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Assessing cognitive flexibility in anorexia nervosa using eye tracking: A registered report

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Abstract

Objective: Cognitive flexibility research in anorexia nervosa (AN) has primarily focused on group differences between clinical and control participants, but research in the general population utilizing the mixed pro- anti-saccade flexibility task has demonstrated individual differences in trait anxiety are a determinant of switching performance, and switching impairments are more pronounced for keypress than saccadic (eye-movement) responses. The aim of the current research is to explore trait anxiety and differences in saccadic and keypress responding as potential determinants of performance on flexibility tasks in AN.

Method: We will compare performance on the mixed pro- anti-saccade paradigm between female adult participants with a current diagnosis of AN and matched control participants, observing both saccadic and keypress responses while controlling for trait anxiety (State - Trait Anxiety Inventory) and spatial working memory (Corsi Block Tapping Test). Associations with eating disorder-related symptoms (Eating Disorder Examination Questionnaire), flexibility in everyday life (Eating Disorder Flexibility Index), and the Clinical Perfectionism Questionnaire will also be assessed.

Results: Data which controls for individual differences in trait anxiety and assesses flexibility at both the task- and response-set level may be used to more accurately understand differences in performance on cognitive flexibility tasks by participants with AN.

Discussion: Clarifying the effects of trait anxiety on flexibility, and differences between task- and response-set switching may advance our understanding of how cognitive flexibility relates to flexibility in everyday life and improve translation to therapeutic approaches.

Public significance statement: This research will compare performance on a flexibility task between participants with anorexia nervosa (AN) and controls while observing their eye-movements to examine whether trait anxiety and type of response (eye-movement and keypress) are associated with performance. This data may improve our understanding of why participants with AN perform more poorly on cognitive

flexibility tasks, and how poor cognitive flexibility relates to eating disorder-related issues with flexibility in everyday life.

1 | INTRODUCTION

Issues with cognitive flexibility are theorized to contribute to the cognitive and behavioral rigidity observed in anorexia nervosa (AN; Schmidt & Treasure, 2006; Treasure & Schmidt, 2013). Cognitive flexibility is the ability to shift focus between mental sets in response to changing demands (Diamond, 2013). Meta-analytic results suggest adults with AN perform more poorly on tests of cognitive flexibility than healthy control groups (Hedges $g = -.39$), but results vary greatly according to the test used (Stedal et al., 2021). Empirical research in this area has primarily focused on group differences between clinical and control participants but could be extended by exploring individual differences which may moderate performance across both groups. Eye movement research in the general population has identified that performance on the mixed pro- anti-saccade flexibility task is moderated by trait anxiety (Ansari et al., 2008), and errors are more pronounced for keypress responses than saccadic (eye-movement) responses (Brett & Machado, 2017). These potential determinants of poorer performance have not been explored in AN and may improve understanding and interpretation of cognitive flexibility test results.

1.1 | Slow but accurate switching in AN

Although there is substantial evidence to suggest poorer performance on mental set-shifting tasks by adult participants with AN compared to controls, results vary by task from very large underperformance on Berg's Card Sort Task (Hedges $g = -1.17$), to superior performance for Verbal Fluency (Hedges $g = 0.18$; Stedal et al., 2021). The main assessments used have been traditional neuropsychological tests; the Wisconsin Card Sort Task and the Trail Making Test (Miles et al., 2020). Task switching paradigms are an alternative, and more precise, measure of cognitive flexibility (see Monsell, 2003 for a review) and are utilized in clinical cohorts when more fine-grained data regarding the mechanisms which underlie cognitive rigidity are required (Meiran et al., 2011).

Recent cognitive flexibility research using a cued task-switching paradigm which requires participants to perform one of two tasks in response to a bivalent stimulus, has demonstrated that both currently ill and weight-restored individuals with a history of AN perform as accurately as a healthy control group, but with slower reaction times (Berner et al., 2019; King et al., 2019). A bias towards accuracy over speed was noted in the task-switching results for weight-restored

participants who were *more* accurate than the control group, and the authors suggested that this high level of self-control may be related to trait perfectionism (King et al., 2019). Indeed, meta-analytic results suggest maladaptive perfectionism is higher in individuals with AN than nonclinical controls with large effect (Hedges $g = 1.00$), and control groups with other psychiatric disorders with small-medium effect ($g = 0.41$; Dahlenburg et al., 2019). However, slow but accurate task switching performance in AN is also consistent with the results of a large synthesis of 23 studies and 165 experimental methods across the eating disorder (ED) literature which found a general "slow down" in choice reaction time tasks (Ferraro et al., 2018).

1.2 | Anxiety and switching

Cognitive flexibility research in the general population utilizing a task-switching version of the anti-saccade task, the mixed pro- anti-saccade task, has demonstrated that individual differences in trait anxiety are associated with the speed of switching (Ansari et al., 2008). The standard anti-saccade task is a measure of inhibitory control which requires a participant to inhibit an automatic saccade (eye movement) towards an abrupt-onset stimulus and make a volitional saccade in the opposite direction. Accuracy and speed can be compared to a pro-saccade task, which simply requires the participant to make the automatic response to look towards the stimulus. Anti-saccade performance by participants with AN does not appear to be significantly different to controls, but pro-saccades may be faster (Phillipou et al., 2016). In the mixed saccade task, pro- and anti-saccade trials are randomly interleaved, requiring the participant to switch between the two tasks as cued by the color of a pre-trial fixation point (see Figure 1). Eye movement research in the general population has demonstrated that when switching between pro- and anti-saccades, participants with high anxiety performed with equivalent accuracy but slower reaction times than participants with low anxiety (large effect, Cohen's $d = .85$; Ansari et al., 2008). According to attentional control theory (Eysenck et al., 2007), trait anxiety may impair efficiency on attention tasks which require switching because it alters the balance between goal-directed or top-down attention and stimulus-driven or bottom-up attention, biasing to the latter. These effects appear to be most strongly observed in the mixed saccade task due to the asymmetry in demands on the attentional control system between the two tasks: one requiring inhibition of a prepotent response and one allowing the reflexive response (Gustavson et al., 2017). The mixed pro-anti-saccade task is primarily used in the general population literature

FIGURE 1 Schematic representation of the expected behavior for the pro-saccade and anti-saccade tasks in both saccadic and keypress response modes. Stimuli are not to scale
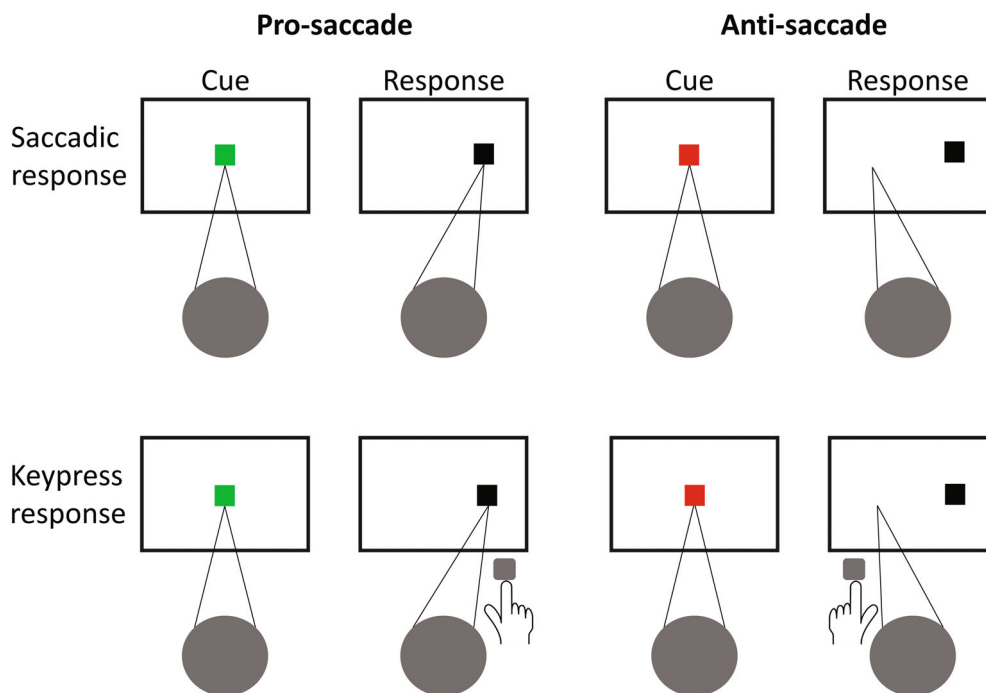
(see Heath et al., 2016 for a review) and rarely in clinical literature (Manoach et al., 2002). However, as a measure of flexibility which controls for inhibition, it may be particularly useful in AN where strong inhibitory control has been suggested to compensate for poorer flexibility in weight-restored adolescents (Weinbach et al., 2019).

The literature examining causal links between anxiety disorders and AN is mixed (Lloyd et al., 2020), but occurrence of co-morbid anxiety disorders in AN is high (Swinbourne & Touyz, 2007), and severity of anxiety-related constructs such as intolerance of uncertainty and worry in participants with AN is similar to that reported in participants with anxiety disorders (Sternheim et al., 2015). There is currently very little direct empirical evidence regarding the specific effects of trait anxiety on cognitive performance tasks in eating disorder research, but a recent systematic review of studies in AN that have assessed associations between cognitive flexibility performance tests and anxiety measures found although the majority (16 studies) did not detect significant effects, nine studies found significant associations (Fuglset, 2021). Data from general population research demonstrating that trait anxiety accounts for significant differences in switching performance (Ansari et al., 2008; Eysenck et al., 2007) particularly under conditions where participants need to switch from an effortfully-established task to a more automatic task (Gustavson et al., 2017; Wilson et al., 2018), suggest that more focused investigation in AN is warranted.

1.3 | Task-set or response-set shifting?

Cued task-switching involves both task- and response-set shifting. Generally, with bivalent stimuli (e.g., circles and squares that are yellow or blue), participants will respond with two keys on a standard keyboard, where each key indicates a color on the color task, and the same two keys indicate a shape on the shape task. When a task-switch is congruent with a response switch (e.g., color to shape task-switch accompanied by a key switch), participants generally make fewer errors than when a task-switch is not accompanied by a response switch. However, in recent research, weight-restored participants with AN did not show this usual benefit of congruent task- and response-set switching (King et al., 2019). This apparent difference in response-set shifting is broadly consistent with neuroimaging flexibility research in AN which suggested that poor performance on set-shifting tasks may be secondary to impairments in response-set shifting (Zastrow et al., 2009).

The mixed pro- anti-saccade task offers an opportunity to further assess the relative contribution of task versus response-set shifting. Direct comparison of saccadic and keypress responses to mixed pro- and anti-saccade trials in a population which displays flexibility decrements has demonstrated that older participants show significant switching deficits when compared to younger adults on keypress measures, but not on saccadic measures (Brett & Machado, 2017). This suggests that rigidity in response-set shifting may be a confound for cognitive switching tasks which are dependent on a keypress response. The anti-saccade keypress version follows the same parameters as the saccadic task, but participants are instructed to respond using the keys on a standard to keyboard to indicate the target direction. Observation of saccadic and keypress responses to the mixed pro- anti-saccade task by individuals with AN to compare task- and response-set switching may provide new data to better understand flexibility at both levels, and further clarify the determinants of differences in task performance.

1.4 | Aim and hypotheses

The goal of the proposed study is to compare switching performance on the mixed pro-anti-saccade task between participants with a current diagnosis of AN and healthy control participants matched for age and level of education while controlling for individual differences in trait anxiety. The relative contribution of task- versus response-set shifting on task performance will be examined by recording both saccadic and manual keypress task responses. Spatial working memory will also be measured and statistically controlled, as higher working memory is associated with fewer errors on the anti-saccade task, but also with greater difficulty shifting away from an effortfully-established task set (DeCaro & Beilock, 2010). Associations with cognitive and behavioral flexibility in everyday life, severity of eating disorder-related cognitions and behaviors, and level of clinical perfectionism will be assessed by self-report. Consistent with past ED research, it is predicted that participants with AN will perform as accurately as controls, but reaction times will be slower. However, consistent with past research in the general population using this paradigm, it is predicted that trait anxiety will be a significant independent predictor of reaction times in both groups. Consistent with previous research that has demonstrated switch costs are more pronounced for manual than saccadic responses, if group differences are due to differences in response-set shifting the effect should be restricted to manual responses, and if group differences are due to differences in task-set shifting the effect should also be observed in saccadic responses. Planned exploratory analyses will examine associations between performance on the mixed saccade task and eating disorder symptoms, clinical perfectionism, and everyday flexibility self-report scales.

2 | METHOD

2.1 | Participants

To aid comparison with recent studies in AN (Berner et al., 2019; King et al., 2019), adult female participants 18 years or older will be recruited. All participants will complete an initial screening process which will include administration of a standardized Eating Disorder Assessment for DSM-5 (EDA-5; Sysko et al., 2015) to determine study eligibility. Clinical participants will be eligible for the study if they have a current formal diagnosis of AN from a medical professional and meet DSM-5 criteria for AN on the EDA-5 interview. Control participants will be eligible if they report no history of an eating disorder or other psychiatric or neurocognitive disorder, and do not meet DSM-5 criteria for any feeding or eating disorder on the EDA-5. Groups will be matched for age and years of education by standard case–control procedure, and all participants will be required to have normal or corrected-to-normal vision. Participants will be recruited through advertisements placed on current research pages on university websites and mental health and eating disorder organizations. Participants will be tested individually in a laboratory session at The University of Sydney. This study is approved by The University of Sydney Human Research Ethics Committee, approval number 2021/189.

2.1.1 | Power analysis

The effect size reported by Ansari et al. (2008) for mean differences in switching latency between participants with high and low anxiety in the general population was large. Taking a conservative approach to sample size estimation, a power analysis using Gpower (Faul et al., 2007) based on a medium effect indicates a minimum sample of 60 participants (30 per group) to achieve 80% power at an alpha of .025.

2.2 | Measures

2.2.1 | Demographic information

Participants will be asked to report their age, country of birth, ethnicity, the year of diagnosis, diagnostic subtype, duration of disorder, whether they have been admitted for in-patient treatment, current medications, and any other diagnoses.

2.2.2 | Mixed pro-anti-saccade task

The mixed saccade task is a task-switching paradigm which measures cognitive flexibility and inhibitory control. Participants switch between pro- and anti-saccade tasks which are presented in random order and are cued by a pre-trial green (pro) or red (anti) fixation point.

2.2.3 | State - Trait Anxiety Inventory

(Spielberger, 1983) includes 20 items assessing for trait anxiety (STAI-T), with higher scores indicating greater severity. Cronbach's alpha of .71 (Sternheim et al., 2020) and .96 (Toppino et al., 2022) have been reported in recent samples of adults with AN.

2.2.4 | Clinical Perfectionism Questionnaire

(Fairburn, Cooper, & Shafran, 2003) is a 12-item self-report measure of clinical perfectionism, defined as being "overly dependent on the pursuit of personally demanding standards... despite adverse consequences" (Shafran, Cooper, & Fairburn, 2002, p. 787). Higher scores indicate higher levels of perfectionism. Cronbach's alpha of 0.82 has been reported for a mixed ED sample (Egan et al., 2015).

2.2.5 | Eating Disorder Flexibility Index

The Eating Disorder Flexibility Index (EDFLIX; Dahlgren, Hage, Wonderlich, & Stedal, 2019) is a 36-item self-report scale assessing general and ED-specific flexibility in everyday life. Total scores range from 36 to 216, with higher scores indicating greater flexibility. Cronbach's alpha for a mixed ED sample reported in the validation study was .91 (Dahlgren et al., 2019).

2.2.6 | Eating Disorder Examination Questionnaire

The Eating Disorder Examination Questionnaire (EDE-Q; Fairburn & Beglin, 1994) is a 28-item self-report questionnaire validated with Australian norms (Mond et al., 2006) used to assess eating disorder attitudes and behaviors over the past 28 days. Items assessing ED-related attitudes comprise a global score with a range from 0 to 6. Higher scores indicate more severe eating disorder pathology. The remaining items assess frequency of ED behaviors: objective and subjective bingeing, purging, laxative use and compulsive exercise. Height and weight are reported, and BMI (kg/m^2) will be calculated from this data. Cronbach's alpha of .93 has been reported in an Australian female community sample (Mond et al., 2004).

2.2.7 | Corsi block tapping test

(Corsi, 1972) is a test of spatial working memory. Boxes in a 9-square grid light up in a sequence, and participants are asked to repeat the sequence. The task will be presented in Inquisit 6 as described in Kessels et al., 2000. Higher scores indicate greater spatial working memory span.

2.3 | Procedure

Participants will provide informed consent before answering demographics questions and mood measures. They will then complete the mixed saccade task in two blocks separated by a short break. The session will end with administration of the working memory task and the remaining surveys. Order will be fixed to minimize any measurement error due to participant × order interactions (Miyake et al., 2001). The protocol for this study is preregistered at Open Science Framework (https://osf.io/czjtp).

2.3.1 | Apparatus

During the mixed saccade task, eye movements will be recorded using a SR Research Eyelink 1000 Plus desktop mounted eye tracker, with a sampling rate of 2000 Hz. The task will be displayed on a 21-in. View Sonic CRT monitor with a refresh rate of 140 Hz. Participants will be seated 60 cm from the monitor, and head movements will be minimized with a chin and forehead rest. Viewing will be binocular, but only the right eye will be recorded. Participants will complete the surveys via Qualtrics on a laboratory PC.

2.3.2 | Experimental task

The mixed saccade task will begin with a brief orientation to the equipment, explanation of the task, and practice trials to familiarize participants with the procedure. Participants will be asked to respond as quickly and as accurately as possible. At the beginning of the experiment, and before each block of trials participants' eye movements will be calibrated using a 9-point calibration procedure. The experiment will be completed in two blocks, one with keypress responding and one with saccadic responding, separated by a short break. Participants will be pseudo-randomly allocated to one of two counterbalanced task orders, completing either the eye-movement or keypress response blocks first.

Stimulus, trial, run, and outcome parameters will be consistent with standardized anti-saccade protocol recommendations (Antoniades et al., 2013). For each response type, participants will initially complete a single-task block of 40 prosaccades and a single-task block of 40 anti-saccades. This will be followed by the mixed saccade task, which will comprise 4 blocks of 40 mixed-task pro- and anti-saccade trials, totaling 320 trials. Mixed trial blocks will be pseudo-randomly ordered to ensure a maximum run of 3-repeat trials. Response stimuli will be presented in a horizontal plane at an amplitude of 8° from the central fixation point, equally to the left and right of screen. Each trial will begin with the presentation of a fixation point (variable interval $M = 1.5$ s) which cues the task - green for pro- and red for anti-saccade trials - followed by the presentation of a 0.5° square target stimulus. For pro-saccade trials, participants will be instructed to look towards the target, and on keypress blocks to press the key on the same side as the target. On anti-saccade blocks participants will be instructed to look to the opposite side of the screen from the target, and on keypress blocks to press the key on the opposite side to the target. The trial will end when the response is detected or 1500 ms elapses.

2.4 | Data analysis

2.4.1 | Data preparation

Saccadic latency will be measured as the time from stimulus onset to initiation of the first saccade. Trials with saccadic latency shorter than 80 ms or greater than 600 ms will be excluded. Dependent measures will be response accuracy and reaction time from both eye movement and key press data. Switch costs will be calculated by subtracting mean reaction time for repeat trials from switch trials in the mixed blocks.

2.4.2 | Statistical analyses

Data analysis will be conducted using IBM SPSS Statistics 28.0 software. To control for the impact of testing multiple dependent measures, an alpha level of .025 will be used. Effects that reach the conventional .05 criterion will be noted as marginal. Hierarchical linear regression will be conducted to examine whether Group (clinical versus control) is a significant predictor of the accuracy and reaction time of eye movement and keypress responses on the mixed saccade task, while controlling for trait anxiety and spatial working memory. Planned exploratory analyses using Spearman rank-order correlation

coefficient (r_s) will further examine associations between performance on the mixed saccade task and eating disorder characteristics (EDE-Q scores), level of clinical perfectionism, and self-reported cognitive-behavioral flexibility in everyday life (EDFLIX scores).

3 | CONCLUSION

Research in the general population using the mixed pro- anti-saccade task has demonstrated that higher trait anxiety is associated with less flexible switching (Ansari et al., 2008), and that switching issues are more pronounced for keypress than saccadic responses (Brett & Machado, 2017). The current research will compare performance on the mixed pro- anti-saccade task between participants with AN and a matched control group while controlling for trait anxiety and measuring both manual and saccadic responses to examine these potential factors that may account for variability in performance across both the clinical and control groups. This data may be used to more accurately understand the determinants of performance differences on cognitive flexibility tasks by participants with AN. Clarifying the difference between task- and response-set shifting levels of flexibility may improve our understanding of how cognitive flexibility relates to eating disorder-related issues with behavioral flexibility in everyday life and improve translation to therapeutic approaches.

CONFLICTS OF INTEREST

P.H. has received sessional fees and lecture fees from the Australian Medical Council, Therapeutic Guidelines publication, and New South Wales Institute of Psychiatry and royalties from Hogrefe and Huber, McGraw Hill Education, and Blackwell Scientific Publications, and she has received research grants from the NHMRC and ARC. She is Chair of the National Eating Disorders Collaboration in Australia (2019–). In July 2017, she provided a commissioned report for Takeda (formerly Shire) Pharmaceuticals on lisdexamfetamine and binge eating disorder, is a consultant to Takeda, and in 2018–2020 received honoraria for education of Psychiatrists. S.T. receives royalties from Hogrefe and Huber, Taylor and Francis and McGraw Hill for published books/book chapters. He has received travel grants, research grants and honoraria from Takeda for commissioned reports, public speaking and consultant work and has chaired their Australian Clinical Binge Eating Advisory Board.

The other authors have no conflicts of interest to disclose.

This study has been preregistered at Open Science Framework: https://osf.io/czjtp Open access publishing facilitated by The University of Sydney, as part of the Wiley - The University of Sydney agreement via the Council of Australian University Librarians.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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