



## Study Protocol

# Effects of the guided disclosure protocol on post-traumatic growth: A randomized control trial designed to observe psychophysiological alterations in traumatic stress subjects

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## Abstract

**Background:** The two constructs traumatic stress and Post-Traumatic Growth (PTG) are distinct and the psychophysiological relationship is yet to be explained. It's a long debate that the victims who survive through the traumatic event only perceive that their suffering has helped them in improving their lives after the event or the experience actually improved functioning. The purpose of designing this randomized control trial is to observe psychophysiological alterations associated with post traumatic growth in traumatic stress subjects.

**Methodology:** This Multicenter study is planned to investigate the effectiveness of the guided disclosure protocol for the promotion of post-traumatic growth (PTG), in the traumatic stress subjects and to determine whether PTG is associated with psychophysiological alterations i.e. (C-Reactive Protein, Brain Derived Neurotropic Factor, Interlukin-6, Cortisol, Heart Rate Variability and brain waves). Study subjects meeting eligibility criteria will be randomized into two groups. Guided disclosure protocol (GDP) will be used as intervention vs the control. Blinded treatment will be provided and the subjects will be made to complete study questionnaires (Screening, Traumatic Stress Scale SSS, Trauma Symptom Checklist, Post-traumatic growth Inventory) at baseline and at post-intervention (3-months later).

**Discussion:** This study might give us insight about application and efficacy of Guided disclosure protocol in a population that is seeking help and underrepresented to be clinical. Moreover, one of the more hopeful findings of this research will be significant information about trauma-related psychophysiological effects.

## Keywords

Guided disclosure protocol, Post-traumatic growth, psychophysiological alterations, Trauma Symptom Checklist.



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## Introduction

Traumatic stress is an outcome of single or a cumulative series of trauma exposure that enduring symptoms conditioned with previous frightening experiences that threatens persons existence and sense of safety in conditions like physical shock, harassment, abusive relationships, sexual abuse, police brutality, judicial corruption, domestic violence, natural disasters, motor vehicle accident, community violence etc. Traumatic stress involves both biological and psychological aspects and as research progress in the field there had been exploration of numerous etiological factors with the main mechanisms remain imprecise<sup>1</sup>. According to the neurobiological findings, the stress and resilience model needs to put together to understand these factors<sup>2</sup> as the underlying biology is the major contributing factor for triggering psychological risk and the resilience factors<sup>3</sup>. It is evident that the symptoms of traumatic stress and Post Traumatic Growth (PTG) co-occur in accordance with trauma type<sup>4</sup>. Where PTG is considered as positive psychosomatic transformation experienced as a result of adversity and other miseries to rise at an improved and quality psychophysiological state.

In response to any traumatic event the neurophysiological factors get triggered like HPA axis<sup>5</sup>, that initiate a cascade to influences neuronal pathways via dopaminergic<sup>6,7</sup>, glutamatergic<sup>8</sup>, and serotonergic systems<sup>9</sup>, to cause changes in the perception and performance. Numerous biomarkers associated with different biological domains such as monoaminergic systems, neuroendocrinological pointers, inflammatory molecules, genomics, psychophysiological markers and neuroanatomical changes had been identified for assessment of post-traumatic stress risk and consequences<sup>10</sup>. The inherent symptomatic diversity among the post-traumatic stress subjects, and other similar psychiatric and medical conditions makes the identification of appropriate biomarker for

post-traumatic stress diagnosis much complex<sup>11-13</sup>.

Inflammatory markers, brain-derived neurotrophic factor (BDNF), and alterations from the HPA axis are few of the Resilience-specific biological factors that had been discovered and studied in the past<sup>14,15</sup>. While cortisol remain the key hormone that release in response to stress stimuli from the adrenal gland and controlled by the HPA axis<sup>16</sup>. The Trauma subjects show increased stress sensitivity as the cortisol level is naturally reduced among these subjects after getting exhaust initially<sup>17</sup>. There is a strong relationship between trauma and inflammatory markers as indicated by a number of comorbidities like physical<sup>18</sup>, inflammation<sup>19</sup> and metabolic illness<sup>20</sup>. The level of pro-inflammatory cytokines such as interleukin (IL)-6, IL-1 and IL-2 are high in traumatic subjects<sup>21,22</sup>. While C reactive protein (CRP) is considered as psychophysiological biomarker of post-traumatic stress with increased level of CRP is observed among traumatic stress subjects<sup>23</sup>. The most recurrent biological finding in traumatic stress is higher autonomic activity and changes in brain functionality that can be detected by numerous recordings such as, HRV measurement, skin conductance, brain waves and facial electromyography responding during internal, mental imagery of the traumatic event and upon exposure to external, trauma-related cues.

According to the Posttraumatic growth (PTG) model, traumatic events function as catalyst and aid in individual growth to develop various coping strategies and it must be considered as a challenge<sup>24,25</sup>. Although the memories and feelings associated with a traumatic event are stressful<sup>26</sup>, but the dealing strategy and experience can be altered by the individual's perspective regarding the event and through this the aftermath could be transformed<sup>25</sup>.

Depending upon psychological symptoms, self-report and patient's observation,



particularly within military personnel, is inadequate as impairment may occur due to various factors, including other combat-related injuries like mild traumatic brain injury<sup>27,28</sup>. Similarly, without the assessment of psychological factors associated with perceived stress, resilience, and struggling experiences and only concentrating on the biological foundation would limit one's knowledge regarding the etiological factors associated with the trauma. The primary mechanisms cannot be studied properly unless the stress related problems are studied along with the coping strategies<sup>29,30</sup>. For assessment, diagnosis, inhibition and treatment, the markers (psychological, biological, and genetic) could assist mainly in the high-risk groups<sup>31,32</sup>.

Several researchers reported immunological differences between studies including participants who disclosed traumatic or upsetting events compared with those in a nondisclosure condition<sup>33</sup>. Results of these type of studies have been interpreted as evidence for the link between inhibition of strong emotions and the development of physical disease<sup>34</sup>. The benefits of disclosure-based interventions may depend on the extent to which individuals become emotionally and cognitively involved in the disclosure process, reorganize the meaning of the traumatic event, and reduce avoidance of the stressful topic<sup>35</sup>.

A number of studies had been conducted including subjects from public healthcare settings, experienced stress due to ill health or trauma<sup>36-39</sup>. It is evident that the expressive writing benefits also extend to the normal population other than students<sup>40,41</sup>. It is noted that the lung function improvises in asthma patients<sup>42</sup> and symptomatic relief is observed in patients with rheumatoid arthritis<sup>43</sup>. Additionally, decreased physical symptoms were observed among the patients of Stage I or II breast cancer having received the medical treatment, after 3 months of the handling with expressive writing showed better outcomes as compared to control group<sup>44</sup>. While there are few outcomes that

indicate reduced health related behaviours due to expressive writing i.e. declining clinical attendance and work absenteeism<sup>45</sup>.

Written disclosure protocols, in which individuals express their thoughts and emotions about traumatic or stressful life events, have been associated with improvements in both psychological and physical health<sup>46</sup>. The effectiveness of GDP in comparison to the standard disclosure protocols is under discussion and various studies have investigated the efficacy of the two. The purpose of designing this randomized control trial is to observe psychophysiological alterations associated with post traumatic growth in traumatic stress subjects.

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## Methodology

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### *Study design*

The study will be conducted as multicenter randomized controlled trial. On the basis of eligibility criteria subjects providing consent to participate in the study will be randomized into two groups, experimental group including those who receive the intervention and a control group receiving control intervention. The study outcomes will be monitored in subjects of both groups at different intervals i.e. at baseline and at 3-month follow-up (post-interventional).

### *Ethical Concerns*

The study protocol was approved by the Ethics Committee of Pakistan Medical Association Committee on Ethics (Reference Code no. 2019/ERC/6-94). And registered by the Clinicaltrial.gov (Registration number NCT04217863)<sup>47</sup>.

### *Participants*

Subjects for the present study will be recruited from 5 centers (based in Karachi, Pakistan). The targeted population includes subjects from diverse ethnicity and considered eligible for participation in the study if they indicated in a pre-screening form that they had experienced traumatic event. These subjects will be invited to



participate in the study through advertisement on notice board of each center. A written informed consent will be obtained from each study subject after providing detailed information regarding objectives of the study and its duration.

### ***Eligibility criteria***

#### **Inclusion criteria**

All subjects fulfilling the below given criteria will be included:

1. Subjects aged 18 years or over
2. Must be disease free, there must be no evidences of any metastatic disease
3. Property of written and spoken English language.
4. Experienced any traumatic event in last 12 Months.

#### **Exclusion criteria**

1. Subjects who received a structured psychological intervention for at least 6 months during the last 3 years performed by a psychologist or psychiatrist will be excluded.
2. Those with codified psychiatric disorder (according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) who received Psychopharmacological treatment during the last 3 years will also be excluded from the study sample.

### ***Interoventions***

The experimental intervention (GDP):

It includes three writing sessions of 20 minutes where the participants will be made to recall the facts regarding the traumatic event first and then the emotions triggered related to the revealed facts will be channelized. The information related to the immediate priority changes due to the revival of the traumatic history and its reflection on current feelings will be collected. Moreover, the learned coping mechanisms will also be inquired and how the traumatic event altered their vision and their personalities and how it helps in coping with future difficulties.

The original instructions will be translated into local language and altered according to

the specific traumatic experience. In the following, a fusion of the tasks concerning each of the three writing sessions is shown.

1. Participants will be required to describe memories associated with traumatic event in a sequential order, with an objective and detached attitude.
2. They will be asked to describe:
  - a. Their opinion regarding the traumatic event and emotions perceived during the experience.
  - b. Its impact on their daily lives, and how it has altered their attitudes toward life.
3. The actual situation will be focused, while reviving the whole traumatic event experience which aids in exploring the following aspects:
  - a. Present thoughts and feelings regarding the traumatic experience, and also clarify the differences between the ones felt at the time of traumatic event in comparison to the current feelings.
  - b. How much they understand and appreciate themselves for successfully dealing with the traumatic event
  - c. To what extent the traumatic event has modified their vision, attitude, knowledge, and skills, and how it can help in their future;
  - d. What will be their future reactions to other similar events.

For the writing session it is mandatory to maintain standard experimental environment with maximum silence so that the subject can write peacefully without getting disturbed. Two weeks after the initial assessment, the first writing session will be performed followed by two sessions once every 2 weeks.

The control intervention:

In control intervention the subjects will be required to take three 20-minute writing sessions, in which they will be asked to write about their daily events of the past week, the writing must focus on the facts and highlight an objective and detached attitude. It has shown potential improvements after the guided disclosure protocol (GDP). Works through the placebo effect. Same protocol



will be followed for these subjects as the one used for GDP.

A day prior to each writing session, in both conditions either experimental or control the researcher will communicate with each study subject via telephone in order to give them a reminder to perform the writing task and to check their understanding regarding the instructions given in the booklet. Details regarding the inability to contact the subject will also be recorded in the patient form.

### **Recruitment & Assessment Procedures**

Recruitment and baseline assessment:

One or more researchers will be involved in the process of recruitment and evaluation. Prior training sessions will be conducted by principal investigator regarding study aims and procedures for all the researchers involved in the study. The participants will be directed towards the researchers who are responsible for explaining the study aims and conduction as well. An information sheet including subject's socio-demographic characteristics will be provided to each individual. A written informed consent will be taken from each subject before initiation of the study. Confidentiality will be maintained during and after the study for both written process and assessment records. A baseline questionnaire (Screening, TSS, PTGI, TSC) and booklet with detailed instructions will be provided to the study subjects according to the groups allocated. The subjects will be kept blinded regarding the study treatment and hypotheses during the study conduction. All the variables (CRP, BDNF, IL-6, Cortisol, HRV, Glutamate and brain waves) will also be measured at baseline.

Post-intervention and follow-up assessments:

After 3 months post-interventional assessment will be performed i.e. Follow-up evaluation, with the same time tolerance as that for baseline. During this the booklets with written scripts will be returned to each of them individually.

### **Procedure**

The Screening questionnaire will be utilized for assessment. Subjects reporting of experiencing at least one traumatic experience are kept inclusive.

### **Study Hypothesis**

1. It is hypothesized that higher scores on the Post-traumatic Growth Inventory (PTGI) will be observed among the subjects enrolled in the GDP group as compared to the control group.
2. We expect the variation in psychophysiological markers i.e. CRP, BDNF, IL-6, Cortisol, HRV and brain waves among the subjects of GDP group as compared to those in the control group.
3. It is expected that lower scores on the Traumatic Stress Scale and Trauma Symptom Checklist 40 (TSC-40) with subscale composition of dissociation, anxiety, depression, SATI, sleep disturbance and sexual problems will be observed among the subjects enrolled in the GDP group as compared to the control group.

### **Measures**

Post-Traumatic Growth (PTG)<sup>48</sup>

PTG will be assessed using the Italian version of the PTGI. This inventory is comprising of 21 questions based on 5 factors. The 1st factor shares spiritual modifications (2 items), 2nd factor relates to self-conception and alterations in viewpoints (Changes in Philosophy) (7 items), 3rd factor describes relationship changes (5 items), 4th factor relates to finding new motivations and interests in life (3 items) and the 5th factor explores the discovery of individual resources attainable by themselves and others (3 items). Respondents will be tracked for the changes that have been produced due to their illness. Likert scale will be used for rating where 0 means no change experienced, to increasing consequently as 5 means change experienced to a greater degree.

Traumatic Stress Scale (Sadaf Stress Scale)<sup>49</sup>

The Traumatic Stress Scale sub section of sadaf stress scale (version 2) measures



exposure to any trauma such as criminal victimization, natural disaster, witnessing or confronting such situations or itself experiencing them as actual or threatened death (or serious injury) to self or others which can dwell a person into traumatic stress. This scale comprises of 8 questions which measures traumatic stress in categories of normal, mild, moderate & severe.

#### Trauma Symptom Checklist<sup>50</sup>

The TSC-40 is a research measure that evaluates symptomatology in adults associated with childhood or adult traumatic experiences. It measures aspects of posttraumatic stress and other symptom clusters found in traumatized individuals. This measure assesses trauma-related problems in categories like Dissociation, Anxiety, Depression, SATI (Sexual Abuse Trauma Index), Sleep Disturbance & Sexual Problems.

#### Brain waves

The voltage fluctuations within the neurons or the electrical activity of neurons due to ionic flow is recorded as brain waves through electroencephalogram while the record itself is the EEG that shows waves or oscillations indicating electrical activity. The (Muse, RRID:SCR\_014418) Brain-Sensing Headband<sup>51</sup> will be utilized to record the brain waves i.e. Alpha waves, Beta waves, Theta waves & Gamma waves.

#### Cortisol

A negative association exists between cortisol and left hippocampal volume among patients with other psychiatric disorders like depression and PTSD due to trauma. Memory and learning skills are affected by elevated cortisol levels. It increases the risk for depression, mental illness, and also decreases the life expectancy. Chemiluminescent micro particle immunoassay (CMIA) will be used for assessment of cortisol levels.

#### Brain-derived neurotrophic factor (BDNF)

The changes in the BDNF Levels are associated with traumatic stress or the changes in the physiological systems in relation to a stress response. Cognitive functioning is mainly altered in cases with alterations in BDNF levels. Human BDNF ELISA (Enzyme-Linked Immunosorbent Assay) kit will be utilized for BDNF assay.

#### C - Reactive Protein (CRP)

For measuring systemic inflammation, CRP is an ideal measure. In vitro immune turbidimetric method will be utilized for the quantifiable determination of CRP in human serum and plasma.

#### Heart Rate Variability

Temperature, heart rate variability, pulse rate, blood pressure will be recorded through Electro Power Lab<sup>52</sup> and analysis through MATLAB.

#### Interleukin-6 (IL-6)

Physical and psychological stress alter plasma cytokines levels particularly interleukin-6 (IL-6). Serum concentrations of IL-6, will be assayed by means of enzyme-linked immunosorbent assay techniques, based on appropriate and validated sets of monoclonal antibodies.

#### Glutamate

Elevated levels of an excitatory neurotransmitter known as "Glutamate" which is an amino acid, is greatly reported in cases of neurotoxicity which causes neuronal death. Glutamate Assay Kit will be utilized for the estimation.

#### Sample size

A sample size of 246 was calculated with at least 123 subjects will be placed in both groups for statistically significant variation of PTG to be observed among GDP versus control groups. It was calculated according to meta-analysis on PTG<sup>53</sup>, where an estimated effect size of 0.36 (equally with both Hedges' g and Cohen's d) with a two-sided test using G power 3.1.3<sup>54</sup>, alpha 0.05 and a power of 0.80.

### Randomization

Subjects on the basis of eligibility criteria will be randomly allocated to the GDP or control group in the 1:1 ratio. Computer generated random numbers are used for randomization. After taking subjects basic information, a unique code will be provided to each included subject by the study center. The code will be mentioned on each form of each individual subject.

### Statistical Analysis

The data will be analysed using  $2 \times 2$  mixed factorial design analysis of variance (ANOVA) in order to calculate whether there exists a significant change in PTG among the subjects of intervention and control group. After intervention if a higher ratio of PTG will be observed in GDP group, the interventional

impact of the five factors of PTG will be examined with further analysis. Sequentially for each secondary outcome further ANOVAs will be used to examine differences between groups at 3 months and after baseline. Adjusted ANOVA will be performed keeping socio-demographic and other variables as co-variants, to determine whether the socio-demographic and other characters could result in alterations in the effect between the two groups. For the effect of GDP on constructed meaning regression-based approach will be utilized. According to previous literature in order to estimate a simple mediation model ordinary least-square regression models is becoming a common practice which is considered as appropriate as structural equation modelling<sup>55-57</sup>.

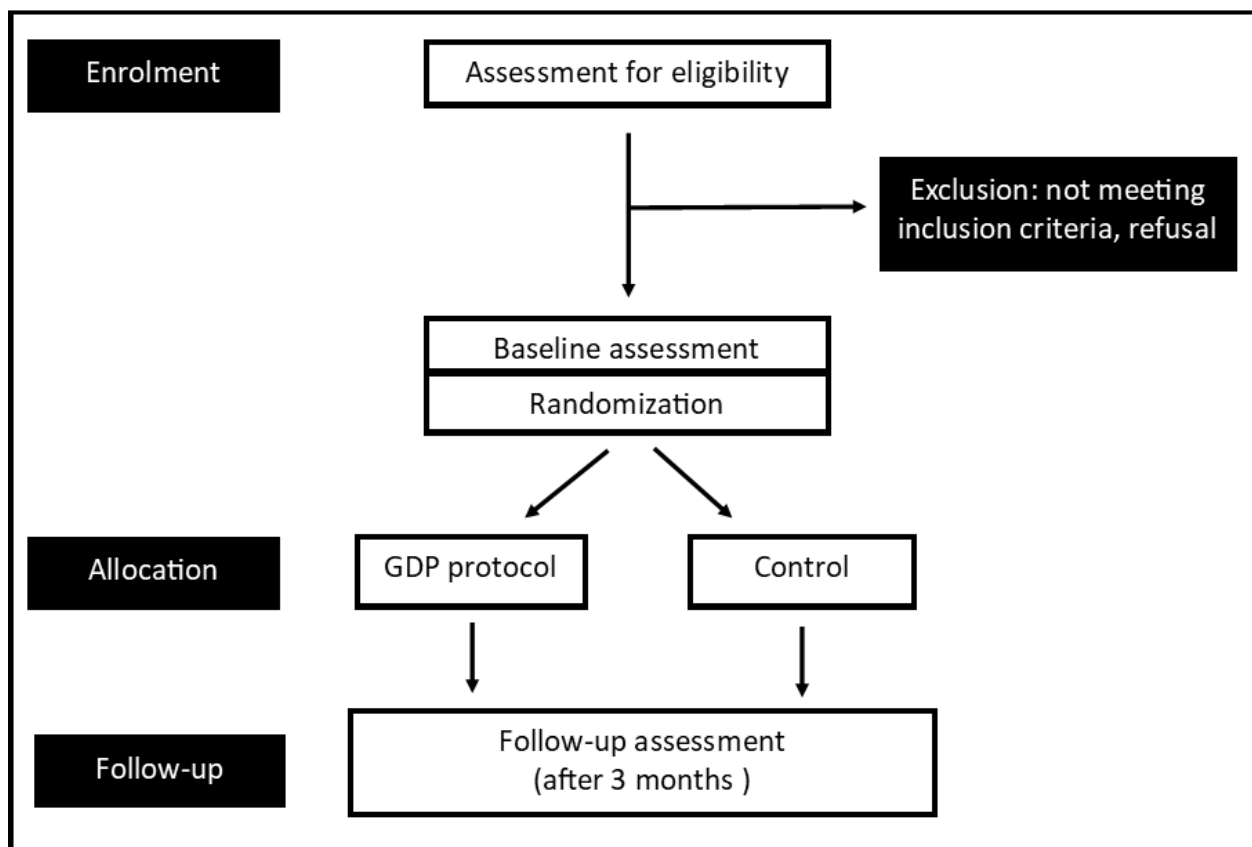


Figure 1: Flowchart of study procedure.



## Discussion

Psychophysiological studies have demonstrated that what individuals think and feel has a measurable effect on the nervous, immune and behavioural responses, demonstrating that the line between physical and mental health is not as solid as we once believed. This might give us insight about application and efficacy of Directed Written Disclosure in a population that is seeking help and underrepresented to be clinical. Moreover, one of the more hopeful findings of this research will be significant information about trauma-related effects that can be managed and possibly reversed and will help trauma survivors for number of specific actions to downregulate their stress response and halt their decline into serious health problems.

Conceptualizing traumatic stress as a disorder of the brain's fear system, with emotional processing dysregulation within its circuitry, has generated a significant body of research over the past decade that has illuminated the neuroimmunological and psychophysiological mechanisms that underlie this problem.

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