x} = 2.19; SD = 0.90$), then memories to neutral words ($\bar{x} = 4.53; SD =1.47$) and memories to positive cue words were rated as the most pleasant ($\bar{x} = 5.51; SD = 1.28$), with all contrasts significant at $p<.05$. This indicates that the allocated valence of the cue words was effective in generating the corresponding valence of memories, i.e. that positive cue words produced more positive memories. Adding to this, the TS/CTD group did not rate their memories as more positive or negative than the control group.

[INSERT TABLE 1]

3.2. Group Differences in Memory Specificity

A 3x2 mixed design ANOVA was used to investigate whether the specificity of memories provided was affected by Group (TS/CTD, control) and by Valence (positive,
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negative, neutral) of the cue word (see table 2 and 3). The ANOVA showed significant main
effects of Valence \(F(2,47) = 3.50, p < 0.05, \eta^2_p = .13\) and a significant main effect of Group
\(F(1,48) = 14.90, p < 0.001, \eta^2_p = .24\). There was no significant interaction between Valence
and Group, \(F(2,47) = 1.77, p > 0.05\). Wilcoxon signed-rank tests indicated that participants
provided significantly more specific memories for neutral cues than negative cues \((T = 414, z
= 2.49, p < .05, r = 0.35)\). There was no significant difference between the number of specific
memories to positive and neutral cues \((T = 133, z =1.91, p = 0.056)\), or positive and negative
cues \((T = 166.5, z = -0.87, p > 0.05)\). Across Valence, the TS/CTD group (\(Mdn = 10\))
provided significantly fewer specific memories that the control group (\(Mdn=13\)), \(U = 490.5, z
= 3.50, p < .001, r = 0.49\). Of note, the difference between the groups remains significant if
the number of overgeneral memories generated is used instead of number of specific
memories, \(U =184.5, z = -2.51 p < .05, r = 0.36\). The same pattern of results was also found
when analyses were re-run excluding those with a diagnosis of ASD, except that the
difference between the number of specific memories generated to positive and neutral cue
words, became significant, \(T = 108, z = -2.27, p < .05, r = 0.33\). These findings imply that the
TS/CTD demonstrated reduced memory specificity compared to matched control participants
across valence.

In addition, we repeated the above analysis to check whether response time differed
between the groups and for different valences. This revealed a significant main effect of
valence \(F(2,47) = 7.19, p < 0.05, \eta^2_p = .23\), but no main effect of group, \(F(2,47) = 2.77, p
> 0.05\). The interaction between valence and group was also not significant, \(F(2,47) = 0.37, p
> 0.05\). Paired samples t-tests revealed that participants were significantly slower in
recalling negative \((\bar{x} = 11.08; SD = 5.00)\) than positive memories \((\bar{x} = 9.50; SD = 4.11, t(49)
= -2.14, p < 0.05, r =0.29;\) or neutral memories, \((\bar{x} = 8.62; SD = 33.97, t(49) = -3.80, p <
0.05, r =0.48)\). There was no significant difference in response times to positive and neutral
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memories (t(49) = 1.53, p > 0.05). This finding implies that there was no difference between the groups in response times but that, across groups, participants were slower to generate negative memories. [Of note, memory specificity did not significantly correlate with either tic severity (positive words, r(24)=0.087; negative words, r(24)= -0.12; neutral words, r(24)=0.037; all p> 0.05) or impairment (positive words, r(24)=-0.041; negative words, r(24)=0.15; neutral words, r(24)=0.34; all p > 0.05) as measured by the YGTSS.]

3.3. Relationship Between Memory Specificity and Depression.

Depression was first included as a covariate in the above analysis. The same pattern of results were identified and, in addition, there was a significant interaction between Valence and depression, F (1,46) = 3.32, p < 0.05, \( \eta_p^2 = .13 \). Regression analyses were therefore conducted to investigate the relationship between depressive symptoms and memory specificity for each valence separately (see table 4). For positive cues, analyses revealed a significant relationship between depressive symptoms and memory specificity across groups (Step 1: F(3, 49) =16.02, p < 0.001, R^2 = .51), such that those reporting more symptoms of depression had fewer specific memories for positive cue words. The second step of the analysis (Step 2: F (4, 49) = 11.76, p < 0.001, R^2 = .51, \( \Delta R^2 = 0.00 \), p > 0.05) revealed that including an additional interaction term did not improve variance explained. Thus, group did not significantly moderate the relationship between depression and memory specificity, implying that the relationship between memory specificity for positive cues and depressive symptoms is the similar for both groups. Although the models at step 1 were significant for negative (F (3,49) = 12.63, p < 0.001, R^2 = .45) and neutral cue words (F (3,49) = 12.71, p < 0.001, R^2 = .45), there was no significant relationship between depression and memory specificity for either. The second step did not significantly add to the model for either negative or neutral cue words (negative: F (4,49) = 10.02, p < 0.001, R^2 = .47, \( \Delta R^2 = 0.019 \), p
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> 0.05; neutral: $F(4,49) = 9.40, p < 0.001, R^2 = .46, \Delta R^2 = 0.002, p > 0.05$. [When analyses were re-run excluding participants with ASD, the same pattern of results was observed.]

[INSERT TABLE 4]

4. Discussion

The current study used an experimental task to investigate autobiographical memory in young people with TS/CTD relative to comparison participants, and whether memory specificity is associated with symptoms of depression in this population (as they are in the general population [17]). Our findings suggest that autobiographical memory in young people with TS/CTD is characterised by over-generality across memories, compared to typically-developing peers, such that young people with TS/CTD struggle to recall a unique memory to a cue word instead generating general memories, routine events or associations. Secondly, we found that across groups those with less specific memories for positive cue words reported more depressive symptoms. Together these results may offer insight into why people with TS/CTD are more vulnerable to developing depressive symptoms than people in the general population, as they have lower memory specificity [4], and suggests that generating more specific memories for positive events could be an appropriate treatment target for this patient-group.

Our findings indicate that young people with TS/CTD may have less specific memories than their peers. This is consistent with findings from other neurodevelopmental disorders, such as ASD, where OGM has been reported [24]. OGM has been most reliably associated with the development and severity of depression [18,19], and is important for the individual’s sense of self and social functioning [15]. Our library of autobiographical memories provides an understanding across time of who we are, with more negative self-beliefs being associated with greater OGM in young people [41]. Being less able to fluently process autobiographical memories in a specific way has implications for daily cognitive
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functioning, with a lack of specificity associated with poorer problem-solving, planning, and impaired social interactions [13]. Therefore, reduced specificity may contribute to difficulties in sense of self, social cognition and functioning documented in this population [21,42]. For example, adults with TS/CTD have been shown to have impairments in making self-other distinctions and on tasks of social cognition [21], such as errors on faux pas tasks [43,44] and errors in attributing intention to random movements [23]. Furthermore, recent neuroimaging research suggests that adults with TS/CTD have atypical activation in brain structures contributing to social and emotional processing as well as memory [29,45]. Whilst further research is needed, these errors could be associated with OGM, as being able to fluently draw on autobiographical memory is likely to aid social understanding.

The relationship observed between memory specificity for positive cues and depression is also in line with existing literature [19], and with our hypothesis that reduced specificity would be associated with increased depression. However, the relationship between depression and memory specificity was not found across all cue word valences. While these findings require replication, it is broadly consistent with research demonstrating that memory specificity to positive over negative cue words are a better predictor of depressive symptoms [46]. The main theories explaining OGM are based on Conway and Pleydell-Pearce’s (2000) model [15], where autobiographical memory is proposed to be arranged into a series of knowledge structures which become increasingly specific. In generative retrieval, a cue guides a controlled top down search of the memory structure and OGM results if there is disruption to this search, for example by functional avoidance. The CaR-FA-X model [16] expanded on this by suggesting that difficulties accessing specific memories result from a number of processes. These include memory search efforts being captured by categorical themes preventing the individual from accessing a specific memory, and that this capture is more likely due to functional avoidance of the specific details of past events which diverts
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processing to the categorical level of autobiographical representation. Therefore, in the short
term, OGM may function to minimise negative affect from past memories [26] and this is
supported by experimental data [27]. The young people in the TS/CTD group are likely to
have experienced more distress than our control group, for example young people with
TS/CTD are at enhanced risk of peer victimisation [1]. Memory specificity may, therefore, be
a strategy employed by young people with TS/CTD to manage negative affect from past
memories. However, research suggests that this is a dysfunctional longer-term strategy as
memory specificity for all memories is reduced as a consequence of this, and this lack of
specificity has been associated with increased vulnerability for later development of
depression [13].

Identifying cognitive factors that may explain why young people with TS/CTD are at
increased risk of developing depression is crucial to develop effective interventions that can
prevent the onset of depression. Early-stage clinical trials in adolescents and adults have
demonstrated that memory specificity can be successfully enhanced using cognitive training
[47] (for example, generating specific memories to cue words e.g. happy). This simple
cognitive training reduced depressive symptomatology and improved day-to-day cognition
[47–49]. Therefore, if these current findings are replicated, they would suggest piloting these
techniques in young people with TS/CTD.

There are several limitations to this study, including limitations in methodology and
sample characteristics. In terms of methodology, a major limitation is its cross-sectional
nature meaning that we cannot understand the temporal links between OGM, tics and
depression. Longitudinal studies that establish whether OGM does confer risk for developing
depression would identify it as a target for prevention. Raters for the Autobiographical
Memory Task were also not blinded to group allocation, blinding in future studies would be
valuable to reduce potential for bias. In terms of individual factors that could affect
performance, it is possible that young people may not provide true autobiographical memories or that the experience of tics during the task may have impacted on the type of memory generated. The AMT is a well-established measure of memory specificity [17] and there is nothing to suggest that one group is more likely than the other to create false memories, so this should not affect group differences. However, the inclusion of a control condition to check whether performance is related to tics and whether the young person is likely to generate false memories would be helpful to reduce these potential influences on performance.

In terms of sample characteristics, limitations include the sample not having clinically significant depression, the presence of comorbidities and the equal sex ratio. Comparing groups of young people with TS/CTD with and without clinical depression with control participants with and without depression would aid understanding of whether OGM is reduced in young people with TS/CTD (generally), in young people with depression (generally), or whether there is an interaction between TS/CTD and depression. Previous research has documented higher levels of depression in children and adults with TS/CTD, compared to healthy controls [4,50,51]. In the current study, there was no significant difference between our groups for symptoms of depression and no participants reported a diagnosis of depression. For the current study, this is highly advantageous as it reduces the possibility that the observed group differences in memory specificity are due to depression rather than the other way around. Nonetheless, there are a number of explanations for why there were no group differences in depression. Firstly, the relatively young age of our sample given that risk for depression increases with age and our sample was younger than the typical age of onset for depression (with peak years for onset considered to be between 15 and 29) [12,52]. Secondly, our TS/CTD participants were recruited from both the community and from a specialist clinic. Studies that have consistently identified higher rates of depression are
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from specialist tertiary services, with only two of five studies from community samples showing significant elevated rates of depression [4]. Thirdly, the internal consistency of the depression scale was questionable, which was surprising as a well-established measure was used. Multiple measures and clinical interviews for depression would improve reliability of diagnoses.

The presence of comorbid ADHD and OCD in the TS/CTD group is another limitation. Comorbidity of ADHD or OCD is reported to be very high in TS/CTD (approximately 70%) [53] and, therefore, it did not seem representative to exclude participants with comorbidity. While there is little data suggesting that poor memory specificity is associated with ADHD and/or OCD, nonetheless, these comorbidities could still impact on task performance. For example, impulsivity is a feature of ADHD which may have meant that young people responded to cue words on the AMT without considering their answer (although this is unlikely given that there were no group differences in response time to cue words). Whether having a diagnosis of OCD or ADHD enhances risk for depression or reduces quality of life (relative to people with TS/CTD alone) is unclear with research reporting mixed findings [40,54]. Furthermore, the sex ratio in our sample was roughly even whereas most studies report a sex ratio of between 2:1 and 4:1 (male: female) [55,56]. This raises issues over the representativeness of our sample relative to other TS/CTDs cohorts.

In terms of future research, it would be helpful to measure the mechanisms that may be contributing to lower specificity in the TS/CTD group. Failures in generating specific memories have been attributed to both retrieval and encoding of the memories [31,38] as well as difficulties with executive functioning [31]. Similarly, it would be helpful to have a measure of peer victimisation/negative life events to evaluate the affect-regulation hypothesis in this population. As autobiographical memory is important for one’s sense of self and for social cognition, it would be valuable for future research to explore links between deficits in
these areas and OGM in people with TS/CTD. It would also be interesting to explore whether there were qualitative differences between the memories generated by the two groups and/or for different categories of words, for example whether one group provided more vivid memories or whether general memories tended to be associated with social situations. Having several samples of different ages would also determine whether typical developmental changes alter the relationship between TS/CTD and OGM, especially during adolescence when depressive symptomatology is likely to emerge.

5. Conclusions

This study found that young people with TS/CTD have reduced autobiographical memory specificity, compared to controls, and that across both groups reduced memory specificity for positive cues was associated with higher depression scores. Autobiographical memory specificity is one cognitive factor that warrants further research and could be a valuable intervention target for this population.
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6. Acknowledgements

We would like to thank all the families that participated in this research study as well as Tourettes Action and the schools for all their help.

7. Funding

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Table 1: Group differences on baseline measures

<table>
<thead>
<tr>
<th></th>
<th>CTD (n=26)</th>
<th>Control (n=24)</th>
<th>Group Comparison (CTD, Control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>11.46 (1.66)</td>
<td>11.36 (2.48)</td>
<td>t(48)= 0.16, p&gt;0.05</td>
</tr>
<tr>
<td>Gender</td>
<td>14 females (54%)</td>
<td>12 females (50%)</td>
<td>χ²(1)= 0.32, p&gt;0.05</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>23 White British (88%)</td>
<td>18 White British (75%)</td>
<td>χ²(5) = 4.87, p&gt;0.05</td>
</tr>
<tr>
<td>IQ</td>
<td>108.08 (11.92)</td>
<td>111.92 (10.94)</td>
<td>t(48)= -1.83, p&gt;0.05</td>
</tr>
<tr>
<td>Depression</td>
<td>52.58 (8.46)</td>
<td>50.54 (8.04)</td>
<td>t(48) =0.87, p&gt;0.05</td>
</tr>
<tr>
<td>Anxiety</td>
<td>51.19 (10.41)</td>
<td>45.96 (8.32)</td>
<td>t(48) =1.95, p&gt;0.05</td>
</tr>
<tr>
<td>YGTSS tic severity</td>
<td>21.04 (8.40)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>YGTSS impairment</td>
<td>22.31 (13.36)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(YGTSS = The Yale Global Tic Severity Scale)
Table 2: Descriptive statistics for specific memories recalled for each valence per group

<table>
<thead>
<tr>
<th>Memory type</th>
<th>TS/CTD (n = 26)</th>
<th>Control (n = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Positive cues</strong></td>
<td>$\bar{x} = 3.35$; SD = 0.94</td>
<td>$\bar{x} = 4.08$; SD = 1.02</td>
</tr>
<tr>
<td></td>
<td>Mdn = 3 IQR = 1.00</td>
<td>Mdn = 4 IQR = 2.00</td>
</tr>
<tr>
<td><strong>Negative cues</strong></td>
<td>$\bar{x} = 2.96$; SD = 1.25</td>
<td>$\bar{x} = 4.21$; SD = 0.98</td>
</tr>
<tr>
<td></td>
<td>Mdn = 3 IQR = 2.00</td>
<td>Mdn = 4 IQR = 1.00</td>
</tr>
<tr>
<td><strong>Neutral cue</strong></td>
<td>$\bar{x} = 3.65$; SD = 1.20</td>
<td>$\bar{x} = 4.38$; SD = 0.77</td>
</tr>
<tr>
<td></td>
<td>Mdn = 4 IQR = 1.00</td>
<td>Mdn = 5 IQR = 1.00</td>
</tr>
</tbody>
</table>

$\bar{x}$: mean; SD: standard deviation; Mdn: Median; IQR: interquartile range
Table 3: Distribution of different memory types for each group and cue word

<table>
<thead>
<tr>
<th>Memory type</th>
<th>TS/CTD (n=26)</th>
<th>Control (n=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Specific</td>
<td>60.69%</td>
<td>53.79%</td>
</tr>
<tr>
<td>General extended</td>
<td>10.34%</td>
<td>13.10%</td>
</tr>
<tr>
<td>General categorical</td>
<td>9.66%</td>
<td>15.17%</td>
</tr>
<tr>
<td>Semantic associate</td>
<td>4.83%</td>
<td>3.45%</td>
</tr>
<tr>
<td>Omission</td>
<td>14.48%</td>
<td>14.48%</td>
</tr>
</tbody>
</table>

Example responses to cue word “excited”

Specific: “I was really excited when I woke up on Monday because my friend was coming over and I was excited to play a new game with them.”

General extended: “I was excited when we were in Florida for a holiday.”

General categorical: “Every year I get really excited just before I have my birthday party.”

Semantic associate: "Birthdays"

Omission: "I can't think of one."
Table 4: Regression analyses with self-reported depression as the dependent variable.

Bootstrapped standard errors, p-values and confidence intervals are reported.

<table>
<thead>
<tr>
<th>Valence of memory cues</th>
<th>B</th>
<th>β</th>
<th>SE B</th>
<th>p</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group</td>
<td>2.53</td>
<td>0.16</td>
<td>2.12</td>
<td>.24</td>
<td>-1.55 to 6.70</td>
</tr>
<tr>
<td>Memory Specificity</td>
<td>-2.09</td>
<td>-0.26</td>
<td>1.02</td>
<td>.046</td>
<td>-4.27 to -.21</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0.58</td>
<td>0.68</td>
<td>0.073</td>
<td>.000</td>
<td>0.44 to .74</td>
</tr>
<tr>
<td>Step 2: Group x Memory</td>
<td>-0.18</td>
<td>-0.034</td>
<td>2.26</td>
<td>.93</td>
<td>-4.90 to 4.14</td>
</tr>
<tr>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group</td>
<td>1.25</td>
<td>0.076</td>
<td>2.42</td>
<td>.62</td>
<td>-3.42 to 5.90</td>
</tr>
<tr>
<td>Memory Specificity</td>
<td>-0.18</td>
<td>-0.028</td>
<td>0.93</td>
<td>.84</td>
<td>-2.06 to 1.53</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0.58</td>
<td>0.69</td>
<td>0.083</td>
<td>0.00</td>
<td>.44 to .76</td>
</tr>
<tr>
<td>Step 2: Group x Memory</td>
<td>-2.79</td>
<td>-0.50</td>
<td>2.50</td>
<td>.23</td>
<td>-8.72 to 1.45</td>
</tr>
<tr>
<td>Neutral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group</td>
<td>1.30</td>
<td>0.079</td>
<td>1.92</td>
<td>.50</td>
<td>-2.58 to 5.00</td>
</tr>
<tr>
<td>Memory Specificity</td>
<td>-.38</td>
<td>-0.049</td>
<td>0.85</td>
<td>.66</td>
<td>-2.15 to 1.61</td>
</tr>
<tr>
<td>Anxiety</td>
<td>.59</td>
<td>.69</td>
<td>0.085</td>
<td>0.00</td>
<td>0.44 to 0.78</td>
</tr>
<tr>
<td>Step 2: Group x Memory</td>
<td>-0.88</td>
<td>-0.15</td>
<td>2.04</td>
<td>.64</td>
<td>-4.20 to 3.89</td>
</tr>
</tbody>
</table>