Common Information for Project: Investigating Predictors of Stress Resilience in Medical Students: A Prospective Cohort Study

Description

Stress affects mental and physical health and significantly contributes to the onset of mental and physical disorders. However, despite its ubiquity in many workplace and other settings, most individuals respond resiliently, i.e., they do not develop lasting problems. Specific populations such as medical personnel are likely to be exposed to severe acute and chronic stress and may therefore be particularly vulnerable. To further elucidate what makes a person resilient despite adversity, we investigate emotion and arousal regulation mechanisms and their neurophysiological correlates as predictors of stress resilience in a cohort of medical interns.

We will recruit medical students about to start their first clinical internship. The internship serves as a real world model of stress, and we will examine factors that should predispose individuals to (not) develop problems in response to stress over a 12-month period following the internship start. Participants' stress burden and mental health will be surveyed via self-report pre-internship (T0), as well as 3 (T1), 6 (T2), and 12 (T3) months later (Figure 1).

Various types of data will be collected at the pre-internship time point to serve as predictors of mental health outcomes. These include questionnaires, a short video interview, fMRI scanning during an emotional regulation task under stress-induction, and blood and saliva sampling. For the first two weeks of the internship, as well as the two weeks following the T1 and T2 timepoints, the participants will complete ecological momentary assessments (EMA) multiple times per day that probe context, sleep, emotional states, stressful experiences, perceived control, coping, self-care, and reflection. From the start of the internship until the end of the T2 EMA assessment, the participants will wear a Fitbit device that will collect data on heart rate, heart rate variability, sleep, and activity. Blood and saliva samples will be taken at the T0, T1, and T2 timepoints alongside the follow-up questionnaires that assess mental health symptoms, stress exposure, and resilience factors including coping and emotion regulation strategies.

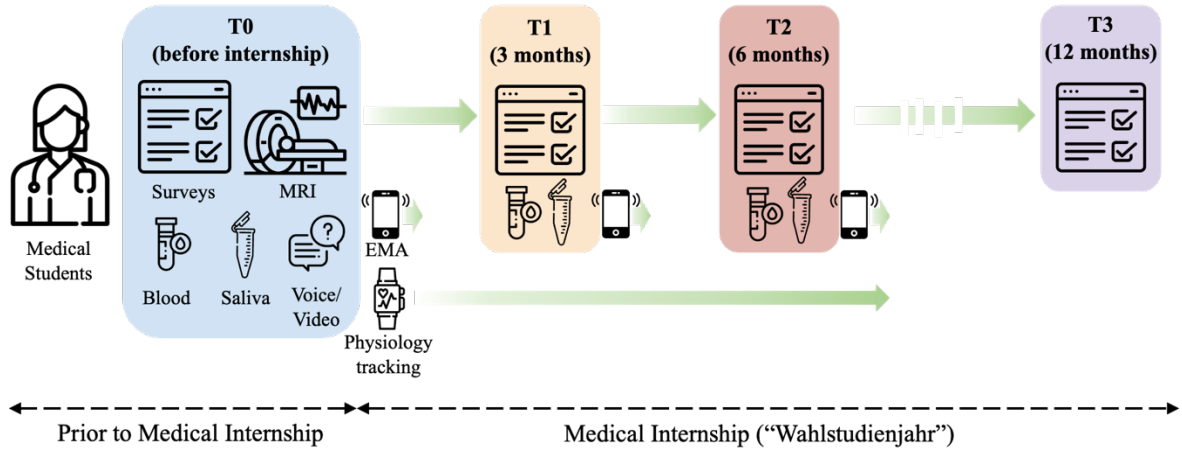

Figure 1. *Prospective cohort study design. Medical students will be assessed with MRI at baseline, prior to their internship (T0) and will be followed up with assessments of self-reported psychopathology and stress exposure at 3 (T1), 6 months (T2), and 12 months (T3). Icons from Flaticon.com.*

Study Design

This is an observational study with no groups. Outcome measures (comprising stress exposure and mental health symptoms) will be measured at four time points - before the start of students' internships (T0), after 3 months (T1), after 6 months (T2), and after 12 months (T3). Measures that will act as moderators, mediators, predictors, and covariates will be mostly assessed at T0, but also as the internship progresses (see Figure 1).

Population, inclusion/exclusion criteria and participant selection

Considering the specificity of the target population (medical students) and time constraints (baseline assessment just before start of participants' first medical internship), we aim to recruit as many participants as possible from the 5th year medical students at the University of Zurich, with the aim of recruiting 150. We may also recruit from other clinics in the greater Zurich area if necessary. Inclusion criteria are the following: (1) being a medical student about to start a clinical internship for the first time, (2) physically and psychologically healthy, as determined by standard interview prior to baseline assessment, (3) fluent in German, (4) not pregnant, (5) over the age of 18, (6) provision of written informed consent. For the fMRI part of this study, a number of standard additional criteria apply for MRI safety. Other than exclusion/inclusion criteria, the participants are selected based on interest to participate. They will be selected and recruited consecutively and therefore are selected without bias.

Recruitment & Compensation

Medical students will be recruited from the University of Zurich with support from the head coordinator of medical education and through standard means, e.g., flyers, mailing lists, posters, student association newsletters, and word of mouth. The participants will be provided with detailed information about the study procedures and will be screened for exclusion/inclusion criteria over the phone. Participation is voluntary, and participants may complete only a part of the study (e.g., not wear the physiological tracker). They will also be told that they can leave the experiment or withdraw from the study at any point without any negative consequences. Participants will be compensated for their contribution up to 212.50 CHF provided they comply to a reasonable degree, and will be offered their structural T1 scan.

Sample Size

We will attempt to recruit up to 150 participants over two cohorts, with the second cohort (2023) much larger than the first. This target sample size was based on data collection constraints and power analysis estimation using G*Power 3 software (Faul et al., 2007) with alpha = 0.05 and power as 0.8. The target effect size of 0.3 was taken from previous work regarding the main hypotheses of the project (Grueschow et al., 2021). This a priori power analysis indicated a minimum sample size of 84 individuals. Considering expected exclusions due to attrition and low-quality data (e.g., caused by excessive movement in the scanner), we aim to include up to 150 participants in total. Participant recruitment will continue until the end of December 2023. As many participants as possible (given participant interest and scanning time constraints) will be recruited up to 150.

Variables

As the primary outcome, we will calculate a resilience score based on Kalisch et al (2021) using change in self-reported mental health symptoms and stress exposure, see indices for a more detailed operationalisation. Mental health symptoms will be measured using two self-report questionnaires, the 28-item General Health Questionnaire (GHQ-28, Klaiberg et al., 2004), and the State-trait-Angst-Depressions-Inventar (STADI, Laux et al., 2013). While stress exposure will be measured with the following questionnaires at T0, T1, T2, and T3: Life Events Checklist (LEC-5, Weathers et al., 2013, plus additional relevant life events based on Canli et al., 2006 and Kalisch et al, 2021) and the Mainz Inventory of Microstressors (MIMIS, Chmitorz et al, 2020). While the LEC-5 assesses major life stressors such as a life-threatening disease or assault, the MIMIS focuses on microstressors or daily hassles within the past 7 days. We adapted the instruction of the LEC-5, so participants report not on their entire lifetime, but only on the last 3 months when assessed at T1, T2, and T3.

Secondary outcomes of mental health symptom change comprise the 10-item Perceived Stress Scale (PSS, Schneider et al., 2020), the Maslach Burnout Inventory (9-item MBI, Kaschka et al, 2011), Intrusive memories (Hackmann et al, 2004), and the World Health Organisation's Well-being Index (WHO-5, Brähler et al, 2007). Assuming little endorsement at baseline, burnout and

intrusions are only assessed following the start of the internships (T1, T2, T3), while all other questionnaires are included at all assessments.

Further variables and their operationalisation will be described in linked preregistrations.

Indices

Mental Health Symptoms Change

Change in mental health symptoms will be calculated as the overall score of each questionnaire at T1 minus that at T0, at T2 minus at T0, and at T3 minus at T0. Positive values therefore indicate greater mental health problems at follow-up compared to baseline. This index will be used to calculate a resilience score (see below).

Stress exposure

Following recommendations by Kalisch et al (2021), we will measure stress exposure through stressful life events (LEC-5) and microstressors (MIMIS). For each timepoint (T1, T2, T3), we will calculate the number of life events reported to have occurred within the past 3 months and the rate of occurrence of microstressors within the past 7 days. Provided life events and microstressors correlate well, we will combine them by taking the mean of the z-scores. Scores will then be used as the stress exposure variable to calculate the resilience score (see below). To generate the stress exposure scores for T2, the average across T1 and T2 for life events and microstressors will be taken, and similarly for T3, the average across T1, T2, and T3 will be taken.

Resilience Score

We will calculate two resilience scores using the residual score method proposed by current resilience theory (e.g., Kalisch et al, 2021; Veer et al, 2021, see Figure 2), one for the first 3 month time period (T0 to T1) and one for the second 3 month period (T1 to T2). This method involves regressing change in mental health symptoms on stress exposure during each period and taking the residual to obtain a continuous score for each participant (see Figure 2). Residuals above the regression line indicate lower resilience, as they reflect a greater increase in mental health problems than expected given the reported stress exposure. Conversely, residuals below the regression line indicate higher resilience, as they reflect a smaller increase in mental health problems than expected given the reported stress exposure. Importantly, scores relate to the observed relationship between mental health problems and stress exposure in the given sample (i.e., the regression line).

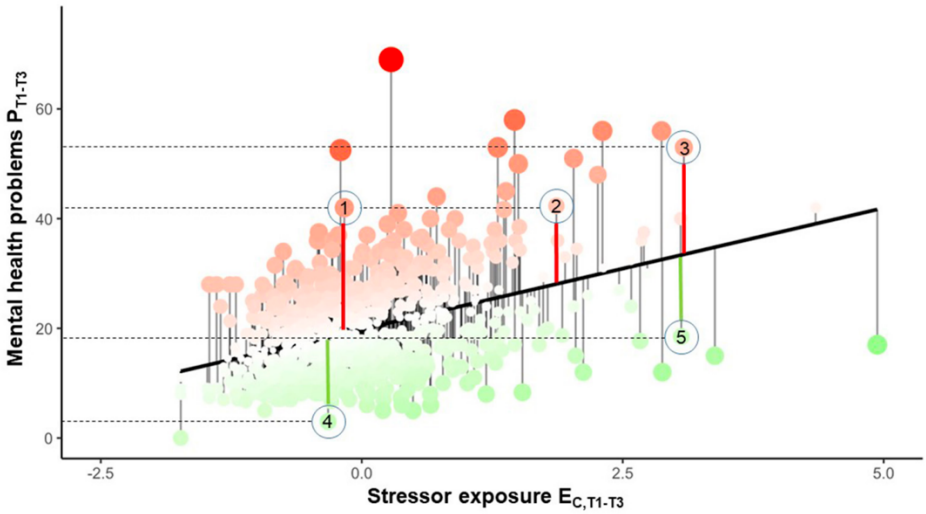

Figure 2. *Operationalisation of resilience as the average increase in mental health problems against the average of stress exposure, with more resilient individuals in green and susceptible individuals in red (Kalisch et al, 2021).*

Analysis

Statistics will be performed using R. For all hypotheses, the assumptions of statistical tests will be verified and if necessary, non-parametric or robust/bootstrapped alternatives will be used instead. Sex will be collected as a covariate. Since we do not expect much variation in age, age will be collected but not included as a covariate. Outlying values and cases with missing data will not be excluded, robust tests and imputation will be used where appropriate.

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