Master's thesis

NTNU
Norwegian University of Science and Technology
Faculty of Medicine and Health Sciences
Kavli Institute for Systems Neuroscience

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Linking Structural MRI to behavior and Real-World Emotional Experiences

Master's thesis in Neurosciences
Supervisor: Dr. Maryam Ziaei
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ABSTRACT

At the core of human cognition lies the complexities of brain-behavior associations, with one influencing the other throughout our lives. Although it is complicated to pin traits with one single region of interest, previous studies imply that *specific personality traits are mediated by neuroanatomy in specific brain structures*, which appear to be the key *determinants of many human behaviours*. Structural magnetic resonance imaging (sMRI) has been proved vital for the research steps in this direction. This thesis followed the same initial pathway through linking sMRI with personality traits to identify brain regions of interest (ROIs) related to psychological well-being. Then correlating these with Ecological Momentary Assessments (EMA). It then took a step further to investigate reliability in everyday life emotions in the young adult population via a novel statistical technique called Multilevel Structural Equation Modelling (MSEM). Participants (N=35) aged 18-35 completed the study in three parts: structural brain imaging, self-reporting of behavioral questionnaires, and daily life emotions surveys. This study aimed to examine the degree to and how ROIs could be associated with everyday negative and positive emotions, with well-being measures orchestrating this paradigm. To bridge the current understanding, I further evaluated the within-individual emotional temporal variation (different times of day; different days) and variability between participants. Insula and caudal anterior cingulate cortex (cACC) were found to influence our negative and positive reactions in life, with anxiety successfully mediating between insula-negative event domains. On the other hand, empathy served as an indirect link between cACC-positive event connections; however, evidence of its direct influence remains inconclusive. Despite reporting higher contentment, participants demonstrated a greater degree of negative emotional variability for both within- and between- individual measures. These results support our existing knowledge of the anatomical relevance of these ROIs, and their roles in psychopathology, real-life perceptions in addition to an exclusive outlook on within- individual mood variations. Furthermore, such analyses could aid efforts in illuminating trait-anatomy relationships and future studies into mental health and illness would likely benefit greatly from also integrating functional imaging.

Keywords: Structural integrity, Behavior, Psychological Well-being, Cortical thickness, Surface area, Experience sampling method, Multi-level modelling, Reliability, Variability

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LIST OF ABBREVIATIONS

sMRI – Structural Magnetic Resonance Imaging
fMRI – functional Magnetic Resonance Imaging
CT – Cortical Thickness
SA – Surface Area
ACC - Anterior Cingulate Cortex
cACC – caudal Anterior Cingulate Cortex
mOFC – medial Orbito-frontal Cortex
T1w – T1 weighted relaxation time
WB – Well-Being
HADS – Hospital Anxiety and Depression Scale
PSS – Perceived Stress Scale
IRI – Interpersonal Reactivity Index
CD-RISC – Connor-Davidson Resilience Scale
ESM – Experience Sampling Methods
EMA – Ecological Momentary Assessment
NE – Negative Event
NA – Negative Affect
PE – Positive Event
PA – Positive Affect
MSEM – Multilevel Structural Equation Modellin

1. INTRODUCTION

Understanding neural correlates and structural brain integrity behind human behavior has always been and remains the backbone of cognitive neuroscience. The rapid advancement in neuroimaging techniques has acted as a catalyst in this research area to investigate brain-behavior relationships and mental health precisely (Goldstein & Volkow, 2011; Kanai & Rees, 2011). In the last two decades, structural imaging has witnessed significant progress in the localization of specific behavior and emotional cues and in observing the relationship between brain regions' structural integrity on personality traits and real-life feelings of emotions. During our lifetime, we have a dynamic range of day-to-day experiences of emotions. This ability lies within and between the strong interconnections of our brains. To explore these interconnections, one must ask, "Could brain morphology affect our daily emotions and not just traits?" or "Does personality help establish a link between the kind of anatomy of the brain as well as a lifestyle?"
As captivating as this area is, associations between morphological features of the brain and its effect on daily life have unique statistical and exploratory issues (McIntosh, 2012). This introduction will first outline the structural magnetic resonance imagining, the composite dimensions gathered from this stage, and the emphasis on personality trait measurements. It will then introduce the widely accepted way to capture momentary behavior and experiences and finally outline the statistical methodologies to address the challenges in linking these three aspects of understanding emotional variability.

1.1 Non-invasive measurements of brain anatomy

From the stages of development till adulthood, the human brain goes through various morphological changes due to genetics that result in varied cognitive abilities. The cerebral cortex expands and changes from a smooth telencephalic structure to intricately well-defined lobular patterns with gyri and sulci. The developmental pathways for neural circuits and brain structures follow independent courses (Shaw et al., 2012; Tamnes et al., 2011) E.g., the maximum peak for grey and white matter differs in life stages as late childhood for the former and early adulthood for the latter (Giedd & Rapoport, 2010). In neuropsychological research and clinical practice, various imaging techniques are in use to study the human brain. Among many, Magnetic resonance imaging (MRI) has evolved as the most widely used *in-vivo,* non-invasive imaging method for high-resolution automated brain segmentations, including structural and functional brain integrity. structural Magnetic Resonance Imaging (sMRI) from >3-Tesla provides static anatomical information about cortical and sub-cortical areas of the brain in exceptional detail with both grey and white matter contrast. The obtained image quality depends on two main characteristics: Signal to noise ratio (SNR) and spatial resolution. While the former is determined by slice thickness and size of pixels, the latter depends on phase encoding directions (Symms M et al., 2004). The information gathered from such high-resolution scans is used to generate T1- and T2-weighted images, which, when processed, provide extensive dimensional measures such as thickness, surface area, and volume of both surfaces (e.g., pre-fontal cortex, insula, Anterior cingulate cortex, etc.) and deep brain structures (e.g., Hippocampus, Amygdala, Thalamus etc.).

In research, three main measures are studied the most: cortical thickness (CT), surface area (SA) and volume, which provide unique multi-dimensional information about the regional brain structures. The width of the grey matter is known as cortical thickness and the boundary occupied by the grey and white matter is termed as surface area (Figure 1), whereas the product of these two gives the volume of a particular area. The radial (Vertical) and tangential (horizontal) neuronal migration driven by progenitors during development gives rise to cortical thickness and surface area, respectively (Geschwind & Rakic, 2013). This separate pattern of migration suggests that the genetic influence on these dimensions is uncorrelated and independent (Winkler et al., 2010). It is also functionally relevant to analyze how cortical thickness and surface area, impact cortical volume. Where the developmental stages are mediated by genetics, the later stages and maturation are driven by the interaction of both genes and the environment (Pallas SL, 2001). Therefore, while exploring the effects of brain regions of interest (ROIs), it is essential to assess all three measures separately due to variability posed by genetic and environmental factors.

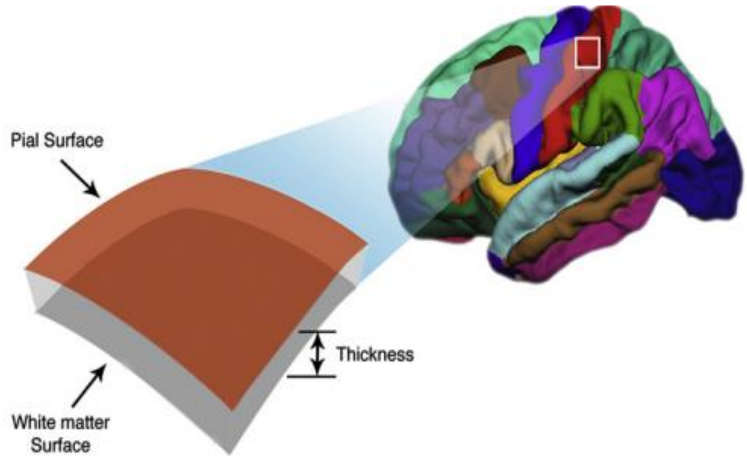


Figure 1 Representation of thickness – the distance between two surfaces and area – is the area of the white matter surface. (Figure from - Lara M et al., 2013) Note how the difference in the two measures arises...

The contribution of thickness, surface area, and volume are unique in structural studies. One measure from a region can provide better information than the other. Previous MRI studies on the brain's structural organization were heavily based on cortical volume as the primary morphometric measure. However, it was found that volume varies across age groups and follows a downward trend as the adolescent stage begins (Giedd et al., 1999). With advances in automation measurements, it was revealed that cortical thickness and surface areas are the two components of volume. Due to its elaborated folding, the cortical thickness and surface area are non-uniform throughout the brain, with thick gyri and thin sulci (Bok, 1929; Campos, Elgeti, & Caspers, 2020; Holland et al., 2020; Holland, Budday, Goriely, & Kuhl, 2018; Zhang, Liu, & Wang, 2015). This distribution pattern is yet to be reasoned; however, cortical thickness and surface area should not be considered as global measures, but rather, a local brain area property that extensively varies spatially. The gyri, sulci, ridges, and grooves increase the SA, which leads to more neurons (Mercadante A et al., 2022). The deep structures of the cortex could potentially be better understood for their functions based on their SA rather than thickness e.g., the insular cortex as insular cortex has a total of six gyral and sulcal subregions (Destrieux et al., 2010) and the microcircuits use one spatial dimension to organize the neuronal types. On the other hand, studies have shown higher dendritic architecture and spines in phylogenetically older areas than the neo-cortex (Nivaldo D et al.., 2020). Greater dendritic architecture may lead to more dendritic arborization and glial support, which lays the basis of the thickness of a brain region e.g., paralimbic structures in the medial region such as the human cingulate cortex. These results suggest prioritizing thickness measures of such parts then the surface area itself for associations and correlations.

Considering this variation and research on the varying degree of thickness and area trajectories, this study was designed to analyze the cortical thickness (CT), surface area (SA), and volume of brain regions in healthy young adults. To execute this step, we used surface-based methods from

Freesurfer to form and compare the three measures. Freesurfer is an MRI-based software tool widely known and used for analyzing neuroimaging data. The extensive algorithm of the program makes it easier to examine the structural properties of the human brain. The tool is highly evolved due to its availability and can be employed using various hardware and software platforms.

In summary, the automated reconstruction of an atlas-based (Desikan et al., 2006) brain model involves a total of thirty-one steps. Major steps include elimination of non-brain tissues such as the skull and meninges (Clarkson et al., 2011; Segonne et al., 2004) and segmentation of grey and white matter tissues for cortex and sub-cortex (Fischl et al., 2004a,b; Salat, 2004), motion correction using a set talairach script which accounts for unnecessary head movement, and finally fitting the grey and white matter by the process of tessellation. Based on these steps, a total of thirty-six brain areas are formed. The thickness of each area (in mm) is calculated by measuring the distance between the grey-white matter surfaces to the sub-millimeter level (Fischl and Dale, 2000). The cortical surface is then inflated according to the cortical folding of gyri and sulci. This provides the surface area (in mm^2) measurement of regions. Based on the morphological properties, it gives more accurate volumetric results (in mm^3). These calculated constructs are further analyzed to understand the brain's anatomical characteristics (Figure 1). Refer to supplementary section 8.1 for detailed information on Freesurfer's Structural-data analysis pipeline and list of codes.

1.2 Psychological Well-Being

One of the most fundamental pursuits in neuroscience, psychology, or cognitive sciences is understanding the intricate relationship between the brain and behavior. As the research progressed throughout history, two main opposing views emerged in the context of this crucial association. Firstly, the idea that the behavior is distinct and controlled by separate brain regions structurally and functionally. This perspective was referred to as the 'localizationist view,' under which one believed that each brain region is responsible for a specific behavioral outcome performed by the mammalian brain (Scoville and Milner, 1957). This view has been supported by various lesion studies, one of which involving the scientists temporarily shutting down a functioning part of the brain through electrical stimulation in patients eliciting symptoms of epilepsy. This experimental procedure led to the discovery of the human homunculus, a brain map of our sensory and motor systems (Penfield and Boldrey, 1937). Contrastingly, it was speculated that behavioral patterns cannot be traced back to one single brain region. Instead, the brain comprehends the outcomes in a more unified way. This was referred to as the 'Reductionist View.' The work by Karl Lashley in 1931, suggested that memory spread across the cortex and cannot be restricted to a specific brain region. In the case of a memory-related lesion, more extensive the damage in the brain, the more severe the cognitive disability (Lashley, 1931).
Many studies followed one or the other perspective as their results supported either localization or unification theory til the end of the last century. The dismay remained as the support to establish one viewpoint was inconclusive until in, 1998, a new methodological perspective of network neuroscience emerged, where the researchers successfully converted the neurons of the central nervous system into a graphical representation. Each neuron was a vertex, and each axonal connection was an edge connecting two vertices. It was suggested that the neural network acts in both high specialization and integration, bringing the previously proposed theories together (Watts & Strogatz, 1998). Following this suggestive approach, many studies have revealed that behavioral patterns are indeed a product of integrating multiple brain areas (Van den Heuvel & Sporns, 2019; Bassett et al., 2018a). Specific but functionally interlinked brain regions continuously process the ongoing flow of information within the networks. This notion holds in terms of emotional and psychological processing as well. This raises several questions, e.g., where do emotions reside in the brain? Previous works aiming to answer this question also fluctuated between region-specific

vs circuit-specific ideas. Today, with the evidence in hand, it is understood that circuit interactions are the basis of the brain's emotional regulation and personality traits. Techniques such as functional magnetic resonance imaging (fMRI) or Electroencephalography (EEG) are used in modern-day neuropsychological research for brain region and region-interaction activation of emotions such as resilience, anxiety, stress, empathy etc. (Bickart KC et al., 2014). However, to understand the individual differences of these basic emotions and to gather essential information and insights on personality traits, self-reported behavioral questionnaires has emerged as a crucial tool. This need to identify attributes, emotional states, and cognitive functions has been extensively used in psychology outside of machine-based apparatus to quantify the results objectively.

1.2.1 Behavioral questionnaires and the Role of the Brain

As stated earlier, the brain undergoes dynamic structural changes during early adulthood. At this age, constant worry about decisions, the future thoughts may lead to anxiety, unhealthy stress, or a possible decrease in empathetic responses. On the other hand, individual mental health states help us be resilient over time. Studies have also suggested this stage of life is a *"vulnerable period"* for poorer mental health (Schofield et a., 2016). Research often resorts to brain and behavioral questionnaires to effectively measure and decipher the level of these states for gathering essential data. This section will highlight the various mental health aspects such as Anxiety, Stress, Resilience ,and Empathy which are the focus of the study and brain regions responsible for these personality traits.

1.2.1.1 Anxiety

The American Psychiatric Association (DSM-IV-TR, 2000) characterized the states of negatively valenced thoughts, avoidance actions, hyperarousal and unusual fear or threat as major symptoms of Anxiety. With a prevalence rate of 29%, it has emerged as one of the most prevalent mental health conditions in the world (Kessler et al., 2005b). Although it is a natural response in worrying situations, anxiety can be induced by unidentified occasional stressors or heightened for some people due to reduced self-regulatory measures, resulting in a more chronic state. The Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5; American Psychiatric Association, 2013), categorized conditions like Generalized anxiety disorders (GAD), Social anxiety, panic disorders, and agoraphobia under anxiety disorders domain. fMRI studies have revealed the dysfunctional circuitry in the amygdala-prefrontal connections as the primary neurobiological mechanism behind such heightened emotional responses (Bishop, 2007). Recent fMRI data obtained from non-clinical participants strongly suggest the role of the insular cortex to be crucial in anticipation of the unidentified occasional stressors and aversive stimuli (Alvarez, R et al., 2015). Self-reports are best-suited analysis for the dimensional assessment of anxiety based on human functional domains such as negative or positive valence for non-clinical subjects. For this purpose, the Hospital Anxiety and Depression Scale (HADS: Zigmond et al., 1983) was formed to measure these states apart from clinical tools.

1.2.1.2 Stress

In everyday life events, we come across several positive or negative encounters, which sometimes are beneficial or often turn out to be traumatic i.e., Stress, anxiety, or the ability to encounter aversive situations. In response, our body generates a "fight-or-flight" mechanism with adrenaline and cortisol hormones (Goldstein D, 2010; Herman JP et al., 2003). Stress can cause dysregulation in our cognitive and decision-making ability leading to irrational behavioral states. Studies have identified the role of the amygdala, hippocampus, and pre-frontal cortex as the brain areas implicated in stressful response (Bremner JD, 2006), where the hypothalamic-pituitary-adrenal (HPA) axis orchestrates the bodily response to "unhealthy stress." The neurobiological mechanism of this axis is beyond the scope of this thesis. Prior work has established the thinning of the cortex during late childhood to early adulthood with increased cognitive performance (Weiranga et al.,2010; Tamnes et al., 2010). However, this thinning can be disrupted by early life exposure to chronic stress through irregular glutamate transmission. Such a situation can negatively affect the brain’s structural integrity (Averill et al., 2018). Marisa C et al. (2020) reported a whole brain cortical thickness study where daily life stressful events and early life trauma in young individuals could affect the neural structure, which leads to a thicker cortex.

1.2.1.3 Resilience

The human brain is adaptive in terms of overcoming stressful situations. When exposed to adverse events, our brain has the ability to ‘bounce back,’ which is associated with better outcomes (Smith et al., 2010). This ability is termed as ‘Resilience.’ This allows us to have lower vulnerabilities to social and environmental risk factors. Psychological resilience has been crucial in positive psychology, with beneficial factors in overall life well-being and satisfaction. It is an essential dynamic process, with evidence from numerous studies suggesting highly resilient individuals lead a more productive life (Hu et al., 2015; Kong et al., 2015d; Staici, 2016). As important as this personality trait is, exploration to underpin the neurobiological mechanisms has been done over the years. Task-based fMRI found that insula activity was prolonged for aversive stimuli when facing a risk, but only low-resilient individuals had prolonged insula activity for a neutral state (Waugh et al., 2008). Consistent recent findings have revealed the role of the orbito-frontal cortex, mainly the medial region (m-OFC), as more influential in psychological resilience (Milad et al., 2009; Sekiguchi et al., 2015). Furthermore, to include quality of life in the research trials, many scales have been developed to measure resilience in healthy individuals. The Connor-Davidson Resilience Scale (CD-RISC) has emerged as one of the most reliable brief self-rated assessments to quantify the results and evaluate potential treatment options.

1.2.1.4 Empathy

We humans, as a specie spend most of our lives engaging with and thinking about other people i.e., being social. These interactions provide us with a response mechanism to perceive and share others’ pain, happiness, and other emotions. This default behavior allows us to understand and engage in actions with consequences for us and others. Such an ability is called empathy (Preston & Waal, 2003), which drives our prosocial behavior i.e., help that could benefit others. Prosocial behavior reduces stress and overall physical and mental well-being (Brown et al., 2008). Emotion contagion, empathetic concern, and sympathy all occur in similar contexts. Empathy is a crucial motivating factor throughout our life and has been found to be altered in many psychiatric and neurological disorders such as psychopathy and autism, evidence of which ranges from animal (Sato et al., 2015) to human studies (Henry et al., 2016). Investigative studies have found the role of the anterior cingulate cortex (ACC) and the presence of oxytocin receptors activated when participants witness their partner in a negative situation (Singer B et al., 2004). Dysfunction in this region is related to autism and psychopathy (Minshew et al., 2010). Moreover, the presence of another individual suffering elicits an empathetic response due to activity in the insula, amygdala, and majorly in the caudal anterior cingulate cortex (cACC) (Boccia et al., 2013). The notion that empathy has many constructs has been measured using self-report scales tapping into personal distress, perspective talking, empathetic concern, and cognitive empathy. The Interpersonal reactivity index scale was developed for this purpose (Davis, M. H. 1983).

1.3 Experience Sampling Method

For overall physical and mental health, a sense of well-being (WB) and happiness can positively impact psychopathology, e.g., anxiety and stress (Diener et al. 2017). Happier and more resilient people tend to have a positive outlook, which is associated with better outcomes in daily life situations (Moore and Diener 2019). Well-being has been studied in its broad context in this thesis, including the two constructs as described in the literature as subjective well-being (SWB), such as high positive and low negative effects and psychological well-being such as positive functioning, savoring, reappraisal (Diener et al. 2018). People can have identical scores in the questionnaire's format, while the individual scores can vary when momentary data on daily life negative, positive, and social emotions are accounted. For this purpose, Experience sampling methodology (ESM), a high-frequency sampling assessment, has been increasingly used to understand the fluctuations and reliability of daily emotions (Stange et al., 2019; Trull and Ebner-Priemer, 2020). ESM helps measure the feelings on a moment basis by asking the individuals the same set of questions in a survey format multiple times a day. This way, it evades the limitations of self-reports such as recall bias, social desirability bias, etc. The concept of daily dairy is not new and evidence of its use in neuropsychological research is as old as the 1920s. Favill and Rennick (1924) used the daily dairy method to collect participant's mood and behavioral data. Over the years, this method has grown and documented its use not just in neuroscience but also in psychology, behavioral medicine under various names such as Ecological momentary assessment (EMA: Stone & Shifman 1994) or Ambulatory assessment (AA: Fahrenberg et al. 2007). The main aim of this methodology is to capture individual behavioral, negative, positive, and observational responses in a natural setting i.e., being part of their lives, such as being at the university, offices, homes , etc. "In the past two hours, has anything happened that made you feel happy or distressed?" (i.e., affective state) can be captured based on momentary assessment. Negative events (NE) can be characterized as emotional distress, concern, and rumination, whereas positive events (PE) have domains like satisfaction, and savoring. Both events can also be rated on how intense the event was. In this thesis, the term ESM accounts for all the interchangeable names (EMA, AA) in the literature.

Previous experimental apparatuses required the participants to carry a beeper or a small diary to document their feelings with every beep, several times a day. With the technological advancements, those were soon replaced by computers and, more recently, smartphones (Runyan and Steinke 2015). However, the concept remained the same where they answered several surveys with options describing and rating the events; the analysis became much easier and more detailed. The calculation of within and between-person variability (cosistency of behavior) became possible with this advancement. Csikszentmihalyi and Hunter (2003) compared the rating of surveys with how the responses and feelings varied in a day and for the whole study duration for both within and between all participants and found that average happiness varied throughout the day, providing excellent use of momentary studies. In economically developed countries like Norway, the use of smartphones has been more than the global average (GSMA intelligence, 2019); hence, smartphone-based ESM studies account for lesser difficulties.

A critical question that arises in using of ESM is, "Could this be linked to neurobiological processes or personality traits?" Studies have shown the overall higher psychological well-being of an individual is linked to higher positive effects in daily life (Burns and Ma, 2015), and individuals have a higher ability to assess adverse events (Rush et al., 2019). A longitudinal study that employed both self-report and ESM measures compared these results with amygdala volume and found that greater volume was linked to more negative effects in daily life than positive and lesser well-being (Puccetti et al., 2021). Equivalent results on anxiety and daily life effects revealed that high academic pressure leads to higher anxiety in young adults which in turn reflects on the daily assessments of emotions being more negative than positive. (Shi et al., 2016; Chin E et al., 2017).

Furthermore, with a time-contingent ESM study like this, two underlying factors can be studied: Compliance rate and Affective yield. Responding to the survey within a fixed time window is known as the compliance rate and the amount of data captured through the surveys is the affective yield. Both factors must be high between 78% - 85%, for a successful study (Rintala et al., 2019; Williams et al., 2021). Moreover, in this investigation, the surveys were designed in a way that each of the NE and PE categories could be divided into sub-categories: different strategies such as intensity, reappraisal, rumination, savoring and social sharing and percentage use of those strategies. Results from ESM depend on numerous factors such as the duration of the surveys, total surveys sent, sample size, and the amount of missing data i.e., total surveys/questions missed by the participants. In a real-world setting, getting responses from all individuals for all the surveys is a challenging task and thus the analysis should account for missing data if the number is significant. Following the guidelines proposed by Liao et al. (2016), these measures can be adjusted for a higher compliance rate. Exclusively, the major challenge in ESM is the interpretation and analysis of data gathered. This thesis aimed to fill the knowledge gap to evaluate how emotions can vary within an individual's life, unlike previous studies, which constantly overlooked this factor by only measuring variation between individuals (Yearick K, 2017; Nezlek et al., 2002; Pinquart & Sorensen, 2000).

1.3.1 Multilevel Structural Equation Modelling

It has been established that in an ESM study, it is essential to determine how the effects vary in the study population. The data based on daily experiences depends on everyone's ability to answer all the surveys which forms the basis for examining the variability of certain emotions. Even the most basic setup of this design can be extremely complex due to the "nested nature" of the data where observations i.e., each survey response, are nested within the participants and participants, in turn, are nested within days of the study. This kind of hierarchal pattern demands an analysis model that can sustain more than one level. Data clustering automatically forms more than one level giving a "multi-level" outlook to the responses which leads to desired within and between-person outcomes (Gottfredson et al., 2015; Shapiro et al., 2013). ESM in this thesis has three levels where observations were at level one; a fixed number of participants were at level 2 and due to the variations, the number of days taken to complete the survey were at level 3 (Figure 2).

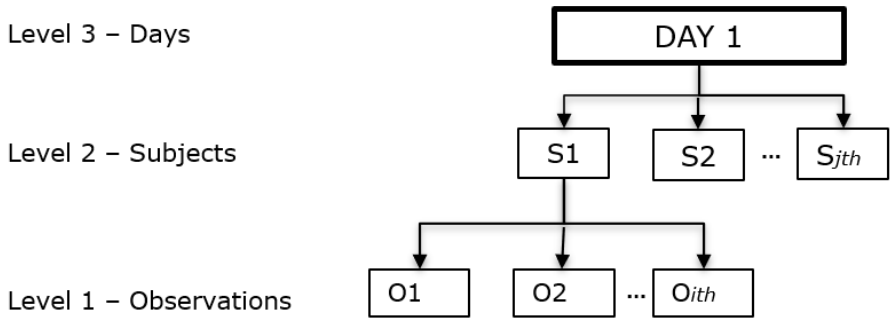


Figure 2. Three-level data structure for ESM. S = subject; O = Observations

A generalized model framework that could be implemented to examine the relationship between variables at various levels, such as in Figure 2, overcomes the challenges of ESM data analysis. Such a statistical model is termed "Multi-level Structural Equation Modelling" (MSEM: Hox, J, 2012). The previous instances of its partial use in research are more than 50 years old (Goldstein & McDonald, 1988; McDonald & Goldstein, 1989; Schmidt, 1969). This method has been extremely useful in studying nested design data with multiple grouping levels as it combines the two traditional methods: Multilevel modelling (MLM: McArdle & Hamagami 1996) and Structural equation modelling (SEM: Meredith & Tisak, 1984). The use of regression analysis and the relation between Level 1 and Level 2 - from MLM and path analysis and relationship within Level 1 – from SEM are extensively used by combining the equations in MSEM. By doing so, it overcomes the limitations posed by these two methods in accounting relationships between variables for all the hierarchies available rather than modelling at one level and disregarding other dependencies within the data. Furthermore, it helps determine previously discussed within- (e.g., individual level) and between- (e.g., group level) subject relations and how they contribute to the outcomes in a combined fashion. It does so by calculating the reliability at each level, denoted by omega *(ω),* where the higher the omega, the greater the strength and variation. It also allows cross-level interactions, which examines if one level interaction could vary or be affected due to other level(s). To capture the relationships in the data, considering all the levels, MSEM has two main parameters: Fixed and Random effect. When the outcome is assumed to be the same for all the individuals, the effect is called fixed, whereas when the outcomes are allowed to vary across individuals, the effect is termed Random. It is worth mentioning that these two effects depend on the variable they have been assigned to and can be used for all variables within the model. Considering the type of effect assigned is essential as it can significantly affect the analysis. However, these effects are assigned in a calculation to provide the 'Effect size' denoted by *(ß)* which is statistically easier to interpret and essential to establish ESM's clinical significance. The magnitude of effect size directly indicates the relationship between two variables. For example, while using the savoring strategy in our ESM survey, the higher the effect size within an individual, the higher the variability of the savoring i.e., the subject was left with a higher Positive feeling after a Positive event had occurred, in a two-hour cycle (Details in the Method section). Previous research (e.g., Lee J. et al., 2018) measured effect size between individuals only to observe the fluctuation in emotion. The primary flaw in this method is that there might not always be any significant variation between individuals. Since the responses are also independent, measuring the effect size within subjects is also essential. This thesis filled this gap by evaluating the reliability and variance at the within level as well. The growing use of MSEM has broadened the statistical tools used to construct the model. Among many, the R-studio version of the platform has emerged as a resourceful platform due to its detailed visualization and straightforward interpretation (Vuorre and Crump, 2021) (details of the codes can be found in supplementary section 8.4).

1.4 Is there a Relationship between Brain and Well-being measures ?

The conventional paradigm in neuropsychological research is investigating correlations among variables such as brain measurements and performance on cognitive assessments, or EMA, in our case. This mainly refers to finding connections, relationships, or links between variables and is usually done using univariate methods. Looking into the relationship between CT, SA, volume, and assessment scores, finding covariances among these variables would be beneficial. These values can help in exploring the relationship between brain ROIs composite measurements, behavioral data and ESM data based on average negative and positive affect, as to how one variable is dependent on the other and inter-effects. In young adults, numerous studies and meta-analyses have tried to establish this relationship by investigating structural brain integrity and psychological well-being such as anxiety and empathy. Higher anxious individuals reportedly had variations in morphological features of the insula (Xiaosi et al., 2013; Pavuluri et al., 2015), cingulate cortex (Frith & Frith, 2006; meta-analyses by Molenberghs et al., 2016; Schurz et al., 2014), and amygdala (Puccetti et al., 2021). Lesion studies have revealed that patients with lesions extending into cACC faced higher difficulty expressing empathetic responses (Shamay & Tsoory et al. 2009). With the help of the background literature, this thesis aimed to determine a linkage between brain regions to fill the knowledge gap by combining these with daily life measures as well. The methodology employed in this study was designed to fulfill this aim.

Once a relationship is established, it is timely necessary to identify and differentiate between the initial cause and its effects. Questions like "Does a brain region's thickness affects our empathetic response?" or "Does higher or lower SA of the brain region affects our daily life experiences?" are common in structural studies. To speculate and methodologically find answers to these questions depends on identifying an independent variable (IV) i.e., which can affect another variable and a dependent variable (DV) i.e., on which the effects are shown. Questions like these also suggest the presence of a mediator who can orchestrate the relationship between IV and DV. Mediating variables are behavioral, biological, psychological, or social factors that relay the impact of one variable on another variable. One approach is to describe the method or technique by which one variable influence another through mediation. Social psychology, neuroscience, and cognitive science evidence emphasize the power of mediating variables forming the basis of many modern theories. For example, memory can mediate the process of information transfer and response. This is the core concept underlying brain-behavior mediation analysis, which identifies relevant cues, detects crucial associations, and, eventually, the impact of/on behavioral outcomes (MacKinnon et al., 2007).

1.5 Research Objectives

Based on the literature and relationships, the objective of the study was to :

i. Investigate the effects of Brain ROI (Insula; mOFC; cACC; Amygdala), extracted from 7-T sMRI on daily life responses and self-report questionnaires.
ii. Examine the relationship between daily life's positive, negative, and social emotions through regular surveys with self-report measures.
iii. To identify the most reliable methodology for the analysis of Ecological momentary assessments concerning between and within individual variations.

2. METHODS

2.1 Ethics

The study received approval from the Regional Committee for Medical Research Ethics (REK), Norway (REK midt, 390390). Prior to joining the study, all participants gave informed, signed consent.

2.2 Study Population

Participants were part of a bigger study aiming to identify neural correlates of resilience in the aging population in Trondheim. The participants were aged between 18-35 (mean = 27.1; SD = 12.02; Male: Female = 13:22) and were recruited through posters, social media, and associated references. Out of 100 people signing up, 78 were selected as per the fMRI safety guidelines. Inclusion criteria included the absence of mood disorders e.g., major depression, Bipolar disorder, Disruptive mood regulation, etc., and MRI compatibility (e.g., claustrophobia, metallic implants). Out of 78 who underwent MRI scanning, 63 participants accepted to be part of the third session of the study, eventually, 12 withdrew or failed to finish the complete sessions. A total of 51 participants were invited to take part in the momentary study, where the final data after ESM criteria was 35 subjects. Exclusion criteria included Invasive brain or heart surgery, prosthetics or metallic implants, epilepsy claustrophobia, Dental braces/bridges, or orthodontic anchorage, neurodivergent diagnoses like autism spectrum disorder (ASD), Attention-deficit/hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD) etc., currently on mental health prescriptions and tattoos above the neck/shoulder area.

2.3 Study Protocol

The study was designed to be conducted in three parts. Firstly, obtaining T1-weighted structural brain imaging data from 7-Tesla MRI. Secondly, the behavioral study session assessed multiple domains of self-reported questionnaires including memory, IQ, emotional well-being, and empathy. Thirdly, a 7-day follow-up ecological momentary survey (ESM) based on their daily life happy, distressing, and social events. The data collection lasted from August 2022 until January 2023. The MRI data were collected at St. Olav's Hospital in Trondheim, the questionnaires in a lab at the medical faculty and Kavli Institute for Systems Neuroscience and follow-up survey data was gathered using a mobile application platform. Each of the participant completed all three assessments with proper training provided.

2.4 Brain MRI

The MRI examinations were performed on a Siemens 7.0 T MAGNETOM Terra scanner (NTNU PET-Senteret) with a circular polarized transmit (1TX) head coil. Participants were provided with earplugs and foam pads for ear protection and to reduce movement and were asked to remain completely still during the 8-minute examination to acquire structural brain imaging. High-resolution T1-weighted images were acquired with Magnetization Prepared with 2 Rapid Gradient Echoes (MP2RAGE) sequence (echo time = 1.99 ms, repetition time = 4300 ms, inversion time 1 = 840 ms, inversion time 2 = 2370 ms, voxel size = 0.8 × 0.8 × 0.8 mm*3*, flip angle = 5°/6°, slice thickness = 0.75 mm, and 224 sagittal slices).

2.4.1 Pre-processing

The structural images from the scanner were extracted for the purpose of this study. In the pre-processing stage, the images were converted into nifti format (nii) by suppressing the noise, sacrificing some of the signal homogeneity for numerical stability, with the MP2RAGE sequence simultaneously acquiring the T1w (GRET1W) image volume. The noise suppression and intensity of the signal were regulated by a regularization parameter (N). The value of N can be optimized depending on the mean signal strength. Adjusting the regularization parameter at N = 10, the SNR was found to be minimum, and the mean signal strength was most; thus, this value was chosen to pre-process all the images gathered from the scanner (Figure 3). (O'Brien KR et al., 2014). The robust T1w images allow MP2RAGE to generate, clinically standard T1w images, which were readily used in the study.

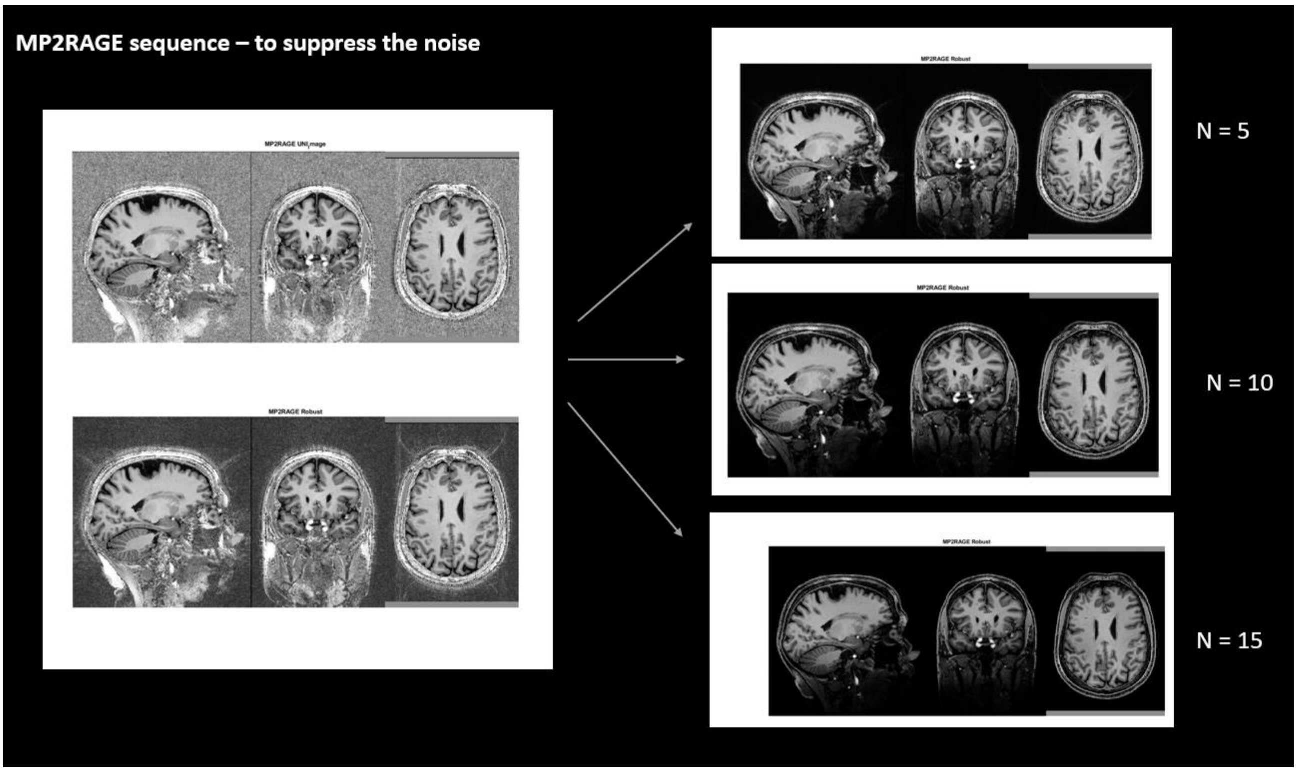


Figure 3 MP2RAGE sequence with different N values concluding N = 10 as ideal for this study.

2.4.2 Freesurfer Analysis

The T1 images generated from the preprocessing steps were analyzed using a set of software tools known as Freesufer, stable v7.2.0 release for ubuntu22 (http://surfer.nmr.mgh.harvard.edu/) to study the cortical and subcortical structural anatomy. The software provides an array of anatomical measures, including cortical and subcortical thickness (Fischl et al., 2002, 2004a), volume, surface area, segmentation of hippocampal subfields and amygdala (Van Leemput et al., 2009), parcellation of cortical folding patterns (Desikan et al., 2006; Destrieux et al., 2010; Fischl et al., 2004b). It labels the cortical and subcortical regions based on the reconstructed surface and pre-existing knowledge of the architecture of a normal human brain as the package within the tool generates surface representations of the cerebral cortex making microscopical structures visible by using any pre-processed T1 weighted image. Parcellation and segmentation are the terms used to describe the labeling of the cortex and subcortical regions, respectively. These libeling's are based on a) The Desikan-Killiany atlas and b) the Destrieux atlas. It divides the brain into the left and right hemispheres for better visualization. It represents the boundary between cortical grey matter, white matter, and Pial surfaces using the software package's default, automated reconstruction protocol (Fischl et al., 1999). The analysis was performed in two categories:

i. **The Cortical reconstruction** is an intricate process where multiple tasks run step by step based on the atlas (Desikan et al., 2006; Destrieux et al., 2010; Fischl et al., 2004b) using the recon-all command. The recon-all command converts the 3D anatomical images into a 2D mesh, comprising edges and vertices (Figure 4). This atlas can be used to align surfaces from individuals using a high-dimensional nonlinear registration approach. First, a high-resolution, T1-weighted, anatomical 3-D MRI dataset was used to construct a normalized intensity image to correct the RF-field inhomogeneities by adjusting the intensity and the contrast of the image. The Second step, known as Skull stripping, involved removing the extra cerebral voxels from the images, by deforming the skull into the shape of the cortex. Third, the geometric grey-white matter segmentation interface segregates both tissue types into light and dark shades. Next, the separation of both the hemispheres including cortical and sub-cortical components through cutting planes. All the interior holes within the white matter are filled. Finally, a smooth and anatomically corrected surface is generated, covered with triangular tessellation. This gives an accurate representation of tissue types and Pial surfaces. Freeview images depicting T1 image, intensity normalized, skull strip, and Pial edits can be found in the supplementary area.

ii. **Segmentation of nuclei of amygdala** – the FS 7.1 version of the Freesurfer hippocampal-amygdala pipeline was used to identify these structures using a T1w image from the ultra-high resolution 7Tesla fMRI. This was performed in 3 major steps. Firstly, the algorithm predicts the location of these areas from the input image through the newly built atlas based on the tetrahedral mesh in the Freesurfer directory (Iglesias et al., 2015a). Secondly, the predictive borders were outlined between the cortex and the sub-cortex (e.g., amygdala, thalamus, etc.), leaving no space or gaps, unlike in cortical reconstruction. Post labeling of the definitive border, the algorithm subdivides the areas marked into different nuclei of the amygdala, such as the Basal nucleus, Central-nucleus, Paralaminar-nucleus, etc., for both left and right amygdala in the two hemispheres (Figure 5). Finally, for analysis, a set of codes can provide the volumetric data of all the nuclei separately, along with the whole amygdala volume. This was performed through the lines of codes provided in the Freesurfer pipeline. (Codes: See supplementary material).

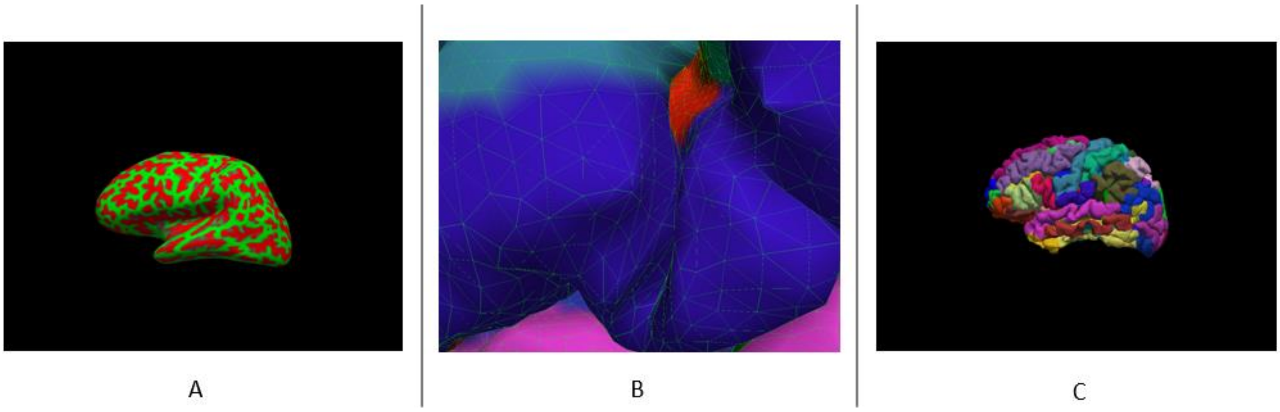


Figure 4. Freesufer Anatomical images. A) Inflated surface to see the sulci; B) A close look at the mesh surface, showing the Vertices and Edges; C) Destrieux parcellation atlas (e.g., lh. aparc. a2009s.annot)

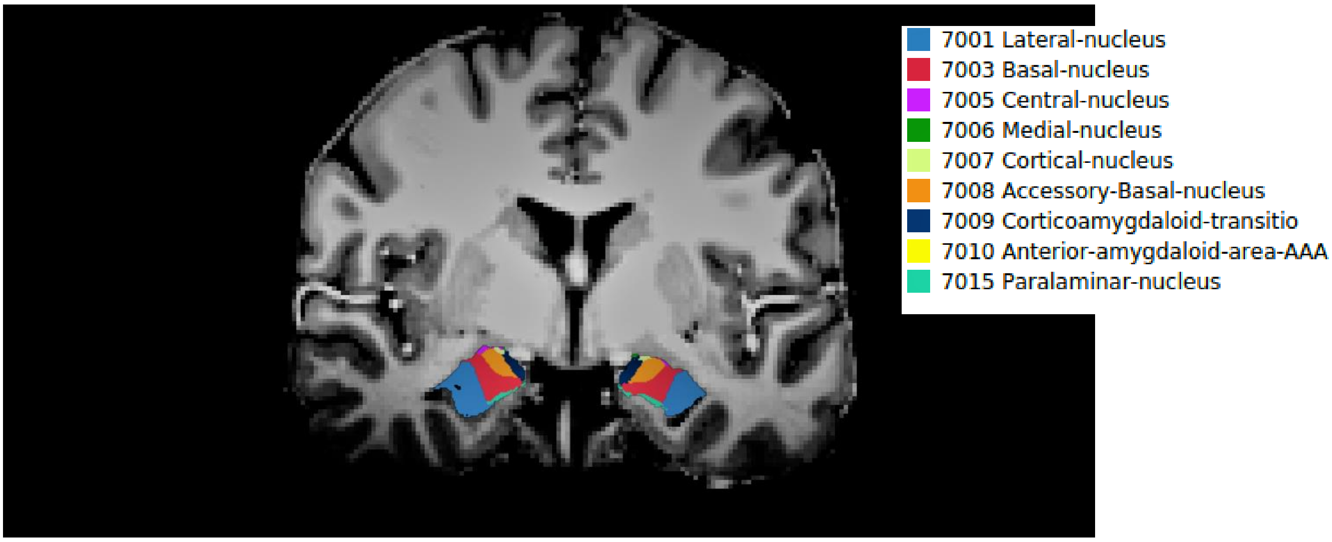


Figure 5 Segmentations of Amygdala obtained from Freesurfer.

2.5 Cognitive behavioral testing

The Self-reported behavioral testing was performed using widely used, valid, and standard set of questionnaires which covered areas including resilience, empathy, quality of life, and stress reactivity. The session was conducted in the behavioral lab at Kavli Institute. All the participants performed the task with one of the lab members guiding the session. The tests under consideration in this study are listed in detail in the following paragraphs. In every test, a higher score represented a higher level of that emotional state. All the instructions were to be followed for the testing to be valid.

2.5.1 Hospital Anxiety and Depression Scale (HADS)

HADS is a self-assessment scale designed by Zigmond and Snaith 40 years ago to estimate these emotional states in the general population (Zigmond et al., 1983). Our task consisted of 14 items , 7 items each for anxiety and depression. Each question had 4 options, each with a number from 0-3 indicated. E.g., "I feel tense or wound up". This was followed by 4 options: "Most of the time" (3), "A lot of the time" (2), "From time to time, occasionally" (1), "Not at all" (0). Participants were required to choose the options closest to how they have been feeling. It was important that they answered at once, keeping the past week in mind. The test took around 3-6 minutes to complete on average. Finally, the total scores were calculated by adding the options picked for each of the 14 items, indicating the range of Normal (0-07); Borderline abnormal (08-10); and Abnormal (11-21).

2.5.2 Perceived Stress Scale (PSS)

To assess how stressful our subjects perceive their circumstances in life to be, we used the PSS consisting of 10 items (Cohen S. et. al., 1983). "In the last month, how often have you been upset because of something that happened unexpectedly?" here, participants were asked to choose from the following options 0=never; 1=almost; 2=sometimes; 3=fairly often; 4=very often. Some items had shared similarities but were treated differently where they had to think about the situation and give their best estimate. The scores were calculated by the addition of the numeric choices (0-4), 2 set of items had reverse order (4-0); eventually, the higher the score, the higher the stress.

2.5.3 Connor-Davidson Resilience Scale (CD-RISC)

To set up a quantitative measure for resilience, we used the CD-RISC (Connor K. et al., 2003), which comprised of 25 items, all had a 5-point range of responses: "I am able to adapt when changes occur." which had the following options, "not true at all" (0), "rarely true" (1), "sometimes true" (2), "often true" (3), and "true nearly all the time" (4). The scale was rated based on how the participant felt in the past week. The total scores range was 0-100 which was added from all 5 columns finally giving one individual score, with a greater score associated with higher resilience.

2.5.4 Interpersonal Reactivity Index Scale (IRI)

The scale was developed to measure different multi-facets of the global 'empathy' concepts(Davis, M. H. 1983). The version of the test included 28 items, designed to tap the thought process of individuals about how they feel in a variety of situations and how well it describes them. The questionnaire was divided into 4 sub-scales consisting of 7 questions in each, namely: Perspective-talking, Fantasy scores, Empathetic concern scale, and Personal distress scale. E.g., "I daydream and fantasize, with some regularity, about things that might happen to me." Scoring was based on answers A-E where "A = Does NOT describe me," "C = In the middle," "E = Describes very well," which correspond to A=0; B = 1; C = 2; D = 3; E=4, except for the personal distressed scale which was A=4 and E=0.

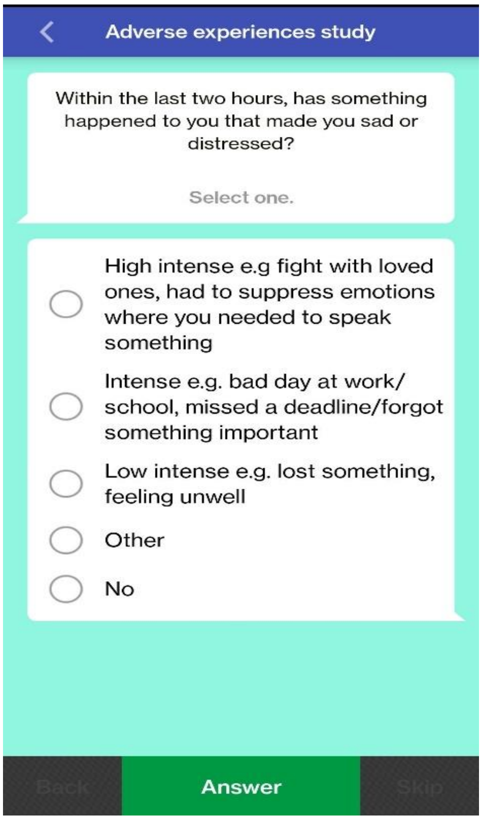
2.6 Experience Sampling Methodology

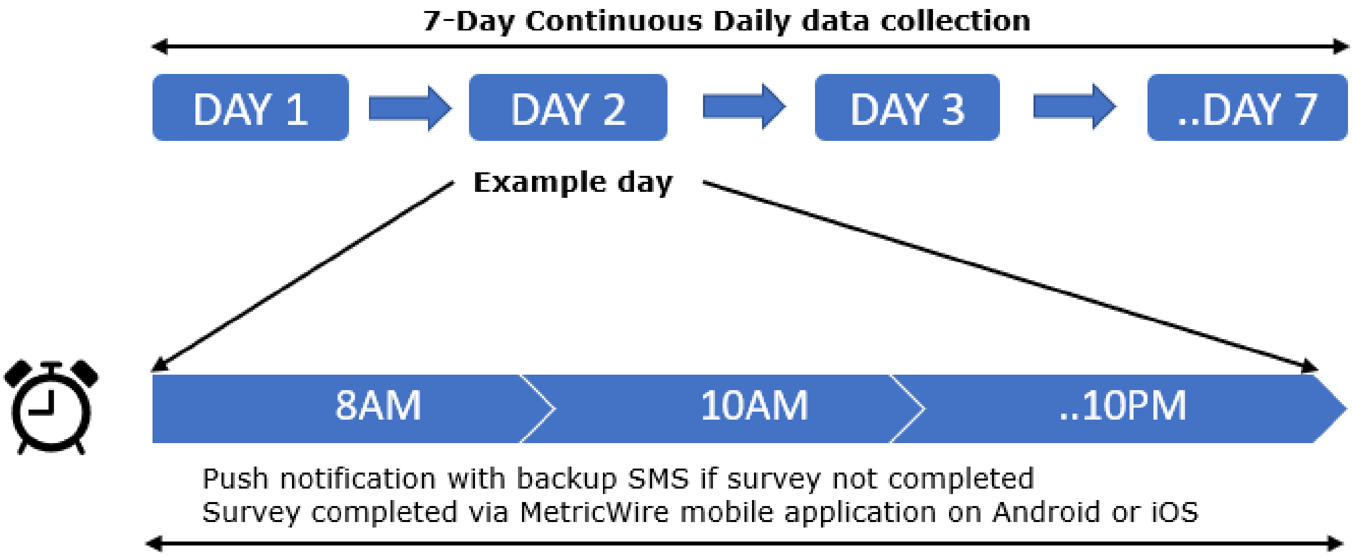
Experience sampling methods refers to the structure of a self-reported mood assessment study where an individual goes through a set of questions about their daily life scenarios (Arthur S. 2007). Being the third section of the study, it consisted of a 7-day follow-up survey after the participant had undergone both brain imaging and behavioral session. The aim was to better understand how individuals perceive and react to environmental cues outside the laboratory, in circumstances such as their daily lives. Out of 78 subjects, 51 participated in the ESM study. The inclusion criteria included time taken and attempt rate both to be ≥0.5 or 50%, average days to finish the study 12 days (M ± 1SD+12; avg. 6.9) so participants that took between 6-19 days were included (Tung et. al., 2022). After these criteria were inducted, a total of 35 participant data was retained for further analysis with the other two parts of the study. Our completion rate was 79.54%.

2.6.1 Design and Procedures

The survey consisted of fifteen questions based on negative, positive, and social aspects of daily life with a ratio of 7:7:1 respectively. Each participant was asked to download the MetricWire mobile application, which sent them survey notifications, ten times a day for the next 7 days (with the possibility to extend further), every morning from 8 am till 10 pm (specific sampling time and details Figure 6). Each survey took 3-4 minutes to complete. In each negative and positive event question, participants had the choice to write or record the audio describing the event using the function on the app. The duration of the study was including both weekdays and weekends.

6.1





6.2

Figure 6. 6.1 Screenshot of the question from the app; 6.2 An example of our EMA procedure with 10 promts each day.

NOTE: All participants started on different days depending on their behavioral session completion. All surveys were closed outside their respective time windows to prevent retrospective reports. All the survey questions were identical over time to reduce participant burden and comparability over time. Subjects could reach a research team member by chat section on the app if they had questions or problems during the sampling period.

2.6.2 Measures

A Negative or a positive set of questions was started by asking them: "Within the last 2 hours, has something happened to you that made you sad or distressed?" (Or happy for the positive side) Which had 5 options on a 5-point Likert scale with high intense - 5, Intense - 4; Low intense – 3; Other – 2; no event – 1. (Fig. 6) This was followed by 7 follow-up questions based on that event. Each question was categorized into sub-scales in both negative and positive sets. The daily negative events had negative intensity – "Following this event, on a scale from 1 to 7 how negative would you rate your emotions to be?"; Rumination – "On a scale from 1 to 7, how upset are you about the event when looking back at it now?"; Reappraisal – "On a scale of 1 to 7 how positive would you rate your emotions to be looking back at this event?"; and Negative social sharing – "Did this occur alone, or in the presence of others?". For the daily positive events, Positive intensity – "On a scale from 1 to 7, how positive would you rate your emotional state to be after this event?" ; Savoring – "On a scale from 1 to 7 how positive would you rate your emotions to be when looking back at the event now?"; Positive social sharing – "Did this occur alone or in the presence of others?" (Hiekkaranta P. et. al.,2021). The last question was based on their social life – "Within the last two hours, have you met with others in a social setting (i.e., visit, meeting, lunch, grocery shopping, conversations, A walk, party, Dinner)". Participant's responses to every question of the survey were analyzed for this study. The study did not analyzed questions based on written/verbal descriptions of events. Three more questionnaires were removed from the analysis due to significant missing values and were often skipped in the survey by the participants. A complete set of surveys was stored in the MetricWire directory of the lab. Questions can be found in Supplementary Section 8.2.

2.7 Analysis

2.7.1 Sample Characteristics

Descriptive statistics of brain data, behavioral measures, and ESM were performed using the IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 29.0.0. The brain data were accumulated for thickness, Area, and volume for the region of interest (ROI) for both the hemispheres Left (lh) and Right (rh) including:

- Amygdala Volume (mm^3)
- Insula area (mm^2)
- Caudal Anterior Cingulate Cortex (cACC) Thickness (mm)
- Region of Pre-Frontal cortex: medial-Orbito-frontal cortex (mOFC) Thickness

All the ROIs were selected based on their association with anxiety, empathy, resilience, and stress. A Bivariate correlation was performed for all the continuous variables (brain data, Questionnaires, ESM). For this Correlation was computed using brain measurements and total scores, followed by a test of Normality to determine the statistical method. Linear regression was performed among the 3 parameters to identify the relationship and finally, mediation analysis to investigate inter-variable effects.

2.7.2 Normality & Correlation

This step was performed to examine any correlations between the ROIs (thickness, area, and volume), results of four questionnaires and Negative, and positive events in daily life. A bivariate correlation matrix was used to study the relationship between brain anatomical statistics and behavioral and ESM assessment scores. This method considers the multi-collinearity among the variables and that one variable is unlikely to be completely independent of the others. Moreover, it highlights the strength among variables through Pearson's and Spearman's correlation coefficients. Such large neuroimaging dataset also comes with the challenge of "false positives." A viable solution to tackle this is to use correction methods such as Bonferroni, False discovery rate (FDR), etc., on the obtained p-values. It is important to choose the right method based on sample size. In the case of small sample size, a too-conservative method like Bonferroni would likely give false negative results. The FDR correction proposed by Benjamini-Hochberg (1993) serves the purpose well. For this Bivariate correlation was conducted, where the Pearson correlation coefficient was computed for all three sets of variables (ROIs, Behavioral data, and ESM), a Two-tailed test of significance at $p=<0.05$. (Figure 11, Table 8). The observed p-values were corrected using FDR correction. The q-value, which is the analog for the p-value, was set at 0.05 to keep the false positive or type I error under 5%. Due to a small sample size of 35, the Shapiro-wilk normality test was performed (significant >0.05), on brain and behavioral data as it has more power to recognize non-normality. This helped select the type of analysis and measure the distribution and normality.

2.7.3 One Sample t-test

After checking for distribution, one sample t-test was performed on behavioral measures to check for the difference between mean values and the standard value that is statistically significant. This step provides population-specific mean, standard errors, degree of freedom, and statistical significance (Sig. 2-tailed, p-value) and showed whether or not the scores of anxieties, stress, resilience, and empathy in the recruited participants differed from the normal standard scale.

2.7.4 Multi-level Structural Equation Modelling (MSEM) steps

For the analysis of daily life measures, a multi-level structural equation modelling was performed which combines the traditional multi-level modelling (MLM) and structural equation modelling (SEM). MSEM addresses the limitations of both MLM e.g., inability to account for several dependent variables and SEM e.g., inability to include level-specific predictors. The analysis was performed using R, version 4.2.3 (R Core Team, 2023), in R Studio version 2023.3.0.386 (Posit team, 2023). Further diagnostics and testing of mixed-effects models were done using multilevelTools, version 0.1.1 (Wiley, 2020), lmer() from lme4 (Bates et al., 2015) packages. lmerTest package was used for the degree of freedom for use in calculating p-values for the fixed effects. Multilevel structural equation modeling assumes individual and group level sampling, with both within-group (individual level) and between-group (group level) variation and covariation. For this study, within-group (individual level) are the observations i.e., each question in the survey and between-group (group level) are the number of days for each participant since observations are nested within participants and participants are nested in Days. Unlike MLM, Multi-level SEM calculates the variations in individual-level variables by keeping a random intercept at the second level (Subject Level). It gives us the within and between-person variability through:

$$Y_{ij} = \mu + \Lambda_w \eta_w + \Lambda_b \eta_b + \varepsilon_w + \varepsilon_b \tag{1}$$

Where Y_{ij} is the response value for the *i*th observation of individual *j*, μ is the vector of group level means, Λ_w is the factor matrix at the within level, Λ_b is the factor matrix at the between level, η_w is the moment (observation) level explanatory variable, η_b is the group (Days) level explanatory variable and finally, ε_w and ε_b are the residual errors at the within and the between level (Figure 7). In this three-level analysis, a new "level" variable 'RespDay' was created, representing the response number for each subject in each day. This was done as lme4 cannot determine nested paradigms automatically. (All the codes used in this step can be found in the supplementary section).

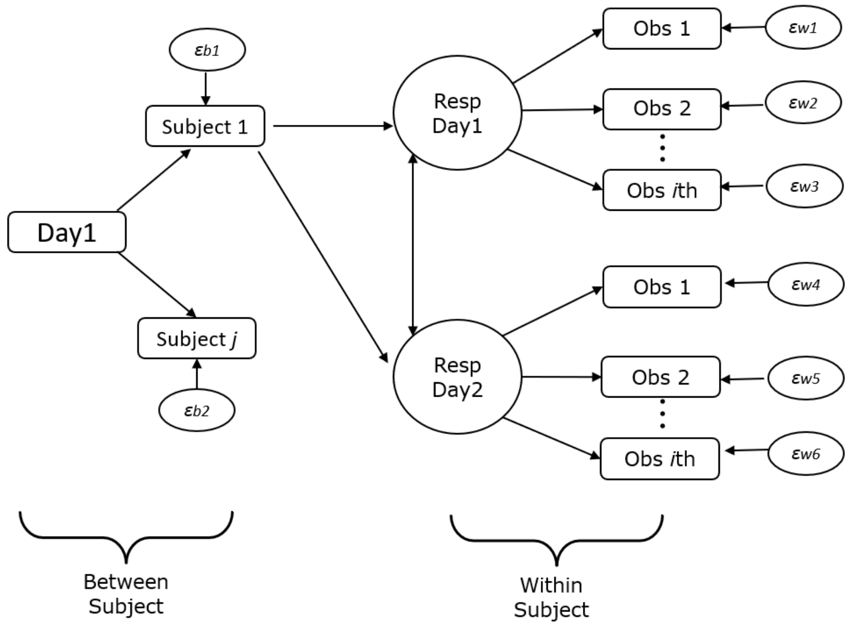


Figure 7 Representation of 3-level MSEM. Level 1 - Obs = Observations i.e., Negative, and positive Survey questions; εw = within residual error; RespDay = response number of each subject in a particular day; Level 2 – Subjects; εb = between residual error; Level 3 – Days of the Study.

The MSEM uses two effect types: Fixed and random effects. The lmer function in R was used to fit the mixed effect model. It was applied for both between and within subject level to calculate covariation, reliability (ω), effect size (ß), fixed and random effect intercept and correlation of fixed effects at each level. To compute between subject model performance, the negative or positive category question was kept as the dependent variable, "Days" were the main effect e.g., Equation 2, where m is the model output; here negative event is the dependent variable predicted by Days. Both the intercept and slope of days were included as fixed and random effects and df2 is the data frame containing all the survey responses.

m <- lmer (NegExp ~ DAYS + (1 + DAYS | Subject) (2)

data = df2)

Similarly, to compute within subject model performance, the negative or positive category question was kept as the dependent variable, "RespDay", was the main effect. Each level was treated as a different part of the model. Since the two levels were already mathematically distinct, no added predictor such as gender or age was added. Since MSEM merges MLM and SEM, MLM was followed to evaluate model fit as the slopes were allowed to vary randomly.

2.7.4.1 Reliability in MSEM

As the ESM data is based on repeated measures, variance exists at multiple levels of the structure (both within level and between levels). To compute the variances, 2-level composite reliability -

omega (ω) was calculated, as it considers the hierarchical structure of the data and provides more accurate estimates of reliability for this nested design study (McDonald, 1999). It does that by estimating the proportion of true score variance in relation to the total observed score variance (Equation 3).

$$\boldsymbol{Var(T)/Var(T) + Var(e)} \qquad \textbf{(3)}$$

where Var(T) is the true score variance, and Var(e) is the measurement error. Both within-subject and between-subject reliability was calculated using the [omegaSEM] function in the [multilevelTools] package in R.

2.7.5 Ordinary Least Squares regression (OLS)

To finally address the first and second objectives of the study, mediation analysis with OLS regression was conducted using PROCESS macro v4.2 for SPSS (Hayes, 2013). Since mediation requires an association between the mediator (M), the predictor (X) and the outcome variable (Y), all three variables needed be inter-correlated. Four parallel mediation models were built, based on the significant Bivariate results (p = <0.05 after FDR correction). Schematics of these models follow this paragraph. An SPSS description can be found in the supplementary section, which describes the process in more detail and provides information covariance matrix, model number etc.

2.7.5.1 Mediation

The main aim of OLS was to investigate the mediation mechanism where behavioral data can potentially mediate the relationship between brain ROIs and our daily emotional experiences (Figure 8).

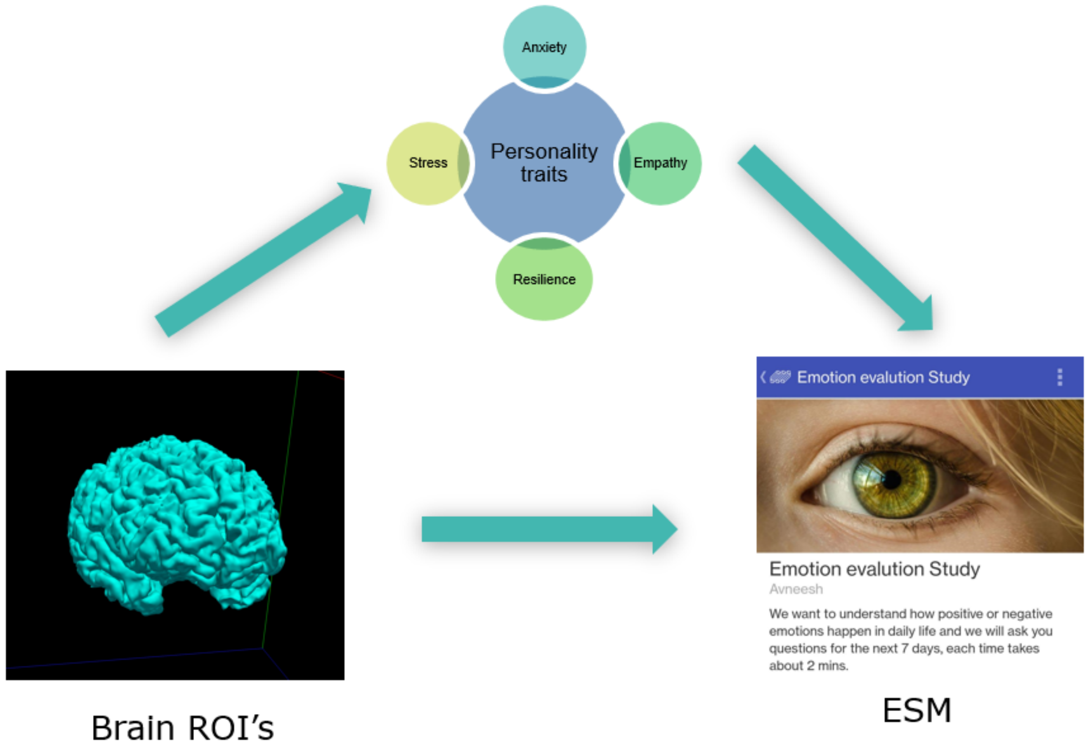
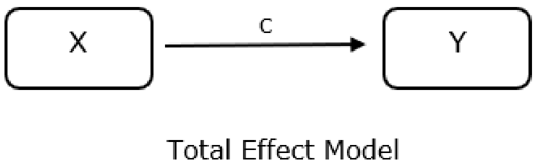


Figure 8 Possible Mediation relationship paradigm. Brain image obtained from Freesurfer; ESM image is from MetricWire Application.

For mediation analysis, the regression coefficient, *a,* and *b* were calculated from path Mediator - M on Independent variable - X (path a) and both M on X and Y – Dependent variable (path b), respectively. The indirect effect (ab) was calculated by the effect of X on Y through M and the direct effect (path c′) was calculated from the effect of X on Y. Finally, the total effect (c) is the effect of the independent variable on the dependent variable. It was obtained by the sum of direct and indirect effect. (Figure 9). For a complete mediation to occur, the total effect should be reduced in the presence of the mediator (the regression coefficient should be smaller for c′ than c). Furthermore, the indirect effect was estimated through bias-corrected bootstrap samples for a percentile bootstrap confidence interval (CI) were 5000 with level of 95% for all CI output, for a successful mediation. (Preacher and Kelly, 2011)

$$\textit{Total effect (c)} = c' + ab$$

9.1.



9.2

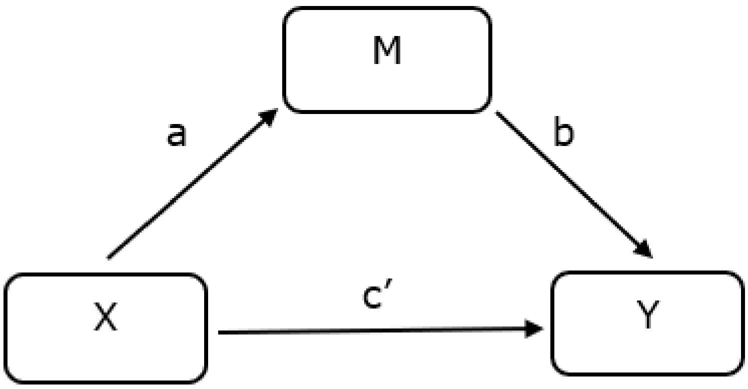


Figure 9 . 9.1) Total effect model i.e., effect of X and Y without mediation. 9.2) Basic Mediation model

The objective of the model was to see the effect of brain ROI on daily life measures with Behavioral data as a mediator. The results obtained from the bivariate correlation between Brain ROI, behavior, and ESM study, were analyzed. These inter-correlation results formed the basis of two mediation models. For each model the brain ROI was the independent variable (X), the ESM study was the dependent variable (Y), and behavioral data was the mediator in this relationship. Two more mediations were performed but were removed from the results due to non-significant results (report can be found in sections 8.3.3 & 8.3.4)

3 RESULTS

3.1 Sample

A total of fifty-one participants completed all three sessions of the study. After evaluating the structural MRI measures, viable behavioral scores, and Survey criteria based on time and number of surveys performed, a sample of thirty-five healthy cohorts was selected for the analysis. Demographic characteristics of the sample population are in Table 1. The excluded participants had tilted talairach for s-MRI (n = 5) and/or did not complete the EMA (n = 11). Otherwise, there were no significant abnormalities in behavioral scores and cognitive testing. Although the desired number of attempted surveys was 70 out of 70 in a 7-day period. Due to lower overall response rate at the start of the study, the average days to complete the surveys was estimated as 9 (5.3 ± 2.7) with 50 (18.15 ± 21.2) or more responses over time. The Overall study completion rate for the ESM was 77.5% with thirty-five participants providing 2444 surveys during the entire study.

Table 1 Descriptive statistics for demographic and Behavioral of the Sample (N = 35)

Variable	Minimum	Maximum	Mean	Std. D
Age (years)	21	35	27.14	10.2
Education (years)	6	29	17.83	5.1
HADS	1	18	7.15	3.98
IRI	41	96	66.54	14.50
PSS	4	29	15.51	6.48
CD-RISC	44	100	70.29	14.23
NEG1	1	5	1.55	0.993
POS1	1	5	2.13	1.102

HADS = Hospital Anxiety and Depression scale; IRI = Interpersonal Reactivity Index; PSS = Perceived Stress Scale; CD-RISC = Connor-Davidson Resilience Scale; NEG1 = Negative events (ESM); POS1 = Positive events (ESM); Std. D = Standard deviation

Performance in the various emotional scales was higher than normal on average for all the 4 sets of questionnaires. Table 2 summarizes the normality. All the scales were normally distributed except HADS-anxiety in the Shapiro-Wilk test. Due to the asymmetry in the anxiety score, the D'Agostino-Pearson test was applied, which showed a non-significant difference from the normal distribution, (χ (2) = 3.61, p = .165). The p-value (0.165 > 0.05) of the data distribution was normal. For the ESM study, the data formed of multilevel data structure. It was observed that the participants did not experience as many adverse events in day-to-day life as they did for positive events. Out of 15, two questions based on 'Has something negative or positive happened in the past 2 hours,' were used to understand the category of events faced in daily life, statistics of which can be found in Table 1 and descriptive distribution of intensities picked through-out the survey can be seen in figure 7. Bivariate correlation analysis results showed that the inter-correlations between ROIs, questionnaires and surveys were significant, with higher structural measures associated with corresponding scores, except, no correlation was found between PSS and ROIs mainly the ventromedial frontal cortex, frontal pole, insula volume. Unlike the other questionnaires, PSS scale was only correlated with negative life events. The brain region inter-correlated with both behavioral score and survey data formed the basis of mediation analysis.

Table 2 Normality and one sample t-test results (N = 35)

Variable	**Shapiro - wilk**		
	W	df	Sig.
HADS	0.992	35	***0.016***
IRI	0.967	35	0.355
PSS	0.975	35	0.601
CD-RISC	0.977	35	0.651
Insula	0.0.958	35	0.205
cACC	0.951	35	0.122
m-OFC	0.907	35	0.126
Amygdala	0.983	35	0.842

W = Test statistic; df = degree of freedom; Sig. = Significant value >0.05 is termed non-significant, meaning that the data is normally distributed. Significant result has been highlighted. cACC = caudal anterior cingulate cortex; m-OFC-T = medial-orbito frontal cortex

Table 3 Results for the one sample t-tests.

Variable	**t-test**				**95% CI of the Difference**	
	Std.error mean	t	df	Sig.	Lower	Upper
HADS	0.673	0.764	34	0.45	-0.85	1.88
IRI	2.43	6.79	34	**0.02***	1.60	11.49
PSS	1.09	2.2	34	**0.04***	0.29	4.74
CD-RISC	2.4	2.1	34	**0.04***	0.4	10.18

Std.error = Standard error mean; df = degree of freedom; Sig. = Significant; CI = Confidence Interval. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$

3.2 Behavioral Tests Performance

The one-sample t-tests were run for all 4 questionnaires to identify whether the scores of Empathies (IRI), Stress (PSS), Resilience (CD-RISC), and Anxiety (HADS) were within the normal standard range (Table 3). For IRI, the normal empathy score was taken as 60. Mean empathy score (66.54 ± 14.50) was higher than the normal empathy score of 60, a statistically significant difference of 6.54 (95% CI, 1.60 to 11.49), $t = 2.43$, $p = 0.02$. For PSS, the normal perceived stress scores were taken as 13. Mean PSS score (15.51 ± 6.48) was higher than the normal stress score of 13, a statistically significant difference of 2.51 (95% CI, 0.29 to 4.74), $t = 2.2$, $p = 0.02$. Similarly, for the resilience score, the test value was set at 65, where the mean resilience score (70.29 ± 14.23) was much higher than the normal score of 65, a statistically significant difference of 5.2 (95% CI, 0.4 to 10.1), $t = 2.4$, $p = 0.03$. Furthermore, for the HADS anxiety scores, the mean anxiety scores (7.15 ± 3.9) were between normal to borderline anxiety range. The t-test results were partially significant (95% CI, -0.8 to 1.8), $t = 0.7$, $p = 0.45$. The first three observations had statistically significant differences between means (p < 0.05); however, for anxiety scores, the level of significance was partial.

3.3 Structural MRI

The regions of interest were selected after multiple correlations with the behavioral and survey scores for thickness, area, and volume data collected from Freesurfer analysis pipeline. Inferential data can be found in Table 4 and images from Freesurfer denoting the location in Fig 11. As expected, a significant correlation was observed between the two variables and 4 ROIs: Insula area; thickness of caudal anterior cingulate and medial-orbito frontal cortex; and the right amygdala volume. p-values after FDR correction are displayed in the correlation matrix in Figure 11.13.

Table 4 Descriptives of brain ROI:

Variable	Min.	Max.	Mean	Std. D
Insula – A (mm^2)	1891	3308	2483.89	372.17
cACC– T (mm)	1.8	2.5	2.16	0.148
m-OFC-T (mm)	2.12	2.86	2.38	0.141
Amygdala-v (mm^3)	450.45	1636.49	1166.95	330.6

Insula-A = Insula surface area; cACC-T = caudal anterior cingulate cortex thickness; m-OFC T = medial-orbito frontal cortex thickness; Amygdala-V = Amygdala volume; Min. = Minimum parameter value of the ROI; Max. = Maximum parameter value of the ROI; mm= millimeter.

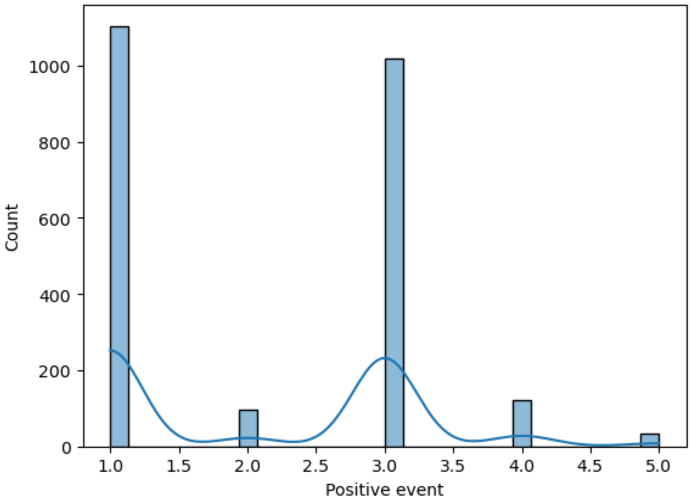
3.4 ESM results

The data set included a multilevel structure in which observations were nested in subjects producing highly clustered data and subjects were nested in multiple days, which varied among subjects. Presented in Table 5 are the details about the ESM measures. The within-person and between-person reliability of scale denoted by omega (ω) shows higher omega indicating greater internal consistency or reliability of the observed variable. For the perfectly dependable scales, for example, in negative events category, reappraisal had 0.98 and 0.94 within-subject and between-subject variance, respectively. For each category (negative and positive), the total percentage of use was estimated, showing the actual average use of that survey question. This was computed for both negative and positive events separately. For example, in the positive event category, out of 100%, a positive event happened was 23%, they used Savoring as a strategy 27%, sharing the experience in someone's company or alone 13%, rating of Intensity 27% (category where they had to rate the negativity in a positive event and how long ago was the event have been excluded due to skips or no ratings). The graphical distribution of the two broad categories, negative and positive is show in Figure 10.

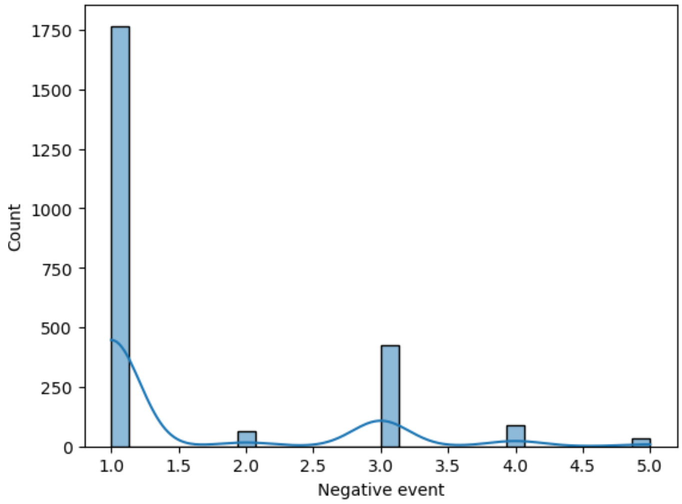
Table 5 Details about measures : Mean, Reliability and % use (N = 35)

	Report	Mean	Reliability	Percentage of use
Daily Negative events	Negative experience	1.5	ω_{within} = 0.897 $\omega_{between}$ = 0.881	33.07%
	Intensity	1.02	ω_{within} = 1.544 $\omega_{between}$ = 1.525	21.97%
	Rumination	0.94	ω_{within} = 1.470 $\omega_{between}$ = 1.444	20.34%
	Reappraisal	0.58	ω_{within} = 0.986 $\omega_{between}$ = 0.947	12.59%
	Negative Social sharing	0.56	ω_{within} = 0.811 $\omega_{between}$ = 0.793	12.13%
Daily Positive events	Positive experience	2.12	ω_{within} = 0.956 $\omega_{between}$ = 0.971	23.37%
	Intensity	2.45	ω_{within} = 2.096 $\omega_{between}$ = 2.072	27.04%
	Savoring	2.44	ω_{within} = 2.087 $\omega_{between}$ = 2.061	26.89%
	Positive Social sharing	1.21	ω_{within} = 1.140 $\omega_{between}$ = 1.149	13.37%

ωwithin = within subject reliability; ωbetween = between subject reliability.



10.1



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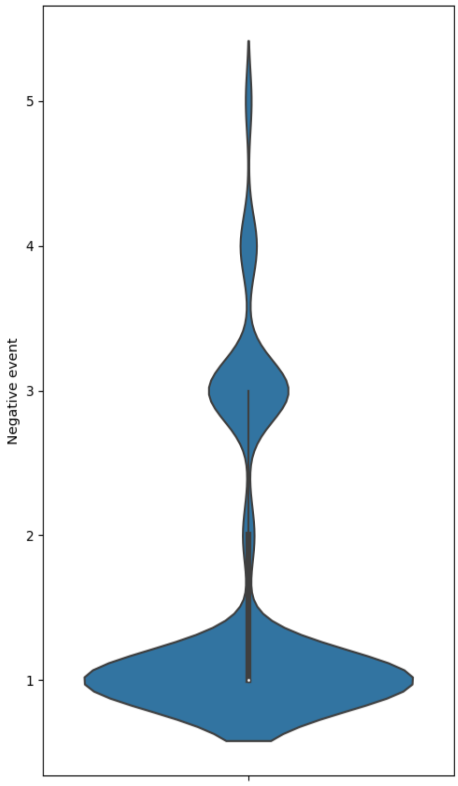
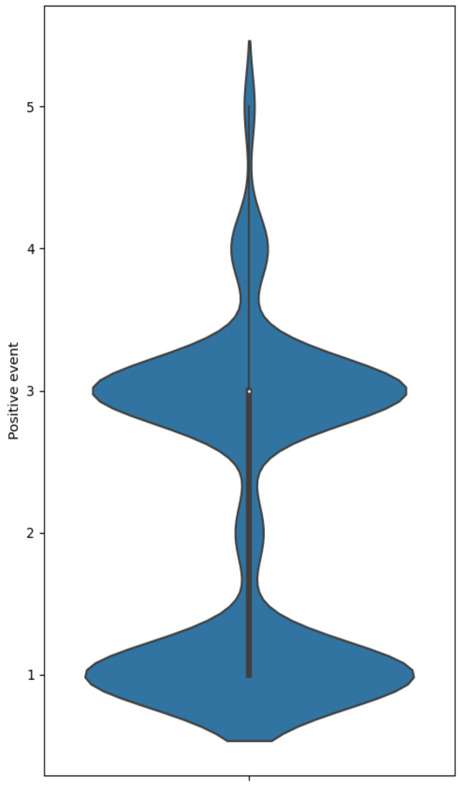


10.3



10.4

Figure 10 10.1 and 10.2 shows the descriptives of total count for each positive and negative event. 10.3 and 10.4 shows the violin plot of frequency for each negative and positive event type – averaged across days, respectively.

Table 6 Results of Multi-level structural modelling. Effect size (ß) (Fixed + Random) for between and within subject for each type of questionnaire.

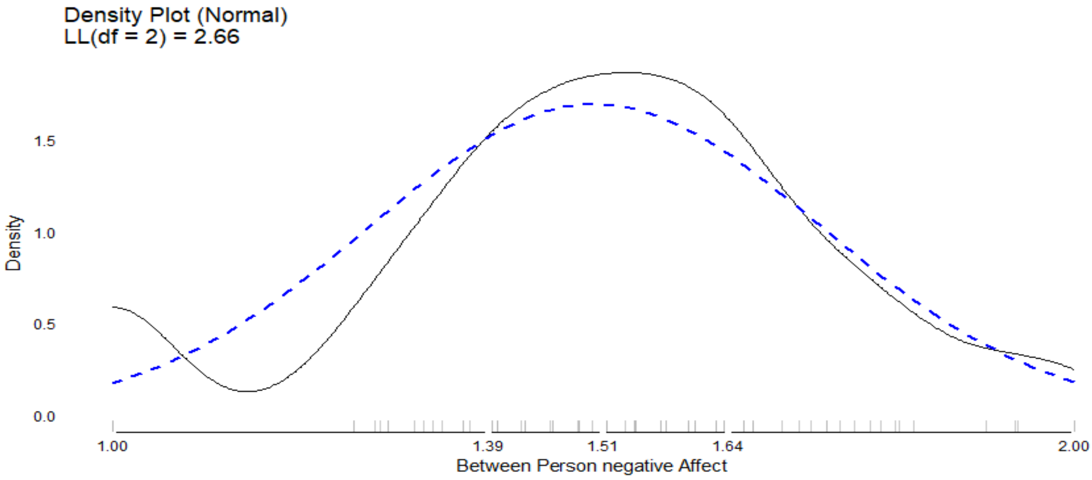
Variable	Effect Size (Fixed + Random) (ß)		p-value	
	Between subject	Within subject	Between subject	Within subject
	EV TV	EV TV		
Negative experience	0.001/0.046	0.001/0.010	p < .001	p = 0.07
Intensity	0.001/0.044	0.001/0.013	p < .001	p = 0.03
Rumination	0.001/0.055	0.000/0.011	p < .001	p = 0.08
Reappraisal	0.008/0.158	0.000/0.000	p < .001	p = 0.45
Negative Social Sharing	0.000/0.081	0.001/0.003	p < .001	p = 0.15
Positive experience	0.01/0.03	0.009/0.023	p < .001	p < .001
Intensity	0.016/0.046	0.005/0.022	p < .001	p < .001
Savoring	0.015/0.048	0.004/0.019	p < .001	p < .001
Positive Social Sharing	0.009/0.026	0.016/0.027	p = 0.003	p = 0.004

*Underlined are the significant Effect size (ß); EV = Explained variance; TV = Total variance; *p < 0.05; **p < 0.01; ***p < 0.001.*

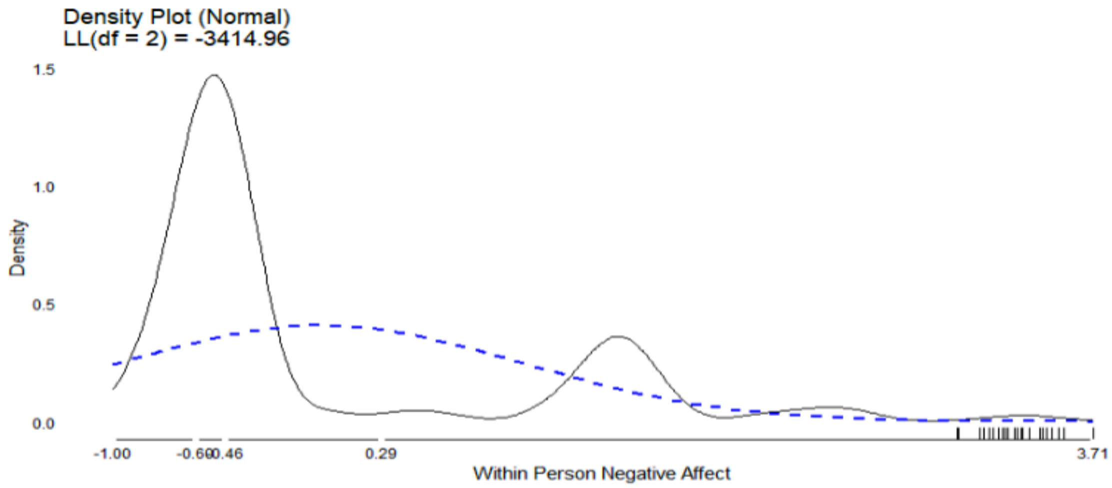
Table 7 Results of Multi-level structural modelling. Effect size (ß) (Random only) for between and within subject for each type of questionnaire.

Variable	Effect Size (Random only) (ß)		p-value	
	Between subject	Within subject	Between subject	Within subject
	EV TV	EV TV		
Negative experience	-0.001/0.044	0.001/0.010	p < .001	p = 0.03
Intensity	-0.001/0.042	0.001/0.013	p < .001	p = 0.01
Rumination	-0.002/0.050	0.000/0.011	p < .001	p = 0.03
Reappraisal	0.006/0.154	0.000/0.000	p < .001	p = 0.32
Negative Social Sharing	0.000/0.08	0.006/0.153	p < .001	p = 0.49
Positive experience	-0.001/0.022	0.001/0.009	p < .001	p = 0.008
Intensity	-0.001/0.024	0.001/0.013	p < .001	p = 0.009
Savoring	0.001/0.029	0.002/0.012	p < .001	p = 0.02
Positive Social Sharing	0.001/0.019	0.001/0.006	p = .003	p = 0.004

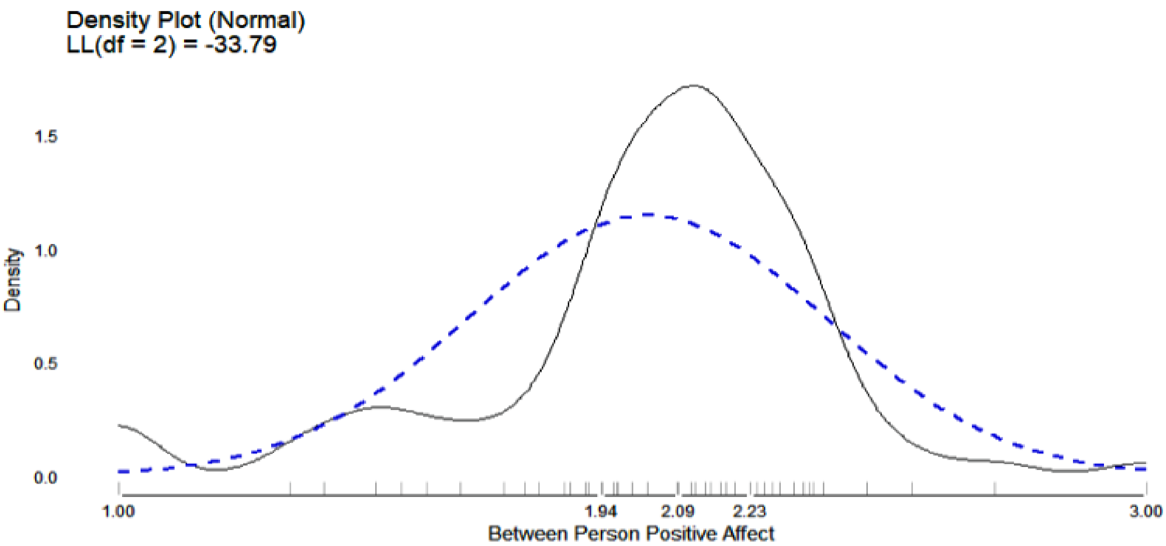
11.1


Density Plot (Normal)
LL(df = 2) = 2.66
Density
1.5
1.0
0.5
0.0
1.00
1.39
1.51
1.64
2.00
Between Person negative Affect

11.2


Density Plot (Normal)
LL(df = 2) = -3414.96
Density
1.5
1.0
0.5
0.0
-1.00
-0.60
0.46
0.29
3.71
Within Person Negative Affect

11.3


Density Plot (Normal)
LL(df = 2) = -33.79
Density
1.5
1.0
0.5
0.0
1.00
1.94
2.09
2.23
3.00
Between Person Positive Affect

11.4

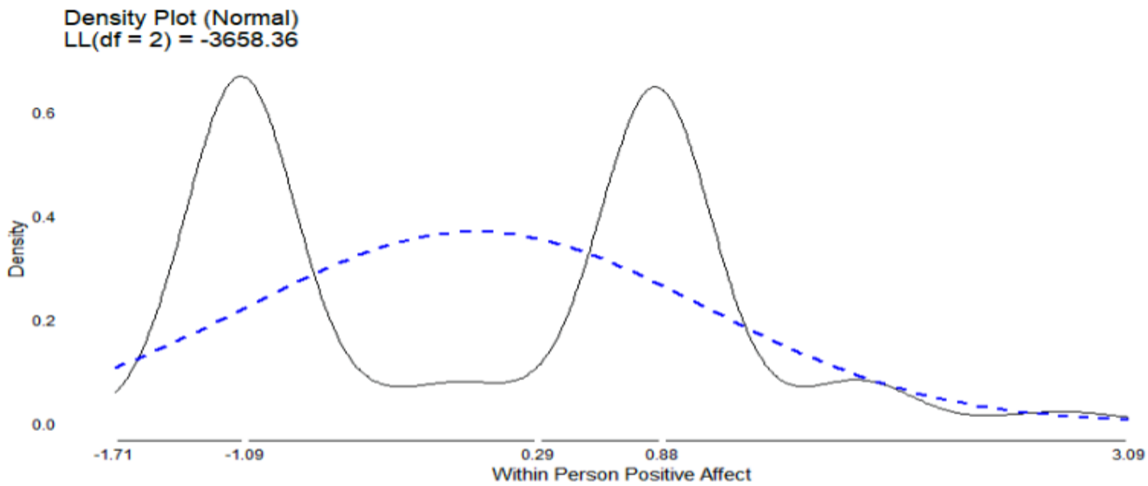


Figure 11 Distribution of between and within person negative (Panel 11.1 and 11.2) and positive (panel 11.3 and 11.4) affect (the two broad event categories from the survey).The graphs show parameter estimates, log likelihood (LL), density plot in black lines, a normal distribution in dashed blue lines, a rug plot showing where individual observations fall, and the x-axis is five options of the question (minimum - 1, first quartile - 2, median - 3, third quartile - 4, maximum - 5).

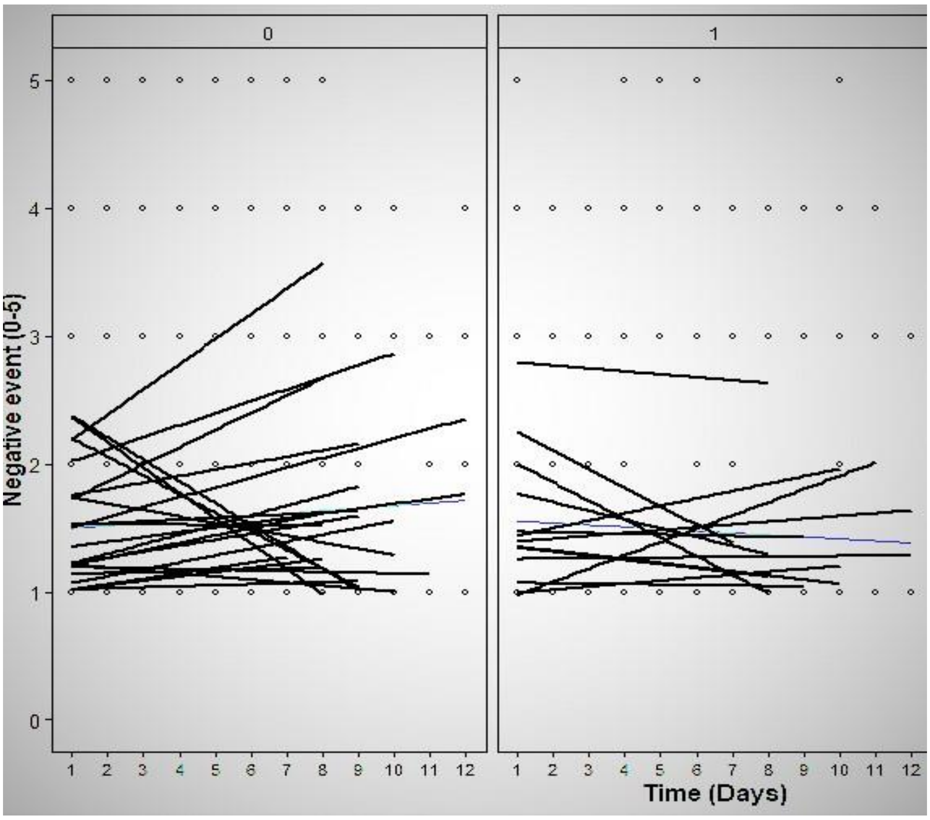


Figure 12. A random intercept, fixed slope representation of thirty-five participants for negative event category with respect to days of the study. 0 -Females; 1- Males.

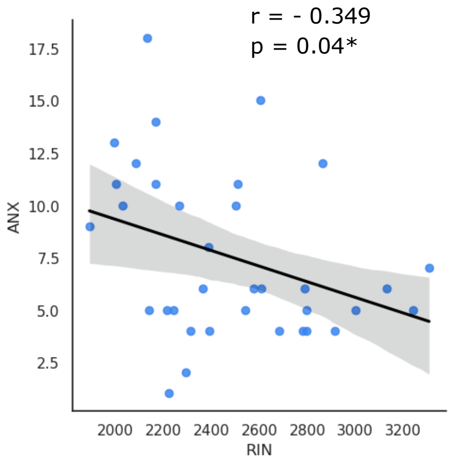
The results of MSEM were fitted by restricted maximum likelihood(REML). The results were obtained in two parts – Between-subject and within-subject for both categories : Negative (Negative experience, Intensity, Rumination, Reappraisal and Negative social sharing) and Positive (Positive experience, Intensity, Savoring and Positive social sharing). Table 6 summarizes the results with between and within-subject effect size (ß) with two values (Equation 4).

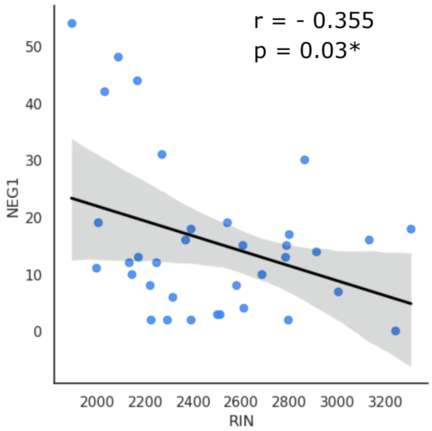
$$\boldsymbol{\beta = \text{explained variance}/\text{Total variance}} \quad (4)$$

Combining the random and fixed effects and p-value. All the variables were positively significant between subjects (Days as a fixed effect), meaning there were correlations with the days of the study when intercept and slope were the fixed and random effects e.g., Negative event (ß **=** 0.02; P<0.001). However, some crucial differences were observed within subjects (RespDay as a fixed effect) where except for negative intensity, the remaining four variables in the negative event category were not significant where all the variables for the positive event category were significant with immense variation within a single subject e.g., Positive event (ß **=** 0.39; P<0.001). It was observed that for the effect size for days as random effects only, broad categories : negative event (ß **=** -0.02; P<0.001) and positive event (ß = -0.04; p<0.001) were negatively associated between subjects (Table 7). Similar characteristics were observed in negative intensity and rumination as well. Reappraisal and social sharing were insignificant within subjects when the effect size was random only. It is important to note that, although they were significant, the effect size for savoring (ß **=** 0.03; p<0.001)and positive social sharing (ß **=** 0.05; p= 0.03) was minimal (Table 7). Furthermore, negative event was significant in within subjects unlike in Table 6. There was no change in the effect size for intensity, rumination, reappraisal, and negative social sharing. Positive event category showed a decline in the effect sizes but were still significant at the order of p<0.001*** The model was first fitted for random intercept and fixed slopes which means with every increasing level, the intercept changed giving different means of dependent variable but the relationship between DV and IV remained the same for all subjects (Figure 12). The intercept is calculated for each person and the slope is for entire study. Second, the fitting with both intercept and slope as random, which means both intercept and slope were calculated for each person.

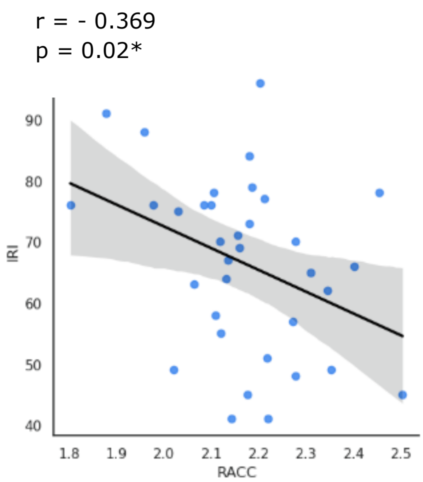
3.5 Correlation between ROI – Behavioral - ESM

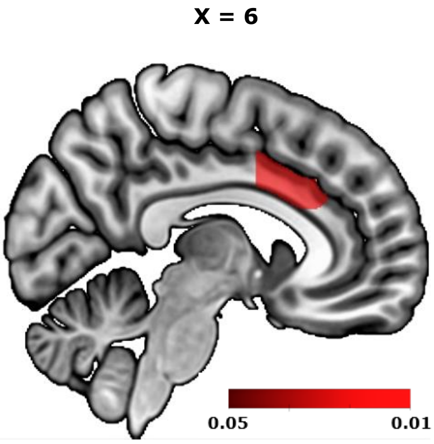
The 3-stage correlation was consistent with the literature, a negative correlation was found between Insula area and HADS anxiety scores among participants (r= -0.349; p = 0.04*). Contrastingly, after multiple comparison of empathy with various other brain region measures, a negative correlation was found between the cACC thickness and empathy scores of participants (r = - 0.369; p = 0.02*). Interestingly, a positive correlation was found between amygdala volume and anxiety (r = 0.320; p = 0.05) and the resilience scale had only significantly correlated with medial-orbito frontal cortex, negatively (r = -0.485; p = 0.003**). A strong positive correlation (r = 0.458; p = 0.006*) was observed between anxiety scores and negative events questions and, as expected IRI scores were positively correlated with positive events (r = 0.376; p = 0.02*). Additionally, PSS showed only one significant positive correlation with negative events from the survey (r = 0.360; p = 0.03*) and no other viable results were found. The insula area was also negatively correlated with the negative events questions from the survey (r = -0.355; p = 0.03*). Similarly, cACC was correlated with positive daily life events, resulting in a negative correlation (r = -0.377; p = 0.02*).Apart from these findings no other correlations were found between mOFC, amygdala and other daily life measures. The brain ROIs were used in the mediation models - to examine the cause-effect relationship after identifying the potential strength of significance between these variables.

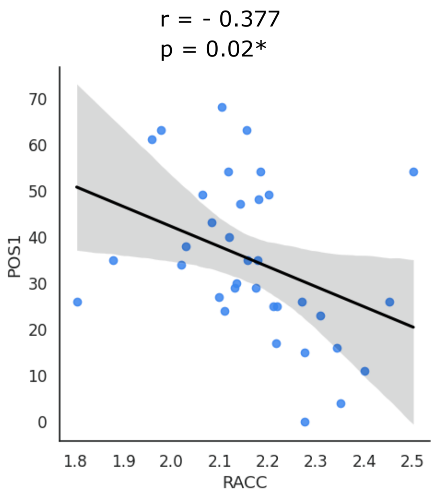




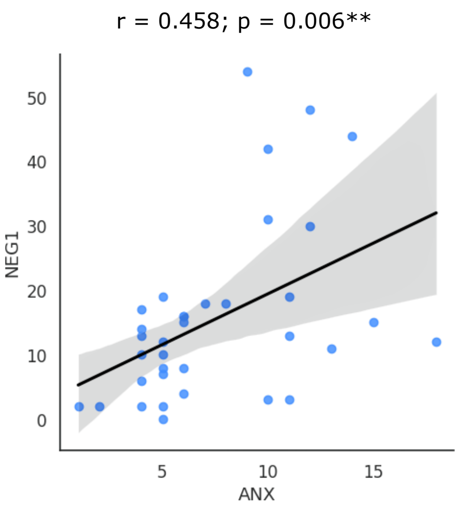
13.1 **13.2** **13.3**



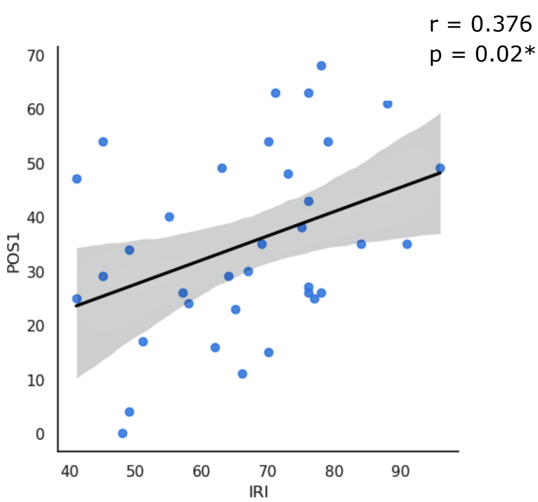




13.4 **13.5** **13.6**

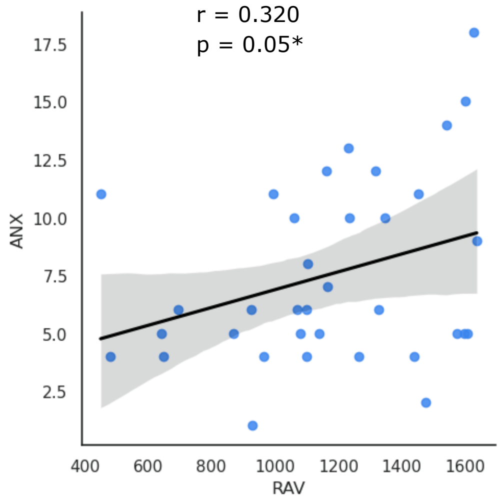


13.7



13.8

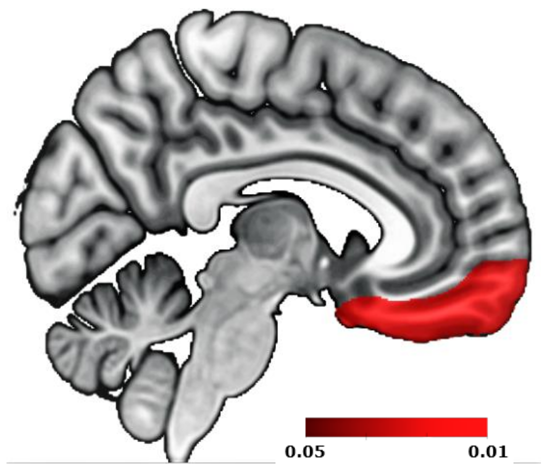
Y = - 3

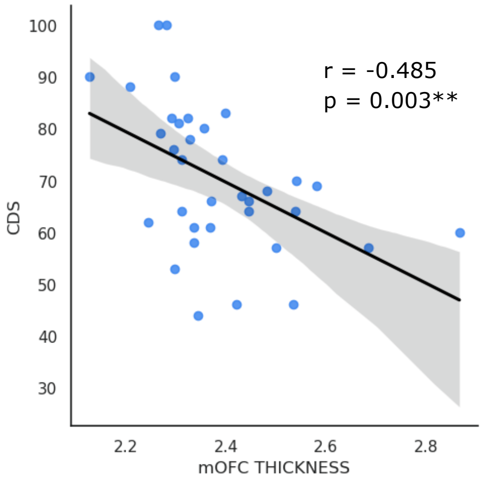


13.9

13.10

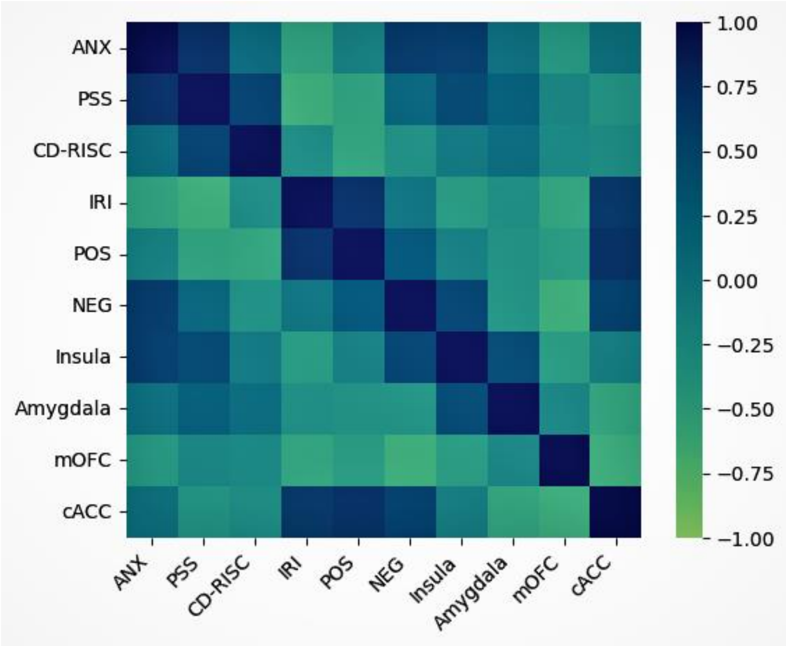
X = - 7





13.11

13.12



13.13

Figure 13 Statistically significant associations between. 13.1. Insula (RIN) – Anxiety (ANX); 13.2 Insula MNI Freesurfer; 13.3 – Insula and Negative events (NEG1); 13.4 – caudal anterior cingulate cortex (RACC) and Empathy (IRI); 13.5 – caudal anterior cingulate cortex, MNI Freesurfer; 13.6 RACC and Positive events (POS1); 13.7 Anxiety and negative events; 13.8 Empathy and positive events; 13.9 Right amygdala volume MNI Freesurfer; 13.10 Right amygdala volume (RAV) and Anxiety (ANX); 13.11 medial-Orbito frontal cortex (m-OFC) MNI Freesurfer; 13.12 medial-Orbito frontal cortex (m-OFC) and Resilience scale (CDS); 13.13 Correlation matrix, obtained from Python.

NB: All correlations are corrected using False discovery rate by adjusting the p-value – computed by R p. Adjust function; Brain images obtained from MRIcroGL SPM152, highlighted manually representing p-value gradient; X and Y are MNI coordinates.

3.6 Mediation analyses results

Based on the descriptives, significant correlation matrix and structural measures, mediation analysis was performed to explore further whether brain ROI directly affects daily life emotional events or indirect effects where behavioral results function as a mediator. A simple mediation model was built to assess the magnitude and strength of variables affecting each other. The correlation results suggested four different models are possible to observe the direct effect (Brain ROI – ESM) and indirect effect (Brain ROI to ESM via behavioral data). This section reports two models based on the order of strength of correlation. The variables assigned as IV, DV and Mediator were per the study objective to see the indirect effects of personality traits over Brain and ESM. For Model I, the independent variable (X) was insula area, dependent variable (Y) was negative events in daily life and mediator (M) were HADS-anxiety scores. Similarly, for Model II, the X was caudal anterior cingulate cortex, Y was Positive events in daily life and M were IRI-scores. Age and education were regarded as covariates in all mediation analyses. As expected, Mediation analysis I showed that anxiety mediates the relationship between insula area and negative life-events (path a = - 0.34, p = 0.01; path b = 0.38, p = 0.02; path ab = -0.35, bootstrapped 95% CI = -0.01, -0.0002; (Figure 14). For mediation analysis II, it was seen that IRI does not mediate the relationship between cACC and positive events (path a = - 0.3, p = 0.01; path b = 0.2, p = 0.1;

path ab = -0.3, p = 0.02; Bootstrapped 95% CI = -32.1790, 1.0856; (Figure 15). NOTE: As stated, two more mediation analysis were conducted but due to lower strength of correlation, those analysis were not significant and could not survive this analysis, hence are not reported in this section. Detailed analyses of all the processes can be found in supplementary section 8.5.

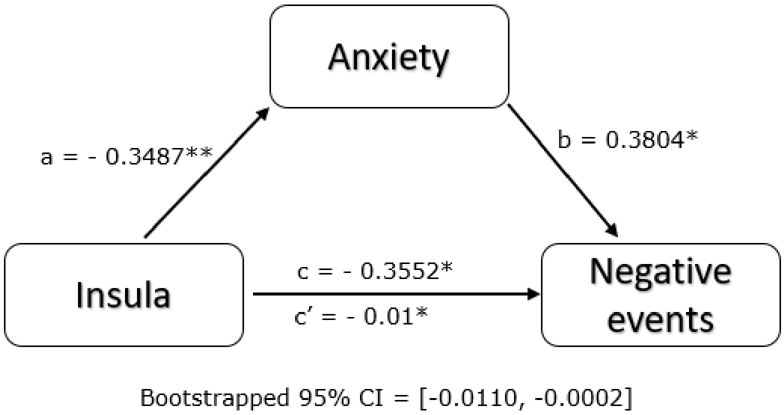


Figure 14 Mediation analysis between Insula, Anxiety and Negative events. Paths a, b, and c′ are statistically significant (bootstrapped 95% CI: -0.01, -0.0002). The mediation results suggest that anxiety **completely mediates** the association between insula and Negative events. *p < 0.05; **p < 0.01; ***p < 0.001.

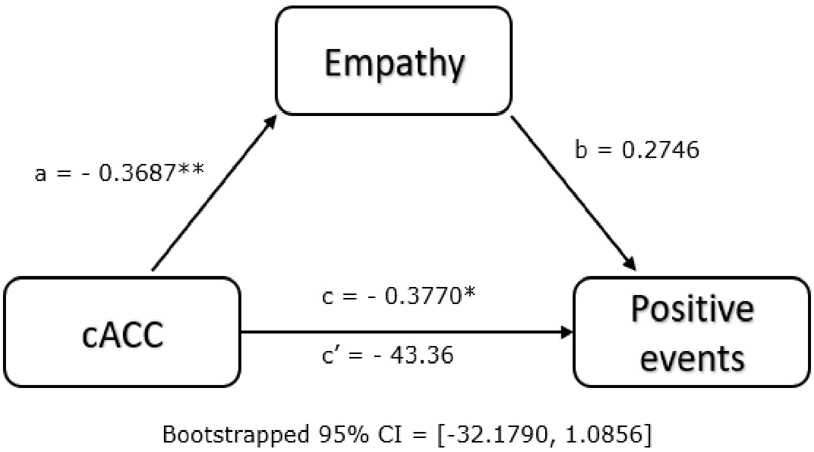


Figure 15 Mediation analysis between caudal Anterior Cingulate Cortex, Empathy and Positive events. Paths a, b, and c′ are not statistically significant (bootstrapped 95% CI: -32.17, 1.08). The mediation results suggest that IRI **does not mediates** the association between cACC and positive events. *p < 0.05; **p < 0.01; ***p < 0.001

4 DISCUSSION

Following the first two research objectives, this thesis investigated the influence of anatomical brain data (CT, SA, and Volume) over emotional experiences during daily life, indirectly through emotional and well-being health measures in a sample of healthy young adults. Behavioral and ESM scores calculated from self-reports and daily surveys were combined with anatomical statistics through a correlation matrix to establish the relationship between these variables. This step formed the basis of ordinary least square analysis (OLS) regression-based mediation analysis to examine the cause-effect relationship. The third research objective was to evaluate the reliability of MSEM analysis for the ESM study design. This section will first discuss and justify the results from sMRI, behavioral and ESM data separately and will finally bring the triad together to support the aims of this thesis.

4.1 View at the Brain anatomy

To obtain an accurate brain extraction after T1w pre-processing is one of the most challenging tasks. Brain extraction means removing the unwanted skull and meninges from a T1w input image to get the correct anatomical data such as CT, SA, and volume measurements (Puccio B et al., 2016). The execution of this step generally occurs within an algorithm pipeline, irrespective of the software used. Apart from Freesurfer, there are two other platforms, Statistical Parametric mapping (SPM) and volBrain which provide promising structural statistics as Freesurfer. However, the CT, SA, and volume steps in Freesurfer outperform the other alternatives in terms of robustness due to two main reasons a) unlike volBrian and SPM, Freesurfer uses surface-based rather than volume-based registration to create WM segmentation then tessellate the mesh to find both GM and WM. This tessellation provides the opportunity to quickly find topological errors such as skull strip, abnormal intensity etc., which are visible in Freeview and can easily be rectified. In contrast, Voxel-based registration gives one segmentation output and creates thickness measures from the same, which limits its ability to detect errors and can provide false CT or SA data (Clarkson MJ et al., 2011). b) The regularization method and optimization strategy used by Freesurfer provide superior and more accurate structural results. This is due to its separate registration of cortical thickness and cortical folding like gyri and sulci for in order to avoid mistaking two adjacent gyri into a single structure which can certainly lead to higher SA data then the true measure (Klein A et al., 2009; Rajagopalan, V et al., 2015). Although all these methods use General linear model (GLM) for primary analysis, results from Freesurfer can better fit the model as its robustness is maintained despite using different scanners and field strength (Clarkson MJ et al., 2011).

Given the varied genetic influence over the development of CT and SA not just in humans but across species, it is established that these measures are local properties of a region and should therefore a region-specific analysis be needed (Rakic, 1995; Panizzon et al., 2009; Lemaitre et al., 2010; Winkler et al., 2010; Eyler et al., 2011; Håberg AK et al., 2018). It is important to note that MRI data obtained from Freesurfer provided separate CT, SA, and Volume of each of the thirty-six regions from the atlas. However, only **four** ROIs were eventually picked for further analysis: Insula area, thickness of cACC and mOFC and Amygdala volume. This was done due to **three** reasons **a)** Location of these areas which demanded the need to prioritize area over thickness and vice-versa (Raznahan et al. 2011; Shaw et al. 2012), **b)** The unique role of these areas over various emotional experiences such as anxiety, stress, resilience, and empathy in a life of a healthy young adults and **c)** These measures showed statistically significant relationship with self-reports and ESM study data as shown in Figure 12 and detailed in Section 4.4. Finally, the ROI measures in this study were normally distributed as all four had $p>0.05$ in Shapiro wilk test. Our cohort of 18-35 years showed normal age specific measures with Insula area, cACC thickness, mOFC thickness

(Raz et al., 2004, 2010; Spreng et al., 2010). The Amygdala volume showed rapid increase with age right from early adulthood to mid-life (Russel JD et al., 2021).

4.2 A Psychopathological perspective

Self-reports have made statistically simple documentation of positive e.g., Empathy and Resilience (Wagnild & Young, 1993)and negative e.g., Anxiety and Stressful emotional states. Studies have used brain structural data such as CT, SA and volume and test results to compare symptoms, effects, and assess a personality trait of an individual (Lerch et al., 2017; Hilland et al., 2020). These results show crucial linkages between brain areas and emotions associated to those areas or networks. In this thesis, I simultaneously analyzed the positive and negative personality traits for young adults through preliminary tests such as test of normality and one sample t-test to validate the responses then Bivariate correlation was performed (Section 4.4). For positive traits: empathy and Resilience, the scores were above the normal range; higher the score, the more empathetic and resilient the individual was. Empathy scale also had sub-scales Perspective talking, Fantasy scale, Cognitive empathy, Empathetic concern, Personal distress scale and Emotional empathy. None of the subjects had lower scores in these areas except for personal distress revealing the overall higher empathetic response in the individuals. Given that cohort was healthy, these results suggest that the participants in the study carry high positive trait value (Waddimba AC et al., 2021). For the negative traits: Anxiety and stress, the scores were above the normal range but not extreme as per the rules of questionnaires used. Being above normal may suggest that younger individuals experience higher anxiety and stress as a trait due to their current lifestyle and various other factors in life such as physical toll of diseases, financial distress, concerns about the future, and career. It is worth mentioning the effect of a large-scale SARS-CoV-2 pandemic (COVID-19) which led to drastic changes in people's lives across the globe (Li et al., 2020; McGinty et al., 2020; Pierce et al., 2020; Hetkamp et al., 2020). This was one of the reasons to employ multiple self-reports of the above four personality traits in this study and compare the trait results with state i.e., evaluating similar emotions in their daily lives (section 4.4). Nevertheless, these results suggest that the overall psychological well-being of the participants was in the normal range, with no evidence of abnormal behavior or physical symptoms were found during the course of the entire study.

4.3 Evidence from daily life experiences

The use of daily life experience sampling aimed to capture momentary emotions and experiences on a daily basis in the lives of healthy young adults. At the end of the survey session, the study yielded an overall compliance rate of 79% as reported by other studies (Rintala et al., 2019; Soyster et al., 2019). Our results supported the notion that the compliance rate does not decreases as the investigation progresses (Soyster et al., 2019) however, a diurnal pattern was found which is participants tend to miss the early morning surveys as compared the mid-day or evening ones (Courvoisier et al., 2012; Rintala et al., 2019). To counter this missing data, subjects had a slightly extended response time window for the first survey (e.g., Ben-Zeev et al., 2009). Although this step did not work in case of no event/no response, those questions were removed from the analysis. As the results were accumulated (Table 5), the responses were divided into two categories : Negative event (NE : 1.5; 33.07%) and Positive event (PE : 2.12; 23.37%). Each category had different strategies where NE had - how intense was the event - intensity, How negative did they feel after 2 hours - Rumination, Did they find anything positive in that negative event – Reappraisal and did they share this with someone – Negative Social sharing. These strategies are a representation of daily life nervousness, irritation, concerns, and distress (Armey et al., 2015). Intensity, Rumination and Reappraisal were based on a 7-point scale. The means and percentage use of these measures reveal that on average the cohort did not experience high intense negative emotions during the survey duration.

The average intensity and rumination out of seven were low meaning even if the event was intense, the subjects neither rated high intensity nor did they felt its effects after a time had passed. Intensity as a strategy was observed the most in the negative event category, but this only means how much the subjects rated their feelings and not the feeling itself. However, comparing the means of rumination and reappraisal suggests that despite the lower intensity, rumination was higher than the other both on mean and percentage use of strategy. Persistent effect of the event may undermine positive feelings and enthusiasm (Heininga & Kuppens, 2021). It can be an underlying reason for the development of borderline anxiety and stress higher than normal in the cohort, as a characteristic of mood disorders (Myin-Germeys et al., 2009; Peeters et al., 2003). On the other hand, PE reflected the daily feelings of enthusiasm, good relations, productivity and positive life changes (Watson & Clark, 1998). Strategies in this category were - how intense was the event – intensity; How positive did they feel after a time had passed – Savoring and did they share this with someone – Positive Social sharing. The means and percentage use for Intensity and savoring were similar. Both suggest that the individuals not only rated higher but also had a persistent positive effect after that, despite overall lower response of Positive event questions then negative event. This also points out that unlike NE where an average of 1.5 would mean something happening to no event happening, the average of 2.12 in PE would mean a low intense event to occurrence of some event (option provided as other). Overall higher use of PE over NE typically would be a response of positive attitude, meaningful events, happiness and most importantly healthy stress (Cohen & Pressman, 2005; Fredrickson & Losada, 2005). During the occurrence of an event, it was found that participants used both NE and PE to respond to the same event suggesting the co-existence of both where Positive attitude can impact the rumination and negative intensity into lower scores (Sin et al., 2015).

Taken together, these findings implicate the need to overcome an unpleasant experience i.e., to be more resilient, and savor the good moments but also to result indicate such experiences can have long-lasting effects on an individual's day-to-day life (Table 5). Previous research has explored the between-person variability and interactions (Yearick K, 2017; Nezlek et al., 2002; Pinquart & Sorensen, 2000), whereas this study took a step further to evaluate the within-person variability and reliability as well due to the momentary nature of ESM. Shrout (1998) suggested a criterion to categories the reliability values as 0.00–0.10, virtually no reliability; 0.11–0.40, slight; 0.41–0.60, fair; 0.61–0.80, moderate; 0.81–1.0, substantial; >1, high. Both between and within-person reliability were calculated for both the broad NE and PE emotional categories. As per the results, all the strategies including NE & PE had a higher reliability then 0.8. For NE, intensity (within 1.5; between 1.5) and rumination (within 1.47; between 1.44) had the highest value >1 meaning the data varied both between and within-person reflecting high consistency in the responses and complete true variance. For reappraisal, the reliability was less than 1 but in moderate category as per the scale. For PE, both intensity and savoring demonstrated higher validity of the results with higher reliability and estimate of true variance within and between-individuals. Between persons negative social sharing was lower than within person indicating a fair to moderate effect yet individuals tend to not share a NE, which is also proved by the fact that both the variables were >1 in positive social sharing. As stated in the previous paragraph that the overall mean of PE was higher than NE, the trend was followed in the case of reliability as well, revealing higher degree of fluctuations of positive emotions. These measurements clearly indicate the overall validity of the ESM and overcoming the limitation of previous studies, which assume the responses each day or each time from each participant are independent (Nezlek, 2001; Verhagen SJ et al., 2016; Habets P et al., 2022). Observations from different surveys, days, time are not independent, as they are provided by the same person hence higher estimates of variance in each category provides evidence for the same. The following section discusses the results to resolve the complexities, coherently.

4.3.1 Does MSEM explores the true Hierarchal nature?

In the present model, all three levels i.e., Observations (Level 1), Subject (Level 2) and Days (Level 3), had at least one random effect. The model was first fitted for random intercept and fixed slopes. With every increasing level, the intercept changed giving different means of dependent variable since the responses are not independent (Evan M., 2017). However, the relationship between DV and IV remained the same for all subjects (Figure 12).

This step formed the basis for calculating the effect size between and within-subject responses. This overcomes two main challenges a) to identify the variation at each level of the study as there is lack a of evidence to quantify this step in previous research, and b) Since effect sizes are measured for clinical significance rather than statistical significance, this provided valid results which can be meaningful in clinical practice as effect size is dependent on population and should therefore be clinically meaningful (Cohen, 1988; Oleson et al., 2019a). Between subject effect sizes were all significant at the order of $p<0.001$ for both NE and PE (Table 5) for the all the strategies used in the survey proving that there is a large fluctuation in emotions and differential variance in the responses between individuals when the both fixed (subjects) and random effects (Days) were allowed to vary. Related results were seen in PE and all its strategies for within-subject effect size. In contrast, for within-subject NE the variance was not significant leading to fewer fluctuations in negative emotions (Table 6). This could indicate that the subjects did not experience high degree of NE during a given day and the entire study, which is also supported by the lower reliability and mean for NE, as stated in the previous section.

On the other hand, when the random effect was only allowed to vary between subject at level 3, the Effects size for NE and PE was statistically significant ($p<0.001$). Still, it was in negative order, and for the strategies. This, however, reduces the clinical significance in a way that when fluctuations in emotions are only accounted for days, they appear to be stable or extremely low (e.g., Reappraisal ß = 0.003). This contradicts the fact that the participants in the study had higher than normal stress and anxiety scores on self-reports and a higher mean and percentage use of strategies. The flaw in this process was filled by estimating the effect size within individuals varying across days which provided significant and positive order ß for both NE and PE along with their sub-scales indicating more substantial discrepancy in the data. Furthermore, for Reappraisal and negative social sharing, the SE was extremely small and was not significant within individuals (Table 7) indicating if there are any fluctuations in these emotions, it is not noticeable. This can be explained by the fact that this thesis had a smaller sample size of thirty-five, study duration of 7 days and higher rate of no response to some survey questions in the negative event category posing a limitation in the design. Maas and Hox (2005) found that a sample size as low as twenty is sufficient for estimations of variance and reliability but a small size at within-person level where one random slope is easily measured, more complexity cannot be estimated (Newsom, 2002; Kenny & Kashy, 2011). Although the significance level and other measures in this ESM study is high and provide ample information about the emotional fluctuations or variations in the given sample size, some changes are recommended. For example, the fundamentals of MSEM are based on its ability to determine within and between level covariance, to achieve the full strength of MSEM, a sample size of at least fifty should serve the purpose (Hox et al., 2010). Limitations posed by the small sample size with respect to sMRI and self-reports are discussed in section 6.

Furthermore, unlike the single level, the effect size is rather complex to estimate and understand in multilevel models. The variance needs to be estimated at each level. ESM analysis in the past (e.g., Raudenbush & Bryk, 2002; Snijders & Bosker, 1999) demonstrated this by simply reducing the variables at each level and it does not explain the negative variance as reported in this study. Several solutions were proposed to overcome this problem, but that in turn had their own flaws (Roberts et al., 2011). This thesis tried to solve one of the issues but adding the slopes at each level rather than reducing, however another limitation of negative variance in this thesis can be achieved by the concept of grand mean centering of predictors could help is explanation of this step as proposed by Hox (2010). A major issue still to be resolved in a hierarchal design structure is the incomplete data i.e., questions needing to be answered or being missed. Although MSEM combines the standard equations of MLM and SEM, it still lacks the flexibility to estimate a desirable missing data methodology. A crucial reason behind this is thought to be the bias of response style i.e., repeated time-contingent surveys create similar responses to all questions among participants (Baird et al., 2017; Nestler et al., 2021). A relatively large sample size can eliminate this bias with the statistical power to detect and explain all variations in effect size (Brose A et al., 2020).

Regardless of these limitations, the MSEM design used in this study evaluated the strength of effect sizes of daily emotions by assuming the homogeneity in both the between and within individual level which is relatively new and was a major drawback in past ESM (Geldhof et al., 2014; Nezlek, 2016). The density and normal distribution of distinct levels of study were represented using maximum likelihood procedure (Figure 10) (Hamaker et al., 2017) which revealed the diverse nature of the daily life emotions. This step cannot be computed using a traditional MLM or SEM (Van Buuren, 2011). A study by Hayley and Robert, (2018) reportedly use MSEM in their cannabis study to evaluate changes in behaviors at various levels and validated its use in modern ESM. As evidently described, MSEM is extremely valuable in a complex structure paradigm and has the ability to detect even the smallest change or fluctuation in emotions leading to exceptional reliability of data (e.g., Conner & Barrett, 2012; Ganzach & Yaor, 2019; Neubauer et al., 2020). Together with these strengths, discussion on the reliability and variance , and possible limitations, MSEM has been proven to be a valid statistical tool in identifying and interpreting the clustered hierarchal nature of ESM which provided crucial information on the daily life experiences of emotion in our young adult community.

4.4 Identifying the Relationships

4.4.1 Brain and Psychological Well-being

This Thesis's final and most important aim was to investigate the relationship between brain ROIs, self-report measures and ESM. The study examined the inter-variable effects by employing a series of tests and statistical methods in each of these sections, then through combinatory assessments. As mentioned in the introduction, the studies on brain structure and behavior associations have fundamentally observed them with localized lesions or behavioral deficits (Genon, S et al., 2018). This study explored these patterns in the healthy population with neuroimaging technique and self-reports. The findings from thirty-four brain region's CT, SA and volume suggested significant relationships mainly between four measures of the brain namely Insula (area), cACC (Thickness), mOFC(Thickness) and Amygdala(Volume) with the four personality trait questionnaires across the cohort. It was found that insula and amygdala had a significant relationship with HADS – anxiety where it was negatively correlated with the former and positively correlated with the latter. Several research have emphasized the role of insula and amygdala in managing anxiety proneness and processing in normal individuals (Critchley et al, 2004; Paulus et al., 2005; Stein et al., 2006; Alvarez R P et al., 2015). The positive correlation between amygdala and anxiety indicates higher anxious individual have a larger amygdala volume which explains its heightened activity during anxious stimuli, untreated GAD activity and severity symptoms (Liu et al., 2015; Osuch et al., 2008; Wang et al., 2002). These results are also supported by studies in rodents and primates

(Iordanova et al., 2006). One study measured the amygdala volume between two groups of rats. Postmortem neurochemical analysis found lower anxiety had low ventral-striatal serotonin levels in the and significantly less volume of amygdala (Schwarting et al., 1998; Iordanova et al., 2006) functional analysis of amygdala activity has constantly been found to be high in anxiety related tasks or studies (Kalin et al., 2005; Jensen et al., 2003; Essau at el., 2014). The negative correlation between insula and anxiety revealed that more anxious individuals had a smaller insula, evidence of which are both for and against this finding. A study found larger insula in GAD patients compared to healthy individuals, revealing remarkable role of insula in social anxiety disorders (Klumpp et al., 2013; Atmaca et al., 2021). Studies on aging have shown equivalent results where older adults with high anxiety had a smaller insula (Potvin et al., 2015) however Qi et al., (2014) suggested a larger insula in various anxiety related measures. Normal aging is associated with reduction if PFC and insula (Fjell et al., 2013; Good et al., 2001) thus, it is possible that the insula-anxiety association may alter drastically as we age. Contrastingly, a larger group of studies have suggested otherwise that higher anxiety positively correlates with higher insula activation, signaling and size. (Nagai et al., 2007; Shah et al., 2009; Brooks and Stein, 2015; Albacete A et al., 2019). Healthy individuals shown to have enhanced activity in the insular cortex in humans suggesting a turn in the understanding of insula and its role.

Furthermore, I found a negative correlation between participant's cACC and empathy (IRI) scores. cACC and its connections with amygdala are known to be the underlying pathway for empathetic response. This is mainly due to the high activity of oxytocin on cACC which drives helping behavior (Etkin A et al., 2006; Bissière et al., 2010; Jhang J et al., 2018). A smaller cACC thickness was associated with higher scores on personnel distress and emotional regulation (Eisenberg et al., 2010) suggesting lower CT of cACC could lead to higher empathetic individuals in this study. While our structural results, as mentioned in this study using T1w were able to better differentiate between high or low empathy scores compared to a study on resting state fMRI by Uribe C et al. (2019), which did not show such effects. However, research based on resting state and task-based fMRI have revealed higher activation of rostral and caudal ACC when a person engaged in empathy-related behavioral tasks (Danziger N et al., 2009; Chang S et al., 2013). Another interesting finding in this study was lower thickness of mOFC was associated with higher resilience among individuals. A region-specific study with fractional amplitude of low-frequency fluctuations (fALFF) revealed that higher resilience is linked to lower fALFF activity in the medial and lateral OFC (Kong et al., 2018). However, a structural brain study by Shikimoto R et al. (2021) suggested mOFC to have higher thickness with higher resilience-based scores, the primary flaw in this study was the adaption of univariate analysis which has its drawbacks. This thesis had opposite findings by using a bivariate approach. Literature has documented the role of ACC (Kahl et al., 2020; Dickie et al., 2013), and amygdala (Gupta et al., 2017) in empathetic and resilience responses in healthy individuals but none of these results were found during analysis in this study. Moreover, considering these results ESM data was also taken into account for a better perspective.

4.4.2 Brain and daily life emotions

In the second part of relationship, ROIs were correlated with two broad categories of daily life emotions i.e., NE and PE. The results had two main findings: First a negative correlation was found between daily negative emotions and the insula, suggesting a greater area of insula leading to lower reaction of negative emotions i.e., although all participants had the same five options. However, how they react could lead to variation in their choices of intensity of the negative experience. The role of the insula in self-monitoring and assessing of emotions is well documented (David, 2012; Sperduti et al., 2011). Our results extended the current notion in identifying the relationship between insula and these emotions. In abnormalities like schizophrenia and psychosis, patients found greater difficulty assessing deviant stimuli due to hypogyral structural changes in the insula (Makris et al., 2006; Moran et al., 2013; Palaniyappan et al., 2013). The Second crucial finding in this context was a strong negative correlation between cACC and positive emotional experiences in daily life. The key role of posterior cingulate in the recognition of daily emotions in terms of happiness and satisfaction has been pointed out several times (Menon et al., 2020; Deen et al., 2011) however those results suggested a larger ACC with respect to positivity which was not found in this study. This could be explained due to the fact that participants in the study experienced more positive emotions than negative ones. The effect size discussed in section 4.3.1 revealed greater variation within negative emotions and higher rumination then positive events leading to less discrimination between the intensities of positive questionnaires. Hence lower thickness of cACC reported higher positive scores.

4.4.3 Self-reports and ESM

The third part of the analysis in the Bivariate correlation section was between behavioral questions and the NE and PE survey results. Here the thesis explored relationships between emotional well-being questionnaires and conventional situations which provided three main results with positive correlations in each category a) Anxiety and NE b) Stress and NE, and c) Empathy and PE. These results were consistent with findings in the literature. E.g., Younger participants experience more NE and subsequently rate higher intensity when they feel more anxious and are in distress. This could be due to high academic (Shi et al., 2016; Chin E et al., 2017) or non-academic pressure e.g., family issues (Allen et al., 2018). These results were neither in extremely high intensity nor demonstrated severe anxiety or stress which is a sign of a healthy individual. It is important to note that studies on patients with mental disorders have reported relatively higher levels of NE and its intensity (Kiff et al., 2018; Schleider et al., 2015). The significant relationship of PE with empathy found in our study is supported by another correlation study that has shown higher empathetic people have greater outlook, care for others and positive emotions in life (Morelli et al., 2015). Interestingly, Devlin C et al. (2014) showed that more positive emotions are indeed linked to higher self-empathy, but it tends to affect empathetic performance in daily life negatively. Furthermore, as reported by Holz et al. (2019), it was speculated that resilience trait would have connections with the question "How positive do you feel now after this negative event has passed," i.e., reappraisal but the positive correlation observed was not significant leading to inconclusive results.

4.4.4 Personality traits mediate the influence of ROIs on Daily life

To examine whether self-reported questionnaires mediate the relationship between brain and ESM, multiple mediation analyses were performed. Interestingly, the HADS anxiety fully mediated the association of Insula and negative emotions. Individuals with large insula tend to have lower anxiety, whereas higher anxiety leads to more negative reaction in daily life. Larger insula also had a negative impact on emotions, and finally anxiety indirectly mediated the relationship (Figure 13) concluding that high anxious individuals have a relatively smaller insula and tend to offset emotions in their lifestyle. This notion is also supported by study on perceived control in life with related results as reported by Alvarez et al., (2015). These results suggest that insula plays a crucial role in the emotional assessment of negative lifestyle and that structural morphology can help in significant predictions of aversive feelings with the help of anxiety related self-reports. Corroborated with previous findings, our results support the current understanding that insula directly orchestrates feelings of resentment in life (Xiaosi et al., 2013; Pavuluri et al., 2015). Another important relationship was that individuals with a smaller thickness of cACC have high empathy, whereas high empathy leads to more cheerful outlook. A less thick cACC also leads to higher positive emotions, however the hypothesis that empathy could mediate this relationship was not true (Figure 14). Indeed, the structural morphology of cACC could potentially affect trait empathy and daily life but this study found that it cannot form the basis of any predictions based on just structural measure or empathy cannot directly affect the relationship. As reported earlier, evidence regarding the role of cACC in managing positivity, awareness and overall empathy in life are growing and this thesis also contribute to this objective (Lockwood, 2016; Vogt BA, 2015). A significant indirect effect in the absence of direct effect could be due to multiple reasons such as length of ESM (James et al., 2006; Pardo & Román, 2013). It is possible that the total duration of the survey (7days) was insufficient as required to have a higher data establishing a direct effect. Another reason could be empathy as a domain is related to other functional associations in the brain and cACC alone could possibly be insufficient despite its stronger correlations. Furthermore, to extend the current findings from this thesis and previous work, two mediation analysis where it was hypothesized that a) resilience could mediate the effects of mOFC on reappraisal and b) Anxiety can indirectly play in role in relation between Amygdala and NE. Both results had a common shortcoming where no correlation was found between these ROIs and ESM, thus disproving that the traits as mentioned earlier could play any role in influencing and predictions. Nevertheless, recent studies have reportedly founded links between amygdala to real-world emotional experiences and psychological well-being (Puccetti et al., 2021; Burns & Ma, 2015).

5 LIMITATIONS & FUTURE PROSPECTS

The findings of this study pose some limitations. This section will highlight those limitations step-by-step and suggest potential future directions for each. First, one of the primary reasons for limited reproducibility is low statistical power which is mostly reported due small sample size. Due to relatively low participant sign-up for the ESM and high movement during sMRI (7T), a sample size was 35 out of the total 78, was analyzed in all the sections, which limited the ability to detect higher power. Lower power often causes problems like low positive predictive value as seen in the case for mediation analysis within the study (Button et al., 2013). It was found that sample size below 40 leads to lower replicability and to enhance the statistical power a size of 40 or above is recommended. A size of 100 and including more variables could generate lower overestimation of the effect size (Turner et al., 2018; Geuter et al., 2018). These suggestions could be considered by planning two sets of studies simultaneously a) an exploratory study to detect the potential effects and relationships within the variables and b) an estimation study to estimate those relationships more precisely by optimizing the sample size (Wilson et al., 2020). Thus, picking a larger size would have been appropriate to counter these statistical challenges in a much better way such as generalizability of the results and future studies pertaining structural measures, self-reports, and ESM i.e., a three variable analysis should take this into consideration. However, the cohort of this study was a younger population where age of onset of mental health measures begins, and hence structural brain changes are expected to be lower (Olabi et al., 2011). Second, no differences between males and females were observed in contrast to previous structural studies. This could be due to the uneven number between the two categories (13:22). Genetic influence on CT and SA due to cortical trajectories is different in both the genders and hence a future comparative study could have the potential to detect gender variation and its effects on behavioral data (Raznahan et al., 2011; Lenroot et al., 2007).

Third, this study supports the localizationist view that various emotions are not the due to one single brain region but are a product of functional connectivity between multiple regions. This however should not be perceived as a drawback of sMRI as it forms the basis for recognition of origin point of these connections. Nevertheless, using functional correspondence (fMRI) along with morphological data in further research methodologies could help identify the areas of overlap between structural and functional correlates within and between individuals. Moreover, the generalizability of inter-variable relationships (section 4.4) might not hold for clinical patients. This is because all the participants in the study were healthy with no history of mood disorders in the last five years. Future studies using fMRI should also investigate the measures from this study on healthy and affected groups for a better understanding of positive and negative personality traits with the support of structural data.

A fourth limitation of the study was to examine self-reported traits based on only self-reports. Although these are ecologically valid and provide a unique perspective on individual's overall behavior (Phelps et al., 2001), they cannot reflect upon state measures, or expression and can be biased due to social desirability (Devaux & Sassi, 2016). One way to counter this is to include a way to detect minute changes in individuals with anxiety and stress through an ESM, which was indeed the part of this study. Another way is to combine these self-reports with a comparative study between healthy and individuals with pathology and through personal interviews on emotional health with much deeper questions. A third way is the use of event-contingent momentary assessment which records daily fluctuations based solely on triggers that induce negative emotions such as experiencing a loss, huge fight etc. (Sindes et al., 2020). Inclusion of these could be beneficial in future studies to understand the affective dynamics in psychopathology and well-being.

Lastly, our ESM study comprised a 7-day time period with ten daily prompts. Considering time-contingency this was a requirement. Naturally, having missing data with such design is inevitable. This could be a plausible reason behind skipping surveys or no response to certain questions as such high frequency leads to participant burden and overall dropouts or failure to finish the study (Shifman et al., 2009). This also restricts the research ability to collect various kinds of mood changes in daily life. In the future, studies could offer more compensation to the participants for their time and include more personalized questions in the surveys to account for individual differences to incentivize and increase the effectiveness of ESM to its full potential.

Research on emotional well-being has drastically increased in the last few years. The use of newer technology has opened the field for more insights into fluctuations of daily emotions, what makes people happy in their day-to-day life and even hour-to-hour. This study benefitted from this momentary design. A wider range of questions that could assess cognitive well-being and help understand the intricate details of people's lives i.e., what influenced the emotion into being happy or sad could be included in diverse future ESM studies. A next bigger step would also be to include intervention methods along with recording fluctuations. A study developed in 2019 does this by asking participants to observe their environment and recall the positive things in that setting. The data has shown furtherance in well-being of individuals (McEwan et al., 2019). Furthermore, smartphone-based ESM studies are relatively new and come with some challenges. One major problem is the issue of privacy, as a huge amount of data is collected from participants including their emotional measures and sensitive information about their lives, the type of device they are using and phone numbers (Trull & Ebner-Priemer, 2013). Some mobile applications often record GPS and gyro meter information passively. This clearly violates participant's privacy and require further ethical approval. However, the rules of this study were strictly controlled, and no such data was gathered. Future studies should take this into thoughtful consideration and put efforts into selective screening for the application used and safe data storage.

6 CONCLUSION

Structural studies in understanding human behavior have mostly focused on integrating structural measures with personality under the mental health paradigm. Work that focuses on not just the traits but also momentary emotions that ultimately give rise to these traits, is relatively less. The instrumental areas of the brain manage and affect these daily emotions, as shown in this detailed three-variable study, which aimed to extend our understanding of human behavior from psychopathology to experiences of emotions in daily life.

It was found that the insula and cACC directly influence our daily negative and positive emotional feelings, respectively. Anxiety plays a crucial role in the relationship between insula and NE directly and indirectly. Higher anxious individuals have a smaller insula area and larger amygdala volume and appear to have more negative reactions in everyday life. On the other hand, empathy indirectly manages the associative characters between cACC and PE, where low empathetic participants experience less PE and show a thicker cACC. Although it cannot be concluded whether or not empathy has any direct influence on this relationship. In support for current literature, it was also found that resilience is thought to be primarily associated with thickness of mOFC; however, evidence to the contrary also exists, as discussed above.

As of the third research objective, MSEM has been proven to be the most reliable method for exploring the complex hierarchy of ESM by providing exceptional results and perspective which needed to be improved to account for within-person variations of emotions. The effect size (ß) was higher in almost all of the strategies within the NE and PE categories. In turn, this resulted in a high variance of emotions among individuals and within their day-to-day routines as well. All the recorded strategies in the study had moderate to high within and between-person reliability (ω) and mood fluctuations, emphasizing the need and power of MSEM analysis.

Furthermore, these results have made translating basic emotions into clinically relevant data possible, enabling us to interrelate brain and behavior effectively. Hopefully this could shed new light and provide future work with a better understanding of stratifying mental health disorders, targeting specific brain areas and their treatments.

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8 SUPPLEMENTARY

8.1 Freesurfer installation steps and codes.

The platform is suitable for Linux or Mac setups only. The following codes are for Linux system. You need to check the system requirements: RAM: 8GB for recon, 16GB suggested for viewing graphics. Size of installed image: 16GB. Typical size of a processed subject: 300MB. *Tip - If you are using the Dual boot system, assign at least 500 GB of space to Linux system for smooth processing.* You need to download the package – (Freesurfer - Linux). Click the latest version as per your Linux setup. For e.g., Ubuntu 22 Linux will support version corresponding to the same version number (either Tar or DEB can be picked). Installation for TAR archive - On Linux systems, if you do not have root/sudo privileges, you can expand the tar archive file (. tar.gz) under any convenient path/subdirectory on your machine you have permission to write to. For example, you can expand the tar archive under your $HOME directory. You can either follow the official Freesurfer step-by-step guide from here or you can follow the Andy's brain book from here Both are a fantastic way to learn. *Tip: Use Freesurfer's guide for step-by-step process's and refer top Andy' brain book to under terminologies, errors, and concepts in a much easier and better way. Make use of both and not just one.* After all the 3 steps. Open Terminal in your Linux system and run the following commands for step-by-step processing: All the commands are from the Freesurfer surface based pipeline as shown :https://surfer.nmr.mgh.harvard.edu/fswiki/FreeSurferAnalysisPipelineOverview

1. Call freesufer:

```
<> export FREESURFER_HOME=/home/avneeshj/Downloads/Freesurfer
<> source $FREESURFER_HOME/SetUpFreesurfer.sh
```

2. Once, opened, call the GUI interface of Freesurfer - 'freeview' which is used to visualize the data. To do this, run –

```
<>which freeview
<>/home/tester/Freesurfer/bin/freeview
```

3. Now we will call freeview again with following commands to open the first image. Here I am using my own data were:

   i. P1 is my – participant 1.
   ii. good_output is the name of the subject.
   iii. The flag -v is used to open some of the most commonly used volumes including:
      1. brainmask.mgz : skull-stripped volume primarily used for troubleshooting
      2. wm.mgz : white matter mask also used for troubleshooting
      3. aseg.mgz : subcortical segmentation loaded with its corresponding color table and at a low opacity.
   iv. The flag -f is used to load surfaces.
      1. white & pial surfaces are loaded for each hemisphere & with color indicated by 'edgecolor'

```
<>cd /home/avneeshj/Downloads/Freesurfer/subjects
<>which freeview
<> freeview -v
<>P1/mri/T1.mgz -v
<>P1/mri/wm.mgz -v
<>P1/mri/brainmask.mgz -v
```

<>P1/mri/aseg.mgz:colormap=lut:opacity=0.2 -f
<>P1/surf/lh.white:edgecolor=yellow -f
<>P1/surf/recon-all -all -subjid P62
<>rh.white:edgecolor=yellow -f
<>P1/surf/lh.pial:annot=aparc:edgecolor=red-f
<>P1/surf^Ch.pial:annot=aparc:edgecolor=red/bin/freeview

4. Recon all command is used to run the first pre-processing step. This can take 4-8hr. depending on your processor. Run this:

<>cd /home/avneeshj/Downloads/Freesurfer
<>recon-all -i /home/avneeshj/Downloads/Freesurfer/T1w/sub-XXXXX_T1w.nii -subjid PXX
<>recon-all -all -subjid PX -use-mritotal)

5. After the recon-all command is finished, lets visualize our results in freeview. Since similar commands are used all the time, its better to change the first half of the commands so we don’t have to type/paste the same code, to do that for your participant 2 for e.g.

<>cd /home/avneeshj/Downloads/Freesurfer/subjects
<>export currSub="P2"

6. Now just add the above before any command (by changing the P no. as per your data) to view brainmask -
<>export currSub="P2"
<>freeview -v $currSub/mri/brainmask.mgz -f
<>$currSub/surf/lh.pial:edgecolor=red
<>$currSub/surf/rh.pial:edgecolor=red --viewport 3d
The following window should open -

Image from Freesurfer terminal in Linux

7. To view Pial surfaces
<>export currSub="P2"

<>freeview -v
<>$currSub/mri/T1.mgz
<>$currSub/mri/wm.mgz
<>$currSub/mri/brainmask.mgz
<>$currSub/mri/aseg.mgz:colormap=lut:opacity=0.2 -f
<>$currSub/surf/lh.white:edgecolor=blue
<>$currSub/surf/lh.pial:edgecolor=red
<>$currSub/surf/rh.white:edgecolor=blue
<>$currSub/surf/rh.pial:edgecolor=red
The following window should open -

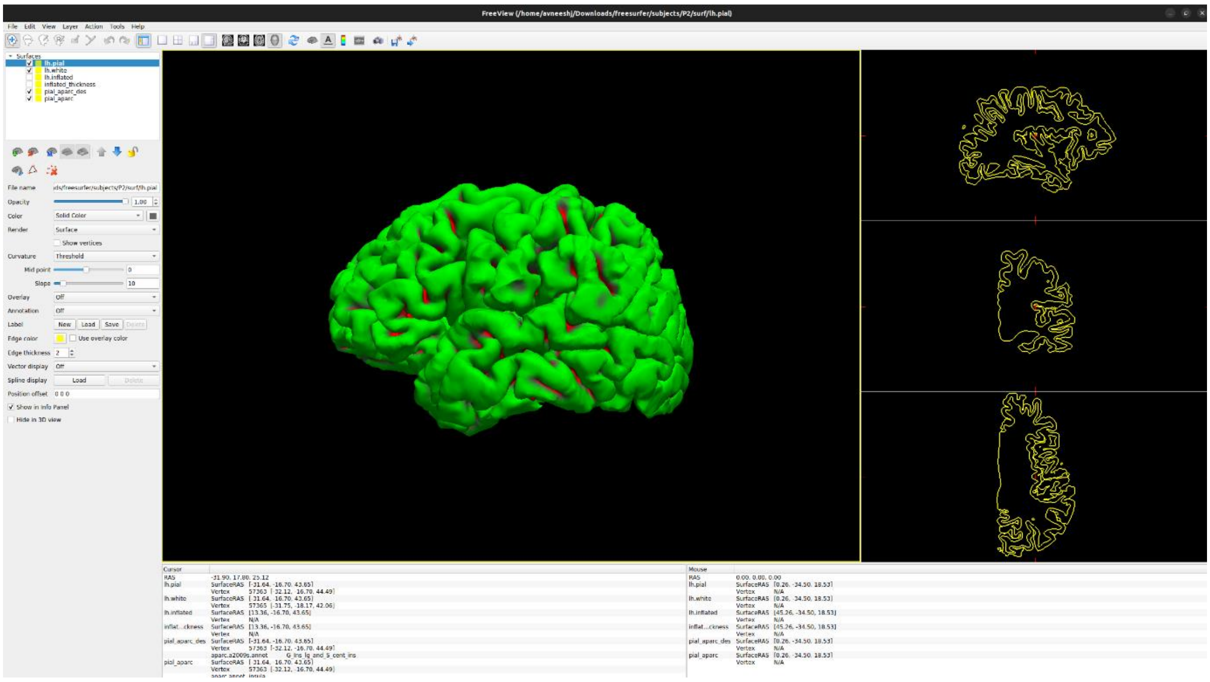


Image from Freesurfer terminal in Linux

8. To view the aparc and inflated surface
<>export currSub="P2
<>freeview -f
<>$currSub/surf/lh.pial:annot=aparc.annot:name=pial_aparc:visible=0
<>$currSub/surf/lh.pial:annot=aparc.a2009s.annot:name=pial_aparc_des:visible=0
<>$currSub/surf/lh.inflated:overlay=lh.thickness:overlay_threshold=0.1,3
<>name=inflated_thickness:visible=0
<>$currSub/surf/lh.inflated:visible=0
<>$currSub/surf/lh.white:visible=0
<>$currSub/surf/lh.pial --viewport 3d
The following window should open -

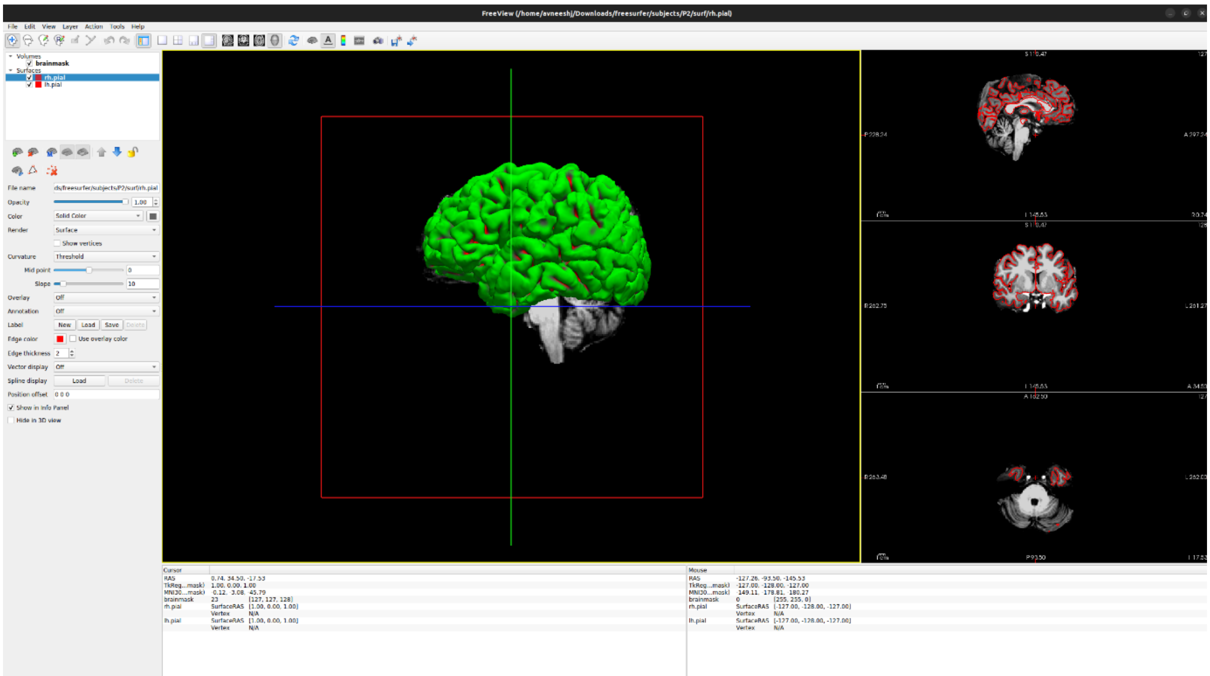


Image from Freesurfer terminal in Linux

9. To view the surfaces with edge color

<>freeview -v
<>$currSub/mri/brainmask.mgz
<>$currSub/mri/wm.mgz:colormap=jet:opacity=.2-f
<>$currSub/surf/lh.pial:edgecolor=blue
<>$currSub/surf/lh.white:edgecolor=red
<>$currSub/surf/rh.pial:edgecolor=blue
<>$currSub/surf/rh.white:edgecolor=red
The following window should open -

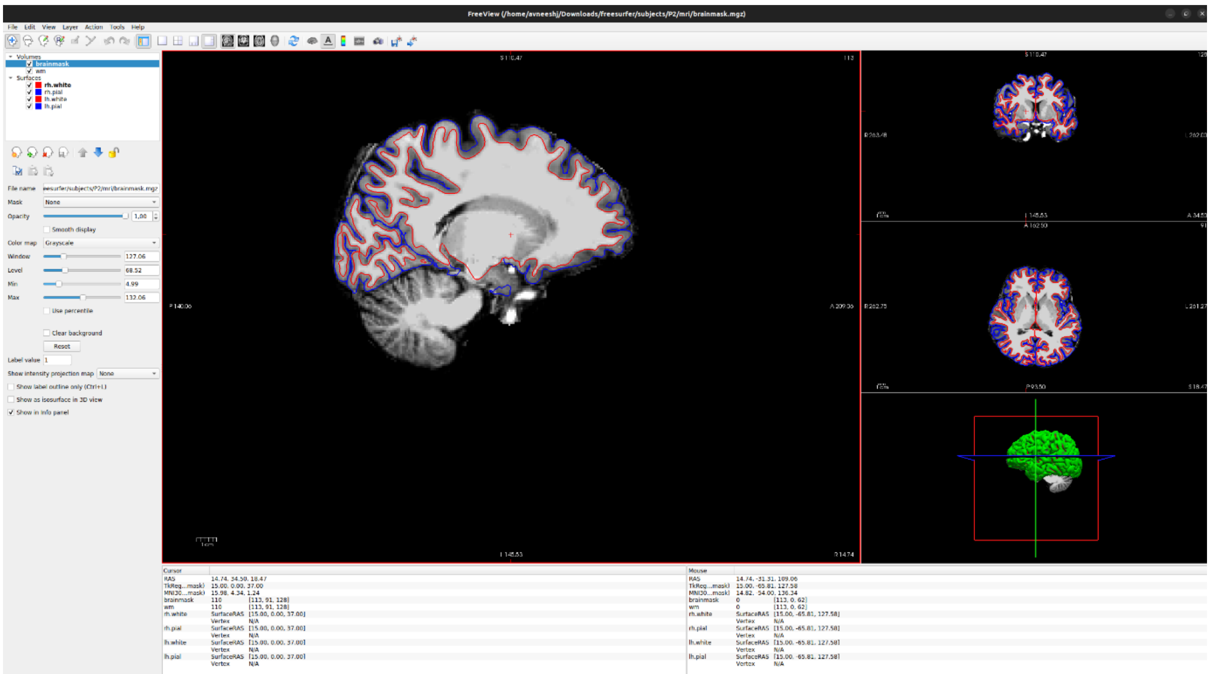
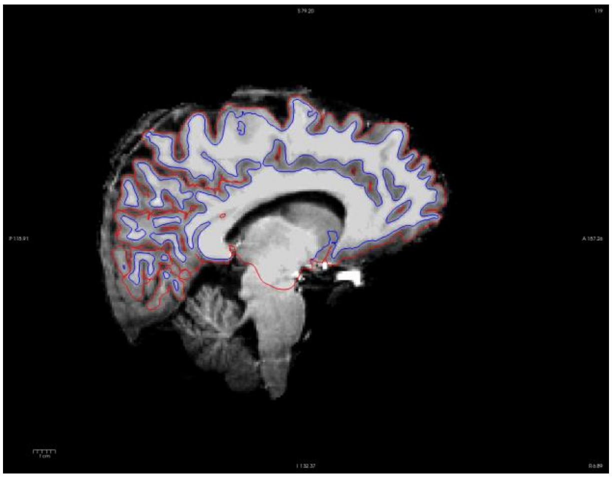


Image from Freesurfer terminal in Linux

10. Failures after the recon-ALL command : These occur when recon-all completes without errors but after close observation to the output in freeview there are some errors which can be all or few of the following, a set of codes has been added after each to fix the issue:

a. Skullstripping errors;



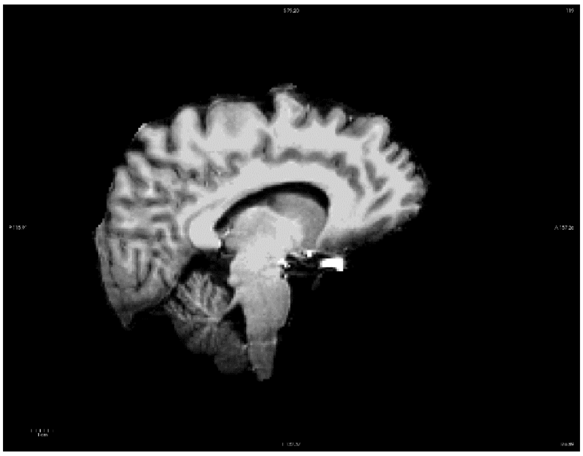
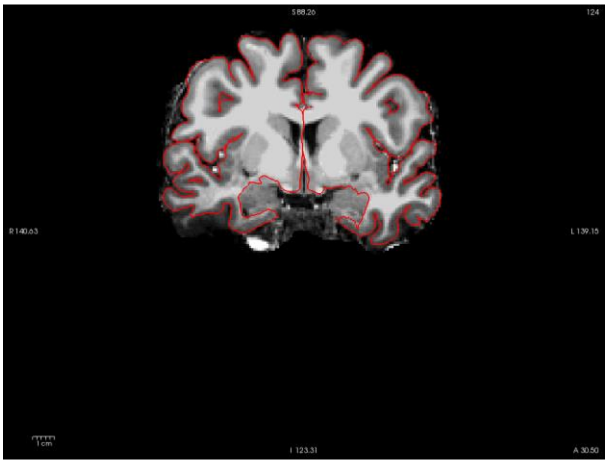


Fig. A Without skulstrip; B. After skull strip

Open your subject who has skull strip issue. More info - SKULLSTRIP
SKULL STRIP
IDEAL VALUE 8-12
<>recon-all -skullstrip -wsthresh <anything from 8-12> -clean-bm -subjid <subject name>
<>recon-all -skullstrip -wsthresh 8 -clean-bm -no-wsgcaatlas -subjid P1
<>recon-all -skullstrip -clean-bm -gcut -subjid <subject name>
<>regenerate surface:
<>POST SKULSTRIP: recon-all -s P1 -autorecon2 -autorecon3
<>POST PIAL EDIT: recon-all -s PX -autorecon-pial

b. Pial Surface errors;
Open your subject with this issue. There is no code to run but this can be fixed manually in the freeview using editing tools. More info - PIAL EDIT FIX



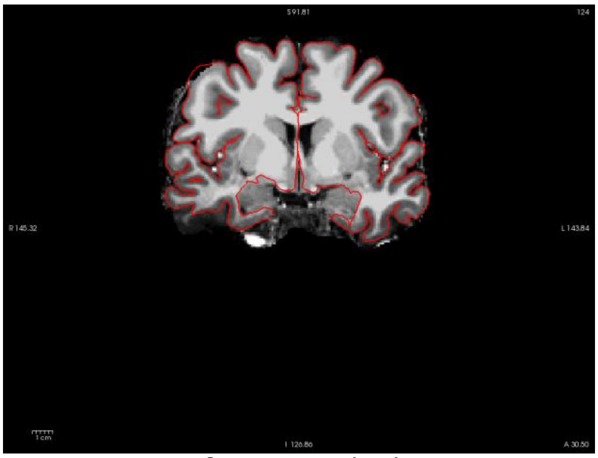
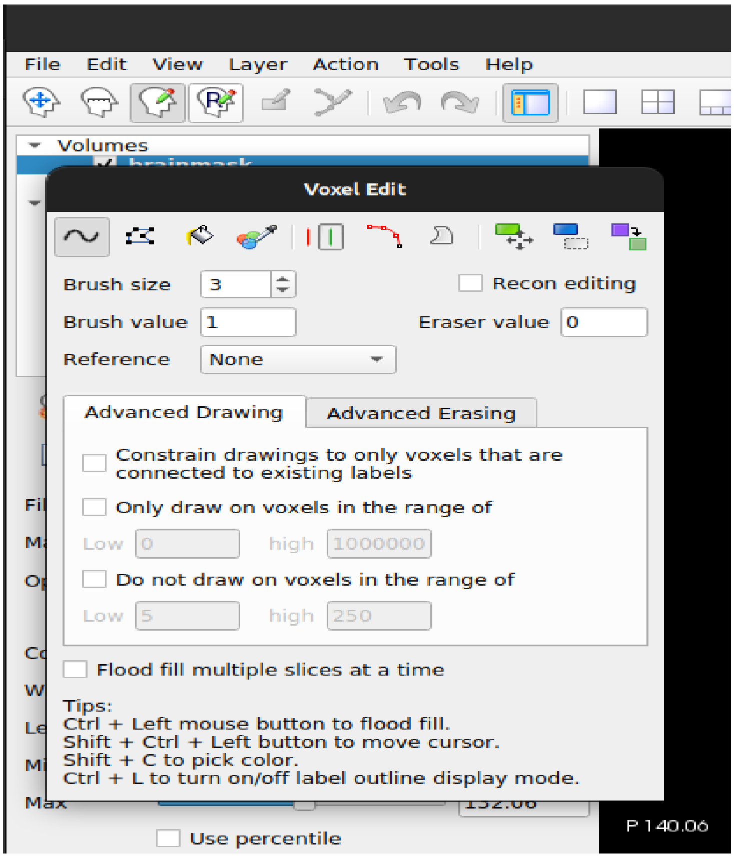


Fig. A. before manual edit; B. After manual edit;



C. Tools section in freeview to edit the extra voxels.

c. Intensity normalization errors;
   Open your subject who has skull strip issue. More info - [INTENSITY NORMALIZATION FIX]
   INTENSITY NORAMLIZATION :
   <>export currSub="P2"
   <>freeview -v $currSub/mri/brainmask.mgz \
   <>-f $currSub/surf/lh.white:edgecolor=blue \
   <>$currSub/surf/lh.pial:edgecolor=red \
   <>$currSub/surf/rh.white:edgecolor=blue \
   <>$currSub/surf/rh.pial:edgecolor=red

d. Topological defects
   This error is very rare but has an easy fix, more info - [TOPOLOGICAL FIX]. Make sure to use your own participant numbers or else the code will not run.

11. For sub-cortical areas.
DO NOT USE FREESURFER CODES PRIOR TO VERSION 7.1 FOR SUB-CORTEX. They are not accurate. The more accurate calculation can be made through the code provided in the Freesufer version 7.1 in this study
Direct command:
subcortical segmentation: segment_subregions (ROI) --cross (subject)
E.G., segment_subregions thalamus --cross (means crossectional) P1 for hippo and amyd
<>segmentHA_T1.sh P1 /home/avneeshj/Downloads/Freesurfer/subjects
<>quantifyHAsubregions.sh hippoSf T1 HIPPO.txt

<>quantifyHAsubregions.sh amygNuc T1 AMYG.txt

12. Now, to gather important structural parameters such as thickness, volume, area. It is advised to use the Freesurfer steps for this, more info - Analysis pipeline. The following codes can be used for large participant groups.

- **FOR CORTICAL THICKNESS**: mris_thickness (participant number) (hemisphere) (name of your thickness file)
- **AVG SUBJECT** : make_average_subject --out avgsubject --subjects P1 P2 P3 P4 P5 P6 P7 P8 P9 P10 P11 P12 P13 P14 P15 P16 P17 P18 P19 P20 P21 P22 P23 P24 P25 P26 P27 P28 P29 P30 P31 P32 P33 P34 P35
- **AVG THICKNESS**: make_average_surface --out avgsubject --subjects P1 P2 P3 P4 P5 P6 P7 P8 P9 P10 P11 P12 P13 P14 P15 P16 P17 P18 P19 P20 P21 P22 P23 P24 P25 P26 P27 P28 P29 P30 P31 P32 P33 P34 P35
- **AVG VOL:** make_average_volume --out avgsubject --subjects P1 P2 P3 P4 P5 P6 P7 P8 P9 P10 P11 P12 P13 P14 P15 P16 P17 P18 P19 P20 P21 P22 P23 P24 P25 P26 P27 P28 P29 P30 P31 P32 P33 P34 P35
- **mris_anatomical_stats** -l lh.cortex.label -b P1 lh - FOR STATS
- **aparcstats2tabl**e --hemi lh --subjects P1 P2 P3 P4 P5 P6 P7 P8 P9 P10 P11 P12 P13 P14 P15 P16 P17 P18 P19 P20 P21 P22 P23 P24 P25 P26 P27 P28 P29 P30 P31 P32 P33 P34 P35 --parc aparc.a2009s --measvolume -t lh.a2009s.meancurv.txt
- **asegstats2table** --subjects P1 P2 P3 P4 P5 P6 P7 P8 P9 P10 P11 P12 P13 P14 P15 P16 P17 P18 P19 P20 P21 P22 P23 P24 P25 P26 P27 P28 P29 P30 P31 P32 P33 P34 P35 --meas volume --skip --tablefile lh.amygNucVolumes.txt
- **asegtats2table** --subjects P1 P2 P3 P4 P5 P6 P7 P8 P9 P10 P11 P12 P13 P14 P15 P16 P17 P18 P19 P20 P21 P22 P23 P24 P25 P26 P27 P28 P29 P30 P31 P32 P33 P34 P35 --hemi lh --meas volume --skip -t lh.amyg.volume.txt

13. How to compute Intra cranial volume:

EstimatedTotalIntraCranialVol (eTIV) - This is the same number as the IntraCrainialVol (ICV) from pre-5.2 verions. The name was changed to help avoid confusion as to what this number is and is not. It is NOT a count of voxels inside the skull. The eTIV is a metric computed from the amount of scaling in the talairach.xfm file. See http://surfer.nmr.mgh.harvard.edu/fswiki/eTIV.
The above metrics are computed using the following function in cma.c:
BrainVolStats = (double *)ComputeBrainVolumeStats(subject);

How to fuse tow lobes together to make one single structural measure:
MANAUL FORMULA: bh.thickness = ((lh.thickness * lh.surfarea) + (rh.thickness * rh.surfarea)) / (lh.surfarea + rh.surfarea)

or much easier by simply usinfg the code

<>mri_annotation2label --subject (enter sub no.) --hemi (rh or lh) --lobesStrictPHCG (name of your lobe file) it will be in annot so annot should be converted to excel or something
<>mris_anatomical_stats -a P1/label/lhlobes.xls.annot -b P1 lh

8.2 Questionnaires of ESM

Q.1 Within the last two hours, has something happened to you that made you sad or distressed?

1. High intense e.g., fight with loved ones, had to suppress emotions where you needed to speak something.
2. Intense e.g., bad day at work/school, missed a deadline/forgot something important
3. Low intense e.g., lost something, feeling unwell.
4. Other
5. NO event

Q.2 How long ago was this negative event?

1. Ongoing
2. Very recent
3. More than 10 minutes ago
4. More than 30 min. ago
5. Over an hr. ago

Q3. Following this event, on a scale from 1 to 7 how negative would you rate your emotions to be?

[1 is not at all negative, 7 is extremely negative]

Q4. On a scale from 1 to 7, how upset are you about the event when looking back at it now?

[1 is not at all negative, 7 is extremely negative]

Q5. On a scale of 1 to 7 how positive would you rate your emotions to be looking back at this event?

[1 is not at all Positive, 7 is extremely Positive]

Q6. Did this occur alone, or in the presence of others?

1. Alone
2. With Strangers
3. With Friends/Family

Q7. Please describe the negative event in audio or type your response

[Participants provide written or verbal description of the event]

Q8. Within the last 2 hours, has something happened that made you feel happy?

1. High intense e.g., new job, trip with family/friends
2. Intense e.g., preparing to move somewhere exciting, First week of school/work
3. Low intense e.g. A nice walk, A good workout, went out.
4. Others
5. No event

Q9. How long ago was this positive event?

1. Ongoing
2. Very recent
3. More than 10 minutes ago
4. More than 30 min. ago
5. Over an hr. ago

Q10. On a scale from 1 to 7, how positive would you rate your emotional state to be after this event?

[1 is not at all Positive, 7 is extremely Positive]

Q11. On a scale from 1 to 7 how positive would you rate your emotions to be when looking back at the event now?

[1 is not at all Positive, 7 is extremely Positive]

Q12. On a scale of 1 to 7 how negative would you rate your emotions to be looking back at this event?

[1 is not at all negative, 7 is extremely negative]

Q13. Did this occur alone or in the presence of others?

1. Alone
2. With Strangers
3. With Friends/Family

Q14. Please describe the negative event in audio or type your response

[Participants provide written or verbal description of the event]

Q15. Within the last two hours, have you met with others in a social setting (i.e., visit, meeting, lunch, grocery shopping, conversations, A walk, party, Dinner)?

1. Yes
2. No

8.3 Correlation Matrix & Mediation

The FDR graph can be found in this page and the correlation matrix with r and p-values can be accessed below on Table 8. Following that, all four-mediation analysis with details from PROCESS SPSS can be found.

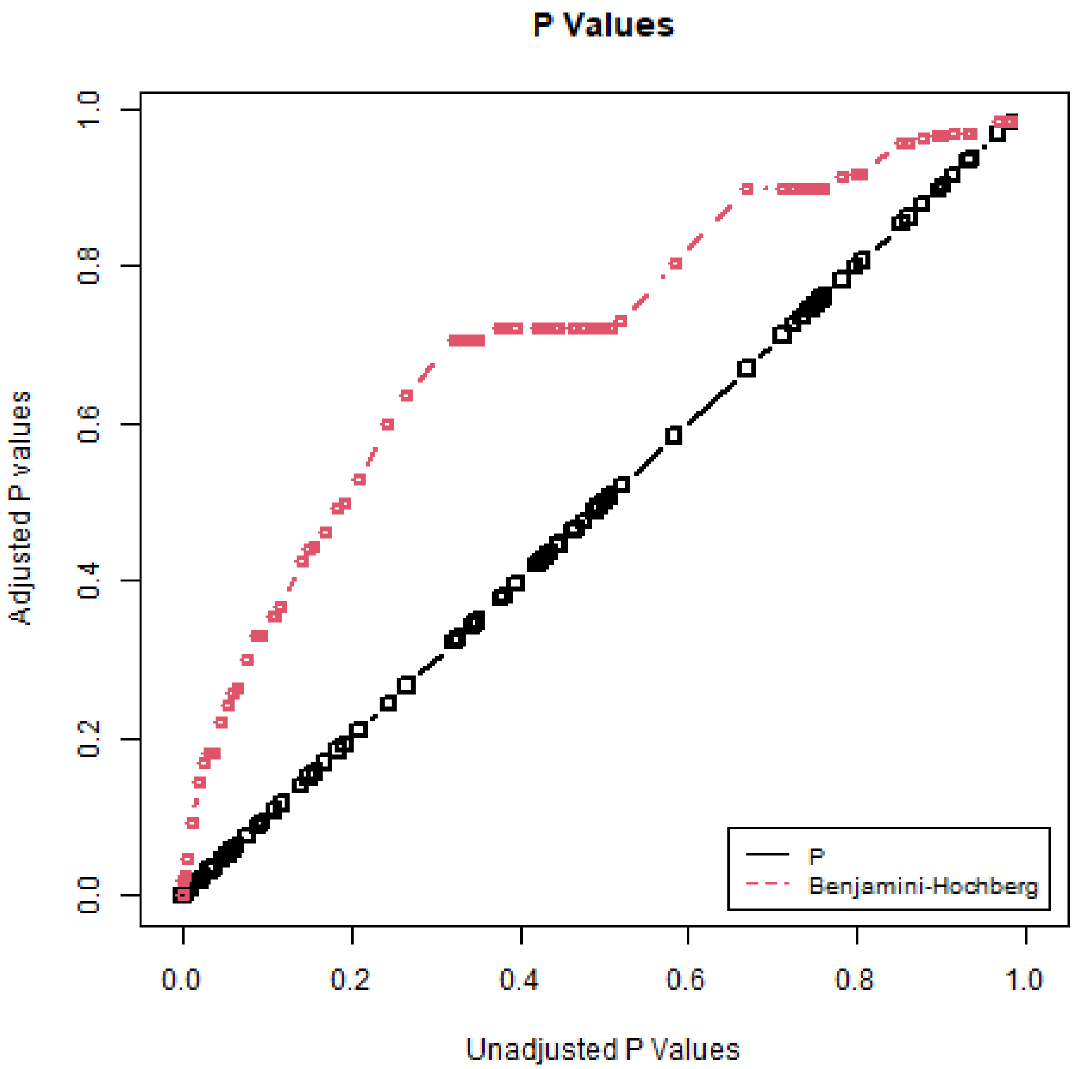


Table 8. Correlations

		ANX	PSS	CDRISC	IRI	POS	NEG	Insula	AV	mOFC	cACC
ANX	Pearson Correlation	1	,659*	-,373*	0,10 0	0,089	,458**	-,349*	0,320*	-0,016	-0,242
	Sig.		0,000	0,027	0,569	0,609	0,006	0,040	0,05	0,929	0,161
	N	35	35	35	35	35	35	35	35	35	35
PSS	Pearson Correlation	,659**	1	-,675**	0,021	-0,007	,360*	-0,269	0,123	0,084	-0,062
	Sig.	0,000		0,000	0,903	0,967	0,033	0,118	0,482	0,631	0,721
	N	35	35	35	35	35	35	35	35	35	35
CD-RISC	Pearson Correlation	-,373*	-,675**	1	-0,017	-0,126	-0,253	0,142	-0,016	-,485**	0,154
	Sig. (2tailed)	0,027	0,000		0,922	0,469	0,143	0,417	0,929	0,003	0,378
	N	35	35	35	35	35	35	35	35	35	35
IRI	Pearson Correlation	0,100	0,021	-0,017	1	,376*	,376*	0,093	-0,001	0,152	-,369*
	Sig.	0,569	0,903	0,922		0,026	0,026	0,596	0,998	0,382	0,029
	N	35	35	35	35	35	35	35	35	35	35
POS1	Pearson Correlation	0,089	-0,007	-0,126	,376*	1	,487**	-0,242	0,118	0,063	-,377*
	Sig.	0,609	0,967	0,469	0,026		0,003	0,161	0,499	0,721	0,026
	N	35	35	35	35	35	35	35	35	35	35
NEG1	Pearson Correlation	,458**	,360*	-0,253	,376*	,487**	1	-,355*	0,243	0,016	-0,272
	Sig.	0,006	0,033	0,143	0,026	0,003		0,036	0,159	0,927	0,115
	N	35	35	35	35	35	35	35	35	35	35
Insula	Pearson Correlation	-,349*	-0,269	0,142	0,093	-0,242	-,355*	1	-,351*	0,065	-0,084
	Sig.	0,040	0,118	0,417	0,596	0,161	0,036		0,039	0,712	0,631
	N	35	35	35	35	35	35	35	35	35	35
AV	Pearson Correlation	0,320*	0,123	-0,016	-0,001	0,118	0,243	-,351*	1	-,341*	-0,073
	Sig	0,05	0,482	0,929	0,998	0,499	0,159	0,039		0,045	0,678
	N	35	35	35	35	35	35	35	35	35	35
mOFC	Pearson Correlation	-0,016	0,084	-,485**	0,152	0,063	-0,016	0,065	-,341*	1	-0,021
	Sig.	0,929	0,631	0,003	0,382	0,721	0,927	0,712	0,045		0,905
	N	35	35	35	35	35	35	35	35	35	35
cACC	Pearson Correlation	-0,242	-0,062	0,154	-,369*	-,377*	-0,272	-0,084	-0,073	-0,021	1
	Sig. (2-tailed)	0,161	0,721	0,378	0,029	0,026	0,115	0,631	0,678	0,905	
	N	35	35	35	35	35	35	35	35	35	35

****. Correlation is significant at the 0.01 level (2-tailed). Green**

***. Correlation is significant at the 0.05 level (2-tailed). Blue**

8.3.2 MEDIATION ANALYSIS Between Insula-Anxiety-NE

Run MATRIX procedure:

***************** PROCESS Procedure for SPSS Version 4.2 *****************

Written by Andrew F. Hayes, Ph.D. www.afhayes.com
Documentation available in Hayes (2022). www.guilford.com/p/hayes3

****
Model : 4
Y : NEG1 (NE)
X : RIA (Inusla)
M : ANX (Anxiety)

Sample
Size: 35

****
OUTCOME VARIABLE:
ANX

Model Summary

R	R-sq	MSE	F	df1	df2	p
,3487	,1216	14,3410	4,5667	1,0000	33,0000	**,0401**

Model

	coeff	se	t	p	LLCI	ULCI
constant	16,7770	4,3815	3,8291	,0005	7,8626	25,6914
RIA	-,0037	,0017	-2,1370	,0401	-,0073	-,0002

Standardized coefficients

	coeff
RIA	-,3487

****
OUTCOME VARIABLE:
NEG1

Model Summary

R	R-sq	MSE	F	df1	df2	p
,5032	,2532	148,2463	5,4261	2,0000	32,0000	**,0094**

Model

	coeff	se	t	p	LLCI	ULCI
constant	26,0331	16,9298	1,5377	,1340	-8,4526	60,5187
RIA	-,0082	,0060	-1,3656	,1816	-,0204	,0040
ANX	1,3061	,5597	2,3337	**,0261**	,1661	2,4462

Standardized coefficients

	coeff
RIA	-,2226
ANX	,3804

************************** TOTAL EFFECT MODEL ****************************
OUTCOME VARIABLE:
NEG1

Model Summary

R	R-sq	MSE	F	df1	df2	p
,3552	,1262	168,2193	4,7643	1,0000	33,0000	**,0363**

Model

	C oeff	se	t	p	LLCI	ULCI
constant	47,9459	15,0062	3,1951	,**0031**	17,4150	78,4769
RIA	-,0130	,0060	-2,1827	**,0363**	-,0252	-,0009

Standardized coefficients

	coeff
RIA	-,3552

************** TOTAL, DIRECT, AND INDIRECT EFFECTS OF X ON Y **************

Total effect of X on Y

Effect	se	t	p	LLCI	ULCI	c_cs
-,0130	,0060	-2,1827	**,0363**	-,0252	-,0009	-,3552

Direct effect of X on Y

Effect	se	t	p	LLCI	ULCI	c'_cs
-,0082	,0060	-1,3656	,1816	-,0204	,0040	-,2226

Indirect effect(s) of X on Y:

	Effect	BootSE	BootLLCI	BootULCI
ANX	-,0049	,0027	**-,0110**	**-,0002**

Completely standardized indirect effect(s) of X on Y:

	Effect	BootSE	BootLLCI	BootULCI
ANX	-,1326	,0661	**-,2757**	**-,0069**

********************** ANALYSIS NOTES AND ERRORS ************************

Level of confidence for all confidence intervals in output:
95,0000

Number of bootstrap samples for percentile bootstrap confidence intervals:
5000

------ END MATRIX -----

8.3.3 MEDIATION ANALYSES Between cACC-Empathy-PE

Run MATRIX procedure:

***************** PROCESS Procedure for SPSS Version 4.2 *****************

Written by Andrew F. Hayes, Ph.D. www.afhayes.com
Documentation available in Hayes (2022). www.guilford.com/p/hayes3

****

Model : 4
Y : POS1 (PE)
X : cACC
M : IRI (Empathy)

Sample
Size: 35

****
OUTCOME VARIABLE:
IRI

Model Summary

R	R-sq	MSE	F	df1	df2	p
,3687	,1359	184,6654	5,1917	1,0000	33,0000	**,0293**

Model

	coeff	se	t	p	LLCI	ULCI
constant	143,9588	34,0538	4,2274	**,0002**	74,6744	213,2432
cACC	-35,7315	15,6818	-2,2785	,0293	-67,6371	-3,8260

Standardized coefficients

	coeff
cACC	-,3687

****
OUTCOME VARIABLE:
POS1

Model Summary

R	R-sq	MSE	F	df1	df2	p
,4553	,2073	246,1243	4,1847	2,0000	32,0000	**,0243**

Model

	coeff	se	t	p	LLCI	ULCI
constant	81,9813	48,8121	1,6795	,1028	-17,4478	181,4105
cACC	-31,7221	19,4764	-1,6287	,1132	-71,3951	7,9508
IRI	,3260	,2010	1,6220	,1146	-,0834	,7353

Standardized coefficients

	coeff
cACC	-,2758
IRI	,2746

************************** TOTAL EFFECT MODEL ****************************
OUTCOME VARIABLE:
POS1

Model Summary

R	R-sq	MSE	F	df1	df2	p
,3770	,1422	258,2874	5,4683	1,0000	33,0000	**,0256**

Model

	coeff	se	t	p	LLCI	ULCI
constant	128,9070	40,2740	3,2008	**,0030**	46,9674	210,8467
cACC	-43,3694	18,5462	-2,3384	,**0256**	-81,1027	-5,6361

Standardized coefficients

	coeff
cACC	-,3770

************** TOTAL, DIRECT, AND INDIRECT EFFECTS OF X ON Y **************

```
Total effect of X on Y
    Effect         se          t          p       LLCI       ULCI      c_cs
  -43,3694    18,5462    -2,3384      ,0256   -81,1027    -5,6361     -,3770

Direct effect of X on Y
    Effect         se          t          p       LLCI       ULCI     c'_cs
  -31,7221    19,4764    -1,6287      ,1132   -71,3951     7,9508     -,2758

Indirect effect(s) of X on Y:
      Effect     BootSE   BootLLCI   BootULCI
IRI   -11,6473     8,7529   -32,1790     1,0856

Completely standardized indirect effect(s) of X on Y:
      Effect     BootSE   BootLLCI   BootULCI
IRI     -,1013      ,0693     -,2503      ,0106

*********************** ANALYSIS NOTES AND ERRORS ************************

Level of confidence for all confidence intervals in output:
  95,0000

Number of bootstrap samples for percentile bootstrap confidence intervals:
  5000

------ END MATRIX -----
```

8.3.4 MEDIATION ANALYSIS Between Amygdala-Stress-NE

```
Run MATRIX procedure:

***************** PROCESS Procedure for SPSS Version 4.2 *****************

          Written by Andrew F. Hayes, Ph.D.       www.afhayes.com
    Documentation available in Hayes (2022). www.guilford.com/p/hayes3

**************************************************************************
Model  : 4
    Y  : NEG (NE)
    X  : AV (Amygdala)
    M  : PSS (Stress)

Sample
Size:  35

**************************************************************************
OUTCOME VARIABLE:
 PSS

Model Summary
          R       R-sq        MSE          F        df1        df2          p
      ,1229      ,0151    42,7012      ,5059     1,0000    33,0000      ,4819

Model
              coeff         se          t          p       LLCI       ULCI
constant    12,7007     4,1071     3,0924      ,0040     4,3447    21,0567
AV            ,0024      ,0034      ,7113      ,4819     -,0045      ,0093
```

Standardized coefficients
AV ,1229
****
OUTCOME VARIABLE:
NEG1
Model Summary

R	R-sq	MSE	F	df1	df2	p
,4124	,1700	164,7655	3,2780	2,0000	32,0000	**,0507**

Model

	coeff	se	t	p	LLCI	ULCI
constant	-5,1743	9,1623	-,5647	,5762	-23,8376	13,4890
AV	,0084	,0067	1,2453	,2221	-,0053	,0220
PSS	,7069	,3419	2,0672	**,0469**	,0103	1,4034

Standardized coefficients

	coeff
AV	,2021
PSS	,3355

************************* TOTAL EFFECT MODEL ****************************
OUTCOME VARIABLE:
NEG1
Model Summary

R	R-sq	MSE	F	df1	df2	p
,2433	,0592	181,1096	2,0765	1,0000	33,0000	,1590

Model

	coeff	se	t	p	LLCI	ULCI
constant	3,8036	8,4583	,4497	,6559	-13,4052	21,0124
AV	,0101	,0070	1,4410	,1590	-,0041	,0243

Standardized coefficients

	coeff
AV	,2433

************** TOTAL, DIRECT, AND INDIRECT EFFECTS OF X ON Y **************

Total effect of X on Y

Effect	se	t	p	LLCI	ULCI	c_cs
,0101	,0070	1,4410	,1590	-,0041	,0243	,2433

Direct effect of X on Y

Effect	se	t	p	LLCI	ULCI	c'_cs
,0084	,0067	1,2453	,2221	-,0053	,0220	,2021

Indirect effect(s) of X on Y:

	Effect	BootSE	BootLLCI	BootULCI
PSS	,0017	,0028	-,0048	,0068

Completely standardized indirect effect(s) of X on Y:

	Effect	BootSE	BootLLCI	BootULCI
PSS	,0412	,0659	-,1111	,1589

********************** ANALYSIS NOTES AND ERRORS ************************

Level of confidence for all confidence intervals in output:
95,0000
Number of bootstrap samples for percentile bootstrap confidence intervals:
5000
------ END MATRIX ----

8.3.5 MEDIATION ANALYSIS Between mOFC-Reappraisal-Resilience

Run MATRIX procedure:

```
***************** PROCESS Procedure for SPSS Version 4.2 *****************

          Written by Andrew F. Hayes, Ph.D.       www.afhayes.com
    Documentation available in Hayes (2022). www.guilford.com/p/hayes3

**************************************************************************
Model  : 4
    Y  : Did you find anything positive in the negative event i.e., Reappraisal
    X  : mOFC
    M  : CD-RISC

Sample
Size:  35

**************************************************************************
OUTCOME VARIABLE:
 CDS

Model Summary
          R       R-sq        MSE          F        df1        df2          p
      ,4853      ,2355   159,6467    10,1650     1,0000    33,0000      ,0031

Model
              coeff         se          t          p       LLCI       ULCI
constant   186,4366    36,4934     5,1088      ,0000   112,1887   260,6846
mOFC       -48,6802    15,2686    -3,1883      ,0031   -79,7450   -17,6154

Standardized coefficients
          coeff
mOFC      -,4853

**************************************************************************
OUTCOME VARIABLE:
 Reappraisal


Model Summary
          R       R-sq        MSE          F        df1        df2          p
      ,3191      ,1018      ,1942     1,8140     2,0000    32,0000      ,1794

Model
              coeff         se          t          p       LLCI       ULCI
constant      ,9377     1,7032      ,5506      ,5857    -2,5316     4,4070
mOFC          ,1614      ,6090      ,2650      ,7927    -1,0791     1,4019
CDS          -,0092      ,0061    -1,5206      ,1382     -,0216      ,0031

Standardized coefficients
          coeff
mOFC       ,0508
CDS       -,2914

************************** TOTAL EFFECT MODEL ****************************
OUTCOME VARIABLE:
 Reappraisal
```

Model Summary

R	R-sq	MSE	F	df1	df2	p
,1922	,0369	,2019	1,2653	1,0000	33,0000	,2688

Model

	coeff	se	t	p	LLCI	ULCI
constant	-,7834	1,2977	-,6036	,5502	-3,4237	1,8570
mOFC	,6108	,5430	1,1248	,2688	-,4939	1,7154

Standardized coefficients

	coeff
mOFC	,1922

************** TOTAL, DIRECT, AND INDIRECT EFFECTS OF X ON Y **************

Total effect of X on Y

Effect	se	t	p	LLCI	ULCI	c_cs
,6108	,5430	1,1248	,2688	-,4939	1,7154	,1922

Direct effect of X on Y

Effect	se	t	p	LLCI	ULCI	c'_cs
,1614	,6090	,2650	,7927	-1,0791	1,4019	,0508

Indirect effect(s) of X on Y:

	Effect	BootSE	BootLLCI	BootULCI
CDS	,4494	,4578	-,1400	1,6809

Completely standardized indirect effect(s) of X on Y:

	Effect	BootSE	BootLLCI	BootULCI
CDS	,1414	,1164	-,0540	,4163

********************** ANALYSIS NOTES AND ERRORS ***********************

Level of confidence for all confidence intervals in output:
95,0000

Number of bootstrap samples for percentile bootstrap confidence intervals:
5000
------ END MATRIX -----

8.4 ESM: Multilevel Structural Equation Modelling

For the negative and positive affect scales in the experience sampling phase, both the within- and between-persons reliability was calculated using multi-level structural equation modelling (multilevelTools package) which calculates Omega - R PACKAGE

8.4.1 Loading the packages

<>load lme4, JWileymisc, and multilevelTools packages
<> (i.e., "open the 'apps' ")
<>Library(lme4)
<>Loading required package: Matrix
<>library(lmerTest)
<>Attaching package: 'lmerTest'
<>The following object is masked from 'package:lme4':
<>lmer
<>The following object is masked from 'package:stats':
#>
<>step
<>library(extraoperators)
<>library(JWileymisc)
<>library(multilevelTools)

8.4.2 R - Codes

1. For Plotting the Density plots:
   <>plot(testDistribution(tmp[["***Neg/Pos event category*** by Subject"]]$X,
   extremevalues = "theoretical", ev.perc = .001),
   varlab = "Between/Within Person ***Name of category***")

2. For getting the statistics of the model :
   <>**m <- lmer (*Name of category* ~ IV + (1 + DAYS | Subject),**
   data = df2)
   here:
   m – Tells R to save the output of the analyses to an object called “m”
   lmer – Command to test a mixed linear model using lme4
   Name of Category – Specifies the categories under Negative or Positive event
   IV – the independent variable i.e. Days for between person and RespDay for within person
   1 – it is added when there are no predictors
   Subject – Specifies that level 1 observations are grouped by level 2 variable called “subject”
   Data – Specifies that the variables (e.g., Subject, observation) are in the file “df2”

3. For model data
   <>*modelPerformance(m*)
   and then by running *summary* function will give the outputs as shown in the two Tables below for Between and within subject, respectively.

Table 9 Model Test for **Between Subject** variables with effect size in last two rows. NegInt – Intensity of negative event; NegSocial – Social sharing in negative event; PosInt – Intensity of Positive event; PosSocial – Social sharing in a positive event

	Negative Effects	Positive Effect	NegInt	Rumination	Reappraisal	NegSocial	PosInt	Savoring	PosSocial
(Intercept)	1.520, p < .001 (1.354; 1.687)	2.320, p <.001 (2.118; 2.522)	0.949, p < .001 (0.665; 1.233)	0.821, p < .001 (0.546; 1.097)	0.779, p < .001 (0.440; 1.118)	0.583, p < .001 (0.390; 0.777)	3.085, p < .001 (2.597; 3.572)	3.060, p < .001 (2.559; 3.561)	1.464, p < .001 (1.256; 1.672)
DAYS	0.006, p= .654 (-0.020; 0.032)	-0.033, p = .009 (-0.057; -0.010)	0.013, p = .571 (- 0.032; 0.059)	0.023, p = .346 (- 0.024; 0.069)	-0.038, p = .181 (- 0.091; 0.016)	-0.002, p = .901 (-0.034; 0.030)	-0.113, p .001 (- 0.165; - 0.060)	-0.110, p < .001 (- 0.164; - 0.056)	-0.043, p = .002 (-0.069; -0.018)
cor_DAYS.(Intercept)|Subject	-0.385	-0.389	-0.476	-0.482	-0.902	-0.586	-0.434	-0.456	-0.332
sd_(Intercept)|Subject	0.439	0.549	0.745	0.727	0.989	0.539	1.354	1.401	0.542
sd_DAYS|Subject	0.066	0.054	0.117	0.120	0.155	0.087	0.124	0.129	0.055
Sigma	0.882	0.965	1.525	1.444	0.945	0.793	2.073	0.129	1.141
Model DF	6	6	6	6	6	6	6	6	6
N (Groups) Subject	(35)	(35)	(35)	(35)	(35)	(35)	(35)	(35)	(35)
N (Observations)	2444	2444	2444	2444	2444	2444	2444	2444	2443
logLik	-3230.278	-3447.932	-4567.253	-4437.338	-3420.757	-2985.906	-5321.420	-5309.676	-3848.239
AIC	6472.555	6907.864	9146.506	8886.677	6853.514	5983.812	10654.840	10631.353	7708.478
BIC	6507.364	6942.672	9181.314	8921.485	6888.322	6018.620	10689.649	10666.161	7708.478
Marginal R2	0.000	0.007	0.000	0.001	0.008	0.000	0.016	0.015	0.009
Marginal F2	0.000	0.007	0.000	0.001	0.008	0.000	0.016	0.015	0.009
Conditional R2	0.223	0.232	0.202	0.220	0.289	0.295	0.278	0.288	0.188
Conditional F2	0.288	0.303	0.252	0.281	0.407	0.418	0.385	0.404	0.231
DAYS (Fixed + Random)	0.000, 0.046; p < .001	0.007, 0.030; p< .001	0.000, 0.044; p< .001	0.001, 0.055; p < .001	0.008, 0.158; p < .001	0.000, 0.081; p < .001	0.016, 0.046; p < .001	0.015, 0.048; p < .001	0.009, 0.026; p < .001
DAYS (Random)	-0.001, 0.044; p <.001	-0.001, 0.022; p< .001	-0.001, 0.042; p< .001	-0.002, 0.050; p < .001	0.006, 0.154; p < .001	0.000, 0.080; p < .001	-0.001, 0.024; p < .001	0.000, 0.029; p < .001	0.000, 0.019; p = .003

Table 10 Model Test for **Within Subject** variables with effect size in last two rows . RespDay – number of responses in one day; NegInt – Intensity of negative event; NegSocial – Social sharing in negative event; PosInt – Intensity of Positive event; PosSocial – Social sharing in a positive event

	Negative Effects	Positive Effect	NegInt	Rumination	Reappraisal	NegSocial	PosInt	Savoring	PosSocial
(Intercept)	1.574, p< .001 (1.384; 1.764)	1.953, p < .001 (1.775; 2.131)	1.053, p < .001 (0.742; 1.364)	0.968, p < .001 (0.674; 1.263)	0.632, p < .001 (0.442; 0.822)	0.527, p < .001 (0.371; 0.682)	2.191, p < .001 (1.748; 2.634)	2.204, p < .001 (1.755; 2.653)	0.950, p < .001 (0.788; 1.111)
RespDay	-0.003, p = .774 (- 0.020; 0.015)	0.042, p < .001 (0.021; 0.062)	-0.002, p = .907 (- 0.035; 0.031)	-0.001, p = .953 (-0.031; 0.030)	-0.006, p = .481 (-0.022; 0.010)	0.013, p = .047 (0.000; 0.026)	0.067, p = .008 (0.020; 0.113)	0.063, p = .011 (0.017; 0.108)	0.063, p < .001 (0.041; 0.086)
corRespDay.(Intercept)|Subject	-0.695	-0.038	-0.628	-0.564	-1.000	1.000	-0.188	-0.167	0.595
sd_(Intercept)|Subject	0.528	0.481	0.857	0.811	0.520	0.424	1.232	1.252	0.398
sd_RespDay|Subject	0.032	0.042	0.066	0.059	0.013	0.008	0.097	0.091	0.040
Sigma	0.892	0.969	1.545	1.470	0.986	0.811	2.096	2.088	1.140
Model DF	6	6	6	6	6	6	6	6	6
N (Groups) Subject	(35)	(35)	(35)	(35)	(35)	(35)	(35)	(35)	(35)
N (Observations)	2444	2444	2444	2444	2444	2444	2444	2444	2443
logLi	-3245.418	-3451.319	-4587.219	-4465.461	-3481.783	- 3011.090	-5342.923	-5333.053	-3838.734
AIC	6502.836	6914.637	9186.439	8942.921	6975.566	6034.180	10697.846	10678.107	7689.468
BIC	6537.644	6949.445	9221.247	8977.730	7010.374	6068.988	10732.654	10712.915	7724.274
Marginal R2	0.000	0.009	0.000	0.000	0.000	0.001	0.005	0.004	0.016
Marginal F2	0.000	0.009	0.000	0.000	0.000	0.001	0.005	0.004	0.016
Conditional R2	0.195	0.227	0.177	0.185	0.176	0.239	0.261	0.268	0.189
Conditional F2	0.243	0.294	0.215	0.227	0.214	0.314	0.353	0.366	0.233
RespDay (Fixed + Random)	0.000, 0.010; p = .074	0.009, 0.023; p < .001	0.000, 0.013; p = .038	0.000, 0.011; p = .087	0.000, 0.000; p = .452	0.001, 0.003; p = .157	0.005, 0.022; p < .001	0.004, 0.019; p < .001	0.016, 0.027; p < .001
RespDay (Random)	0.000, 0.010; p = .033	0.000, 0.009; p = .008	0.000, 0.013; p = .015	0.000, 0.011; p = .038	0.000, 0.000; p = .322	0.000, 0.000; p = .498	0.000, 0.013; p = .009	0.000, 0.012; p = .021	0.001, 0.006; p = .001

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