First Year Report -

Learning in Adolescence: Social and Affective Influences

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Introduction

Adolescence, defined as the period of life between 10-24 years of age (Sawyer et al., 2018), is a key developmental period for learning. In addition to acquiring formal education, which is what we typically think about when discussing learning, adolescents are also learning about their increasingly complex social and emotional worlds. Concurrently, the brain continues maturing substantially during adolescence, into the mid-twenties (Steinberg, 2014; Selemon, 2013) with adolescence representing a 'window of opportunity' for brain development (Fuhrmann et al., 2015). These changes have led researchers to propose that adolescence is a second sensitive period in which heightened plasticity might result in environmental factors exerting substantial influence on brain and behaviour. In recent years, adolescence has been established in the research literature as a life stage characterized by heightened affective and social sensitivity (Hartley & Lee, 2015; Blakemore & Mills, 2014). For example, compared to adults, adolescents are particularly susceptible to peer influence (for review see Andrews et al., 2021; Blakemore, 2018) experience more intense emotions (Nook & Somerville, 2019; Crone & Dahl, 2012) and are less adept at some aspects of emotion regulation (Schweizer et al., 2020). While we have begun to better understand both brain development and social and affective processing in adolescence, much less is known about learning during this stage.

Development and learning are intricately entwined. Both normative development and learning can generate rewiring of neural circuits (Galvan, 2010; Greenough et al., 1987). While the brain maintains a level of plasticity throughout life, there are certain developmental periods in which neural systems are more sensitive to certain types of input. This makes learning easier, more effective and more enduring in specific domains at certain times, with consequences for behaviour and function long term. For example, though we can learn new languages throughout life, it is particularly easy to learn certain aspects of language (in particular language sounds) in the first year of life relative to other life stages. This amplified learning corresponds to a particularly plastic phase in neural systems sensitive to language (Doupe & Kuhl, 2008). Researchers have suggested that enhanced learning in other domains might constitute evidence for sensitive periods (Fuhrmann et al., 2015). Interestingly, research suggests that learning in adolescence may be heightened in several ways.

Adolescence is characterized as a period of increased neural sensitivity to rewards relative to both childhood and adulthood (Schreuders et al., 2018). Though behaviourally it is less clear how reward sensitivity affects reward learning, this sensitivity has been shown to facilitate reward learning in some studies. Increased activity in reward regions of the brain (such as the striatum; Oldham et al., 2018) have been associated with better learning performance in adolescents (Peters & Crone, 2017; Davidow et al., 2016; Depasque & Galván, 2017, 2019). Reversal learning, or the ability to update one's behaviour when the contingencies between choice and outcome change, is also enhanced during adolescence according to both human and animal studies (Eckstein et al., 2021; Afshar et al., 2020). Further, adolescent improvements in reversal learning seem to be driven by rewards, with adolescents more likely than adults to use positive outcomes to update their behaviour (Afshar et al., 2020). These results suggest that adolescence could be an optimal window for learning from rewarding feedback. However, other studies have shown opposite effects, with adolescents preferentially weighting worse than expected rather than better than expected outcomes – with consequences for subsequent memory (Rosenbaum et al., 2021).

In addition to reward, adolescence is also a period of en-

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hanced sensitivity to threat. Several studies have found increased activity in the amygdala (a region important for processing emotional information; Davis & Whalen, 2001) in mid-adolescents compared to adults when looking at photos of fearful faces (Guyer et al., 2008; Hare et al., 2008). Learned fear associations seem to be particularly robust during adolescence – evidenced by decrements in fear extinction, or the ability to unlearn or suppress a conditioned fear response (Pattwell et al., 2012). Further, when adolescents do extinguish a fear response, they are more prone to later experience a re-emergence of that fear response. While studies have shown comparable levels of fear acquisition in adolescents and adults, adolescents have shown diminished extinction and extinction retention (Waters et al., 2017, Johnson & Casey, 2015, Ganella et al., 2018), suggesting that abolishing negative associations could be more difficult during this developmental stage. While evidence for this finding is relatively robust in the animal literature, there are only a handful of human studies that directly compare fear learning, fear extinction and fear extinction retention between adolescents and other age groups.

The evidence is particularly unclear regarding how social factors might affect learning during adolescence. Studies have found elevated sensitivity to all social stimuli (both positive and negative in valence) in adolescents (for review see Foulkes & Blakemore, 2016; Rodman et al., 2017), with uncertain implications for social learning. Because adolescents are especially sensitive to both social rewards (e.g., Douglas et al., 2004; Yates et al., 2013; Altikulaç et al., 2019) and social exclusion (Fuhrmann et al., 2019; for review see Sebastian et al., 2010), both reward and fear learning might be particularly increased in social contexts and by social content. For example, one social context that might influence learning could be when adolescents' social needs are not being met. Across the lifespan there is evidence to suggest that executive and cognitive function (two mechanisms critical for learning) are adversely impacted by social isolation (for review see Hawkley & Capitanio, 2015). While early findings are interesting, much additional research is needed to replicate and extend our understanding of learning in adolescents. Adolescence might be a time in which learning can powerfully influence development, but how learning is affected by social and affective sensitivity during this period remains largely unresolved. Investigating developmental differences as well as social and affective factors that influence learning during this period will enable us to better study and understand mechanisms underlying sensitive periods in adolescence with the aim to optimize adolescent learning to promote well-being.

Aims

My thesis aims to further our understanding of adolescent learning by answering three major questions.

Question 1: How does social isolation affect learning in adolescents?

Question 2: Are there differences in fear extinction learning and/or retention in adolescents compared with both children and adults?

Question 3: Do adolescents preferentially remember and recall social versus non-social information?

Question 1 - Social Isolation Study

Introduction

Background

Loneliness and social isolation are increasing in societies all around the world (e.g., Victor, 2005; Victor & Bowling, 2012). However, the effects of isolation on cognition and the human brain are not clear. Furthermore, while many studies focus on loneliness in elderly people, a recent large survey (Barreto et al., 2021) found that 16-24-year-olds reported higher loneliness levels than any other age group. Other surveys have shown that late adolescence and emerging adulthood are developmental periods in which the highest levels of loneliness are reported in many western countries (Hammond et al., 2018; Twenge et al., 2019). This suggests that individuals in this age group might be specifically sensitive to the effects of isolation. Additionally, loneliness amongst young people has been exacerbated by school closures, lockdowns and social distancing due to the COVID-19 pandemic (e.g., Lee et al., 2020, Luchetti et al., 2020). Using experimentally induced, short-term isolation we will assess: i) the effects of isolation on adolescent (age 16-19) emotion, motivation and cognition; ii) behavioural and brain markers that predict individual sensitivity to isolation and iii) the role of social media usage on the effects of isolation.

We are collecting structural and functional 7T-MRI data (functional data during a monetary incentive delay [MID] task) and assess whether: i) structural differences in brain development (i.e., whole brain cortical volume, intracortical myelination, white matter volume) and ii) functional sensitivity to rewards (i.e., magnitude of activation during anticipation of rewards) predict individual differences in susceptibility to the effects of isolation.

We are collecting outcome measures in the domain of emotion, motivation, social processing and cognition and have derived our hypotheses from findings in animal models showing that isolation in adolescence increases reward sensitivity, decreases cognitive control and increases anxiety and fear. We will also assess whether social media and technology use during isolation alters the effects of isolation and aim to identify brain markers of sensitivity to isolation.

Research Question

Our full set of hypotheses, variables and measures can be found in the preregistration published on the Open Science Framework (OSF; osf.io/kbgsv). For the purposes of this report, I will focus on answering Question 1 of my PhD: How does social isolation affect learning in adolescents? This question has several sub-questions.

Sub-question 1: How does social isolation affect fear learning and reward learning in adolescents?

Sub-question 2: Do adolescents learn better from rewarding social versus non-social feedback and is this affected by social isolation?

Sub-question 3: Can virtual social interactions remediate these effects?

Sub-question 4: Do functional and structural brain markers predict individual differences in these effects?

Rationale

Animal studies have suggested that social isolation in adolescence influences the way individuals process rewards (for review see Walker et al., 2019). Specifically, in rodents, isolation has been found to heighten sensitivity to social rewards (Ikemoto & Panksepp, 1992). It has recently been suggested that acute social isolation might also enhance sensitivity to social rewards in humans, evoking a neural craving response similar to hunger (thereby motivating socially isolated individuals to seek out social contact; Tomova et al., 2020). While enhancing reward sensitivity, social isolation might also reduce cognitive flexibility and control, including impairing reversal learning (Amitai et al., 2014). Studies have shown increases in dopamine release in reward regions of the brain and decreases in dopamine release in prefrontal cortex (Hall, 1998; Novick et al., 2018; Lukkes et al., 2009). Both reward sensitivity and cognitive control are crucial mechanisms for reward learning. Therefore, it is pertinent to investigate how acute social isolation influences reward learning in human adolescents. Further, this developmental period has been characterized as a period of heightened social sensitivity, with neuroimaging studies suggesting that adolescence is a period of heightened neural reactivity to social stimuli (for review see Foulkes and Blakemore, 2016). Despite this, few studies have directly compared learning from social versus non-social rewards in human adolescents, and none has investigated this in the context of social isolation. Social isolation has also been found to increase anxiety behaviours in animal models, with the most detrimental effects occurring in adolescence (Burke et al., 2017). In rodents, social isolation in adolescence has been associated with a significant deficit in the extinction of conditioned fear (Skelly et al., 2015). This suggests that social isolation might contribute to anxiety by disrupting the extinction of a learned fear response and the retention of that extinction learning.

Hypotheses

A) Effects of isolation

H1) Reward learning: Isolation will alter reward learning, as measured by a reinforcement/reversal learning task. Isolation will enhance reinforcement learning, but diminish reversal learning, i.e., participants will initially learn associations between cues and rewards faster but will show perseveration. These effects (faster learning but higher perseverance) will be stronger for social compared to monetary rewards.

H2) Fear learning: Isolation will heighten fear learning and attenuate fear extinction and fear extinction retention as measured by skin conductance responses (SCR; also referred to as electrodermal activity [EDA]) responses and self-report ratings during a fear conditioning task.

B) Effects of social media usage

H3) Social media use during isolation will remediate the effects of isolation on reward learning and fear learning.

C) Brain markers predicting effects of isolation

H4) Participants who show higher neural sensitivity to rewards will be more sensitive to the effects of isolation, especially in outcome measures related to reward processing (i.e., reward learning).

Methods

Study Design

Each participant undergoes three experimental sessions: baseline, total isolation (iso_total) and isolation with social media (iso_media). We collect predictor measures during the baseline session (MRI and behavioural measures; described in variables section) as well as behavioural measures, which are repeated on the iso_total and iso_media sessions (also described in variables section). This will allow us to compare effects between sessions (baseline vs. iso_total; baseline vs. iso_media), the difference in change between the two isolation conditions ([baseline vs. iso_total] vs [baseline vs. iso_media]) and use predictor measures to assess individual differences in sensitivity to isolation. The baseline session is completed first for all participants, while the order of the iso_total and iso_media sessions are counterbalanced between participants. A diagram of the study design can be found in Figure 1.

Baseline.

The baseline session is comprised of magnetic resonance imaging (MRI) scanning (structural and functional) and behavioural and physiological testing. Structural and functional MRI scanning are being conducted on an MRI Siemens 7T

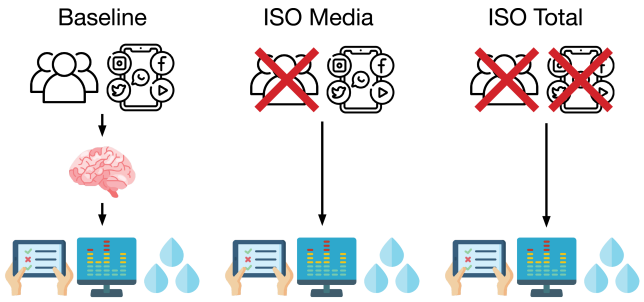

Figure 1

Social Isolation Study Design. At the baseline session, participants are completing a 7T MRI scan, computer tasks, surveys, and physiological recordings (sweat response). During the ISO Media session, participants are isolated from in-person contact, but have access to virtual social interactions before completing computer tasks, surveys, and physiological recordings (sweat response). During the ISO Total session, participants are isolated from both in-person and virtual social interactions before completing computer tasks, surveys, and physiological recordings (sweat response).

Terra scanner at the Wolfson Brain Imaging Centre at the University of Cambridge, United Kingdom (UK). Behavioural and physiological testing are being conducted at the Department of Psychology at the University of Cambridge, UK.

Total Isolation (iso_total).

Participants undergo social isolation by spending 3-4 hours in a furnished comfortable room at the Department of Psychology at University of Cambridge, with access to a bathroom and a stocked fridge. Participants are monitored (but not recorded) by video during isolation and are able to communicate with the researchers if necessary. Participants do not have access to social stimuli (and are asked to give their phones and other electronic devices to the experimenter) but are allowed to bring books and reading material without social content (e.g., textbooks). In addition, the room is equipped with games and puzzles, including video games without social content (e.g., Bubble Shooter, Tetris). Immediately following isolation, participants undergo behavioural and physiological testing (self-administered). Participants are provided with detailed instructions before starting isolation.

Isolation with Social Media (iso_media).

The isolation procedures for isolation with social media are the same as in the iso_total session, except that in the iso_media session participants are able to bring their phones and visit social media and messaging sites (e.g., Instagram, Snapchat, Twitter, or whatever their preferred sites are) and to post, "like", respond to posts, engage in online discussions and live chats, message, call and video call with friends. We ask participants what websites, platforms and applications they used during the session in a self-report questionnaire at the end of the iso_media session. Following isolation with social media, participants undergo behavioural and physiological testing the same way as in the iso_total condition.

Participants

Forty participants aged 16-19 years (approximately half female) are being recruited via local schools, sixth form colleges, the University of Cambridge and the local community. Participant recruitment and data collection for baseline sessions started in April 2021 and the duration of data collection is planned to take approximately one year (assuming no disruptions [for example, due to COVID-19 pandemic restrictions]).

Interested participants complete an initial online and phone screening. To be eligible for participation, participants must be between the age of 16 and 19 years, fluent English speakers, MRI eligible (following standard MRI safety screening procedures of the Wolfson Brain Imaging Centre), share their home with at least one other person, have no diagnosed neurological or psychiatric conditions or special education needs and be at low risk according to current COVID-19 guidance set out by the Department of Psychology. Participants must not regularly consume drugs (including but not limited to misusing prescription drugs, smoking nicotine cigarettes daily or excessively drinking alcohol). The UCLA Loneliness Scale (Russell, 1996; described in the preregistration) is used during screening; participants are not eligible to participate in the study if they score above 50 (one standard deviation above reported mean loneliness levels for students). Additionally, participants are not eligible to participate in the study if they report having had fewer than 10 social interactions in the past month and/or fewer than two close friends on the Social Network Scale (described in the preregistration).

Participants are reimbursed a minimum of £107 for participating in all three experimental sessions and can additionally earn up to £20 depending on their performance in the reward sensitivity task during scanning and the reward responsiveness and reward learning tasks during the behavioural testing sessions.

Pilot data (N = 19; taken from part of the sample in Tomova et al., 2020) from 18–24-year-olds has shown that short-term isolation affects feelings of loneliness (using a self-report loneliness scale ranging from 0-100) after just four hours of isolation with an effect size (Cohen's d) of 0.47. A power analysis showed that 38 participants are required to detect a medium effect size of d = 0.47 in our outcome measures to achieve a power of .80 (1-beta) at an alpha of .05.

Recruitment will be stopped after 40 participants successfully complete all three sessions of the study. New participants will be recruited to account for participants who fail to complete all three sessions.

Variables

Magnetic Resonance Imaging (MRI).

We use structural and functional MRI to measure our predictor variables described below. All MRI data is collected at baseline.

Structural MRI.

Using MRI, we measure regional cortical volume, surface-area, cortical thickness, intracortical myelin and mean diffusivity and fractional anisotropy of white-matter. An MP2RAGE and a DTI sequence is used to capture the structure of grey matter and white matter.

Functional MRI - Reward Sensitivity.

Using functional magnetic resonance imaging (fMRI), blood-oxygen-level-dependent (BOLD) signal at a single voxel in successive scans (a voxel time-series) in response to anticipating rewards of different magnitudes during a monetary incentive delay (MID; Knutson et al., 2000) task is measured. The MID task is a well-established task used to study neural correlates of reward anticipation (i.e., winning of money) and will be used as a marker of reward sensitivity. During the task, participants are able to win either 0.2 GBP (small win) or 5 GBP (large win), or lose -0.2 GBP (small loss) or -5 GBP (large loss). On some trials, participants cannot win or lose any money, which serve as control trials. Participants see a cue at the beginning of each trial indicating whether they can win or lose money on that trial. The cue is a star with the amount of the possible win (or loss) written inside of it (i.e., 0 [control trials], 0.2 [small win trials], 5 [large win trials], -0.2 [small loss trials], 5 [large loss trials]). Following the cue, participants see a white circle on the screen presented for a jittered time interval (range 1.5-4 s, mean 2.5 s) briefly followed by a white square, which is presented for 100 ms and then see the circle again. Participants' task is to press a button as fast as possible when they see the square. Following their response, participants are presented with feedback whether they won (or avoided a loss) or whether they did not win (or lost) money on that trial (presented for 500 ms). Then participants see a fixation cross for a jittered time interval (range 2-6 s, mean 3.5 s). The task is adaptive and the time window for how fast participants need to respond changes depending on their response times during the task. Participants undergo a practice run of the task during the MP2RAGE scan, which is used to calibrate the response window for the MID task.

Behavioural Tasks.

We are using the following computerized behavioural tasks to measure our main outcome measures described below. All behavioural tasks are being administered at baseline, iso_total and iso_media. Several additional tasks (which are beyond the scope of this report) are also being administered. For full details see the preregistration. The fear learning task is being administered near the end of each session to minimize potential fear related carryover effects. The order of the remaining tasks is being counterbalanced between participants to minimize order effects.

Reward Learning.

The ability to learn stimulus–reinforcement associations and to reverse them based on probabilistic feedback is being measured using an adapted learning task (Palminteri et al., 2016). In this task, participants are presented with two slot machines and are asked to choose between them to obtain a reward. One slot machine is rewarded 80% of the time; the other is rewarded 20% of the time. Participants need to learn through trial and error which slot machine is rewarded more often. After seven trials the reward contingencies switch, and participants need to learn the new reward contingencies. Feedback is given via symbols (non-social feedback) and facial expressions (social feedback) in two counterbalanced blocks (28 trials per block, in total 56 trials). Rewards are represented by either a plus symbol (+) or a smiling face, while the absence of a reward is represented by a zero symbol (0) or a neutral face. This task measures learning rate, perseveration and exploration versus exploitation. Reinforcement learning models will allow us to assess how isolation affects these parameters (learning rate, perseveration, exploration/exploitation) and whether it selectively affects learning to social versus non-social feedback. Participants are given 1 s to respond on each trial and then receive feedback for 0.5 s. A fixation cross is presented for 0.5 s between each trial. A simplified task diagram can be found in Figure 2.

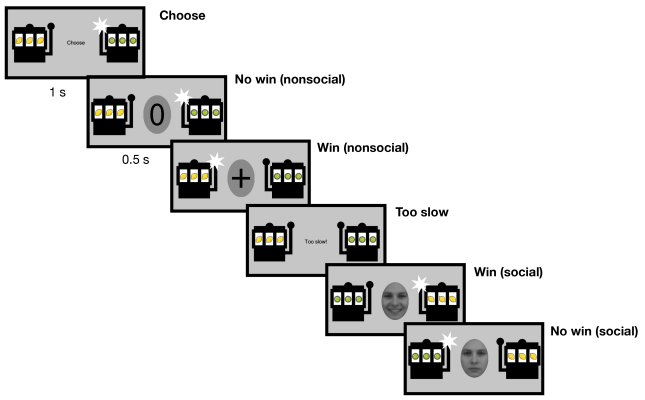

Figure 2

Reward Learning Task. This is a simplified task diagram of the reward learning task. Participants complete a social and non-social block. Block order is counterbalanced between participants. Stimuli are counterbalanced between participants and between sessions.

Fear Learning.

We are measuring fear learning using a Pavlovian differential fear conditioning and extinction paradigm. In this task, participants learn to associate neutral shapes with an aversive sound (e.g., fingernails scraping on a blackboard). The fear learning

task assesses the ability to discriminate between learned threat and safety cues (behaviourally via self-report and physiologically as measured by skin conductance response [electrodermal activity]). Participants hear the sound before the task begins and are given the opportunity to turn the volume up or down to make the sound "unpleasant, but not painful".

The task consists of three phases. During the first phase (24 trials), participants are presented with neutral shapes, one of which is accompanied 50% of the time by the aversive sound. The other shape is never accompanied by the aversive sound. In the second and third phase (each 16 trials), participants see the neutral shapes without the aversive sound. After the third phase, a few distractor trials are presented in which the threat cue is again paired with the aversive sound. These distractor trials are meant to reduce task predictability across three sessions (baseline, iso_total, iso_media). After each phase, participants are asked to judge the valence and arousal of each shape and each sound. For valence, participants are asked "How unpleasant/pleasant do you find this shape (or sound)?". Participants rate valence from (1) very unpleasant to (9) very pleasant. For arousal, participants are asked "How anxious does this shape (or sound) make you feel?". Participants rate arousal from (1) not anxious to (9) very anxious. Differences in valence and arousal ratings between phases represent learned threat and safety associations.

Participants also are having their electrodermal activity (skin conductance response) measured while they are undergoing the fear learning task. Electrodermal activity, a marker of sympathetic arousal (fear learning), is being measured by two small electrode sensors that are placed on the participant's non-dominant hand (on the index and middle finger) to measure very small variations in sweating (Bach, 2014; Back & Melinscak, 2020). To measure these physiological responses, we are using a Biopac (MP36R) skin conductance recording system together with AcqKnowledge software to amplify and record the SCR.

The stimulus type differs across participants and sessions. Different coloured shapes are being presented as the threat and safety cues at each session to prevent carry over effects. Which stimulus is the threat versus safety cue and the order of the stimulus pairs is being counterbalanced across participants. In the task, each cue is presented for 2 s. For reinforced threat trials, the aversive sound is presented after 1.5 s of cue presentation for 0.5 s. Trials are followed by an intertrial interval of 7 s. There is no time restriction for trials in which participants give ratings. A simplified task diagram can be found in Figure 3.

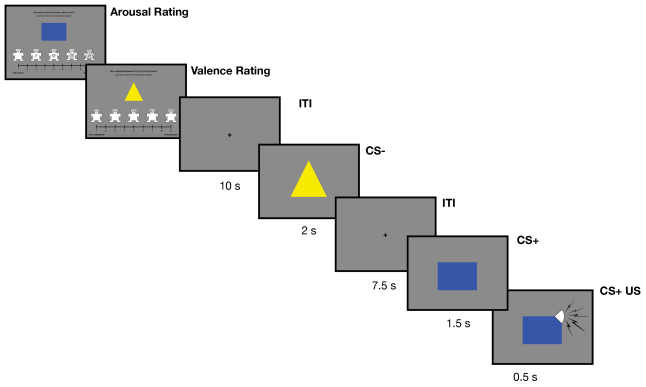

Figure 3

Fear Learning Task. This is a simplified task diagram of the fear learning task. Participants complete acquisition, extinction, and extinction retention phases. Stimuli are counterbalanced between participants and between sessions. Stimuli shown are example stimuli.

Results

Analysis Plan

Behavioural Data Analysis.

Reward Learning.

Participants' choices from the reinforcement/reversal learning task will be analysed using a computational reinforcement learning and decision-making model for probabilistic reversal learning tasks (Ahn et al., 2017; Metha et al., 2020). We will estimate the following parameters for each participant: learning rate, experience decay factor and inverse temperature. The learning rate is based on how much an individual updates their current response based on their most recent response, the experience decay factor is a measure of perseveration, and inverse temperature is a measure of exploration versus exploitation (den Ouden et al., 2013).

To compare differences in these estimates, we will use mixed effects models to test for differences between sessions to estimate the fixed effects of feedback condition (social versus non-social) and session (baseline, iso_total, and iso_media) on our three parameters of interest (learning rate, experience decay factor and inverse temperature), with subject included as a random effect.

Fear Learning (behavioural).

In the fear learning task, participants provide subjective reports (valence and arousal ratings; markers of fear learning) for each condition (threat versus safety cue) across each phase of the task (pre-acquisition, post-acquisition, post-extinction and extinction retention [10 mins post-extinction]) and across each session (baseline, iso_total and iso_media).

To compare differences in these responses associated with our experimental manipulations, we will use separate mixed effects models (for valence and arousal ratings as separate outcomes). We will test for differences between sessions by estimating the fixed effects of condition (threat and safety),

phase (acquisition, extinction and extinction retention) and session (baseline, iso_total and iso_media) with subject included as a random effect. We will also investigate condition by phase by session interactions to determine whether isolation differentially influences responses to threat and safety cues across acquisition, extinction and extinction retention.

Physiological Data Analysis (electrodermal activity).

Fear Learning (physiological).

We will use a model-based approach to estimate sympathetic arousal (SA; a marker of fear learning) from skin conductance response (SCR; Bach, 2014). We will employ a general linear convolution model (GLM) approach using PsychoPhysiological Modelling software (PsPM) on the data from the last half of each learning phase (acquisition, extinction and extinction retention; Bach et al., 2018).

To compare differences in these responses to our experimental manipulation, we will use mixed effects models to test for differences between sessions by estimating the fixed effects of condition (threat and safety), phase (acquisition, extinction and extinction retention) and session (baseline, iso_total and iso_media) with subject included as a random effect. We will also investigate condition by phase by session interactions to determine whether isolation differentially influences responses to threat and safety cues across acquisition, extinction and extinction retention.

MRI Data Analysis.

Preprocessing.

For full details of the preprocessing pipeline, see the preregistration.

Structural Quantification.

The structural measures of interest will be: 1) Whole brain white matter volume, 2) Whole brain grey matter volume, cortical thickness, and surface area and 3) Cortical grey matter volume divided into four lobes (Tamnes et al., 2017).

The Nighres toolbox (Huntenburg et al., 2018) will be used to quantify laminar volumetric layering. The lamination data will then be used to model the distribution of cortical myelin following methods described in (Dinse et al., 2015). We will also perform region of interest (ROI) structural analyses. The main target ROIs for these analyses will be the striatum, prefrontal cortex and amygdala. We will assess grey matter, cortical thickness and surface area in these areas as well as the structural connectivity between them. We will also perform exploratory analyses of other ROIs.

Functional Modelling.

For analysing the functional data from the MID task, we will apply whole brain analyses and region of interest (ROI) analyses. For the ROI analyses, we will include regions that were found to be consistently activated during reward anticipation in the MID task across different studies (identified in a meta-analysis by Oldham et al., 2018). The regions will include the ventral striatum, thalamus, amygdala, midbrain, supplementary motor area, anterior insula and occipital cortex.

Univariate Analysis.

To test our key hypotheses, we will extract the mean response magnitude for the contrast reward anticipation > neutral anticipation (as a first marker of "reward sensitivity") from each ROI which, along with our structural measures, will be used as predictors in our analyses. We will use mixed-effect models to estimate whether reward sensitivity and structural markers predicts effects of isolation (compared to baseline) on reward learning and fear learning.

Discussion

Animal research has shown that isolation during adolescence has unique and detrimental effects on learning, influencing both brain and behaviour. Findings from this study will contribute some of the first evidence to evaluate the effects of isolation in adolescent humans. Further, this study will begin to address the impact of digital forms of social interaction, which are fundamental in the present-day social lives of adolescents. These findings will have implications for evidence based public policy regarding health-related social distancing, online learning and mental health treatment.

Future Plans

I will address Question 2 (Are there differences in fear extinction learning and/or retention in adolescents compared with both children and adults?) and Question 3 (Do adolescents preferentially remember and recall social versus non-social information?) of my thesis with two future studies which are in planning stages. A timeline can be found in Figure 4.

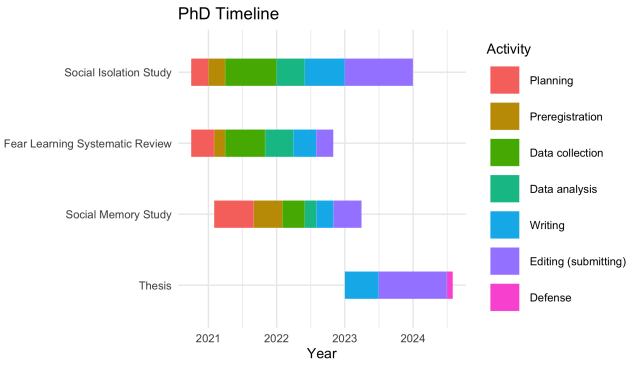

Figure 4

Timeline. A timeline for the completion of the studies and thesis outlined in this first year report.

Question 2 – Fear Learning in Adolescence Systematic Review

Fear extinction learning is a critical part of the most effective exposure therapy-based treatments for anxiety and stress-

related mental health disorders (Craske et al., 2014). Research has identified differences in fear extinction learning and/or retention in adolescents compared with both children and adults (Den et al., 2015; Pattwell et al., 2012; Waters et al., 2017). Specifically, studies have shown reductions in adolescents' ability to diminish learned fear responses and retain that attenuation in the long term. This finding has been replicated in several human and animal studies and has served as an important building block for further lines of research, including fear reconsolidation (Johnson & Casey, 2015), safety signal learning (Meyer et al., 2019), and fear extinction following stress (Gerhard et al., 2020). However, to our knowledge, there has yet to be a systematic review and meta-analysis of fear extinction learning and retention in human adolescents compared to adults. Differences in fear extinction may represent a key vulnerability for the development and maintenance of mental health disorders during this period, including anxiety, which frequently emerges in childhood or adolescence and often persists into adulthood (Kim-Cohen et al., 2003; Merikangas et al., 2010; de Lijster et al., 2017). Given these findings, there is a need to review the literature to clarify and quantify the results, identify methodological and theoretical concerns, and inform future research directions.

In this study, I will focus on answering Question 2 of my PhD: Are there differences in fear extinction learning and/or retention in adolescents compared with both children and adults? I hypothesise that adolescents will show heightened conditioned fear during and after extinction compared to adults, indicating impaired fear extinction learning and/or retention. This question will be addressed by conducting a systematic review and meta-analysis, for which a preregistered protocol has already been published on the OSF (osf.io/f3u9y). The preregistered protocol was developed using the Non-Interventional, Reproducible, and Open (NIRO) Systematic Review guidelines (Topor et al., 2020).

Question 3 – Social Memory Study

Empirical studies have shown that people tend to recall a higher proportion of specific personal events from the ages of 10-30 years than from any other time in life (Rubin et al., 1986). This adolescent/young adult 'reminiscence bump' can be partially accounted for by the fact that many novel and important life events take place during this period that ultimately shape one's identity (for review see Munawar et al., 2018). However, recent evidence suggests that developing neural systems and cognitive abilities may also contribute to memory enhancement during this period (Janssen, 2020; Lynch et al., 2019; Callaghan et al., 2020). Concurrently, brain regions involved in social cognition undergo structural and functional changes during adolescence (for review see Blakemore, 2008) as does the hippocampus (a brain structure critical in supporting episodic memory; Tamnes et al., 2017; Davachi et al., 2003; Davachi, 2006; Eichenbaum et al., 2007).

Investigating social memory development in adolescence is a critical step to help us understand how adolescents learn and remember social information which guides thoughts and behaviours that influence well-being. Adolescence is a particularly vulnerable time for the development of mental health disorders (Kessler et al., 2005), which are often accompanied by altered cognitive and memory processes (for review see Gotlib & Joormann, 2010; Hedges et al., 2019). Further, impaired memory for social information in adults has been linked to various negative outcomes, such as anxiety and depression. Higher social anxiety has been shown to predict poorer social memory for both positive and negative imagined social events (Romano et al., 2020), and positive memory specificity (regardless of social quality) has been associated with reduced vulnerability to depression (Askelund et al., 2019). Emerging evidence suggests that recalling memories richer in social context may even help to reduce stress. As one recent study showed, recalling social memories led to lower cortisol levels after stress exposure, even after controlling for positive feelings (Speer & Delgado, 2020).

In this study, which will be carried out in collaboration with Dr. Talmi, I will focus on answering Question 3 of my PhD: Do adolescents preferentially remember and recall social versus non-social information? I hypothesise that adolescents will display heightened memory for social versus non-social information relative to adults. This question will be addressed by conducting an empirical study, for which a preregistration is in progress.

Conclusion

Adolescence is a transformative period of life characterized by substantial changes in one's social and emotional environment. It is a critical period to learn, attain education, forge social connections, explore career paths and establish one's sense of self. While this developmental stage is rife with opportunity, it is also a potentially vulnerable period for maladaptive learning to shape one's brain and behaviour. Learning is critically related to mental health disorders, which often onset in adolescence and have lifelong consequences to well-being (Costello & Maughan, 2015; Polanczyk et al., 2015). For example, extinction learning and retention are critical for regulating anxiety and fear (Raeder et al., 2020). Fear learning is a critical component in the onset and maintenance of anxiety disorders, such as PTSD (Jovanovic & Ressler, 2010), while fear extinction learning is a critical part of treatment (Milad & Quirk, 2012), such as exposure therapy. Studies have shown reduced reward learning in individuals with depression, along with a blunted neural reward response (Robinson et al., 2012; Safra et al., 2019). Alterations in learning have also been shown in patients with trait anxiety (Riesel

et al., 2019), bulimia nervosa (Hagan & Forbush, 2021) and as predictors of posttraumatic stress (de Haart et al., 2021). Importantly, learning is also a point of intervention – with treatments targeting learning mechanisms (exposure therapy) among the most effective evidence-based therapies (Chorpita et al., 2009). By harnessing inherent neurobiological social and emotional sensitivity in adolescence we might be able to shape learned associations through practice and training with learning as an intervention target (Klein et al., 2021; McLaughlin et al., 2019).

Before we attempt to use learning as a target of intervention, however, it is critical to understand how the changing social and emotional sensitivity that accompanies adolescent development influences learning and whether adolescence constitutes a window of opportunity for brain and behaviour change. There remain many unanswered questions regarding how social and emotional context and social and emotional content are learned, remembered and guide future thoughts and behaviour during this period. Investigating the neural and behavioural mechanisms that underlie differences in the way that adolescents learn will allow us to better understand how learning, development and mental health are related. Critically, it might also help us move beyond observational associations between learning, development and mental health to begin elucidating causal mechanisms, with implications for research, education and intervention.

Note

We used R (Version 3.6.1; R Core Team, 2019) and the R-packages *dplyr* (Version 1.0.5; Wickham, François, et al., 2021), *forcats* (Version 0.5.1; Wickham, 2021a), *ggplot2* (Version 3.3.3; Wickham, 2016), *papaja* (Version 0.1.0.9997; Aust & Barth, 2020), *purrr* (Version 0.3.4; Henry & Wickham, 2020), *readr* (Version 1.4.0; Wickham & Hester, 2020), *stringr* (Version 1.4.0; Wickham, 2019), *tibble* (Version 3.1.1; Müller & Wickham, 2021), *tidyr* (Version 1.1.3; Wickham, 2021b), and *tidyverse* (Version 1.3.1; Wickham, Averick, et al., 2019) to create this document.

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