

Research Article

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Perceptual Asymmetry in Depression: Role of Co-morbid Anxiety

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Abstract

Background: Vulnerability of depression has often been linked with enhanced right hemispheric asymmetry. However, other emotional states such as stress and anxiety have also been found to be associated with greater activity of the right hemisphere. Since, anxiety disorders are the most commonly reported co-morbidity in depression; it would be interesting to examine the role of co-morbid anxiety in determining the pattern of hemispheric asymmetry in depression. In the view of this, the present study investigated the influence of co-occurring anxiety on the observed pattern of hemispheric asymmetry in depression in processing of emotional information.

Method: Twenty-nine right handed sub-clinically depressed individuals and matched controls were assessed for their level of anxiety (trait and free-floating) and perceptual asymmetry in processing of emotional information. Three emotional tasks for assessing perceptual asymmetry were used- Chimeric face test, facial emotion discrimination task and judgment of emotional valence of positive and negative emotional words.

Results: The analysis of the obtained data revealed that the depressed individuals showed increased left visual field (right hemispheric) bias in processing of facial emotional stimuli and no asymmetry was reported in processing of emotional words when the co-occurring anxiety was not controlled. Further, the findings of ANCOVA revealed that the observed enhanced right hemispheric asymmetry in depression for processing of emotional information is not influenced by the co-existing level of trait anxiety. But contrary to it, the neurotic (free-floating) anxiety played a minimal role as evident by reduction in the observed magnitude of right hemispheric asymmetry in depressed group after statistically controlling its effect.

Conclusion: The findings indicated that anxiety does not have any significant influence on the observed pattern of hemispheric asymmetry in depression and further, the findings are discussed under the light of several theoretical observations of role of co-morbid anxiety in the pattern of hemispheric asymmetry in depression.

Keywords: Depression; Anxiety disorders; Perceptual Asymmetry; Co-morbid anxiety

Introduction

Anxiety disorder is the most prevalent psychiatric co-morbidity in depression [1-3] and many researchers argue that it is present in lesser or greater degree in almost all cases of depression [4,5]. The clinical picture and severity of symptoms become worse in patients having incidence of psychiatric co-morbidity in depression and these observations pose a methodological difficulty in uncovering the underlying hemispheric base of depression inasmuch as both anxiety and depression are associated with negative affect and both conditions generally co-occur in a patient. Thus, any study of hemispheric asymmetry in depression is fraught with methodological difficulty of differentiating how far the observed hemispheric changes in depression is due to the clinical syndrome of depression and how far it is associated with symptoms of anxiety. Delineating the difference in hemispheric functioning associated with depression and co-morbid anxiety disorder becomes further complicated by the fact that both are associated with higher prevalence of negative affect that has often been associated with a pattern of hemispheric asymmetry similar to that observed for anxiety and depression. Considering anxiety while investigating brain function in depression has been repeatedly emphasized [6-11] inasmuch as both depression and anxiety may be associated with different pattern of hemispheric functioning [9] and the possibility that co-morbid presence of anxiety disorders can alter the observed pattern of hemispheric asymmetry in depression has been empirically demonstrated in various studies [12-14].

Further, several studies dealing with the nature of hemispheric asymmetry in depression with the intent to measure of co-morbid issues have suggested less consistent findings using perceptual

asymmetry measures and scarce attempts has been done in this area. For example, Pine et al. [15] assessed perceptual asymmetry using verbal stimuli [fused word test] in patients with major depression (with and without anxiety disorder) and observed that both patients with major depression without anxiety disorder exhibited enhanced right ear/left hemispheric advantage in processing of fused words. Whereas, patients with anxiety disorder displayed a reduced right ear/left hemisphere in processing of fused words. This observation suggests that major depression without anxiety is linked with enhanced left hemisphere advantage, whereas depression with anxiety is associated with reduced left hemispheric bias.

The aforesaid review of literature revealed that the co-morbid presence of anxiety disorder may alter the pattern of hemispheric asymmetry in depression inasmuch as several researchers reported a differential pattern of hemispheric asymmetry in depression with and without anxiety [12-15]. For example, Keller et al. [11] found depression to be linked with reduced right hemisphere while anxiety to be associated with increased right hemispheric bias. Similar findings of opposite pattern of hemispheric asymmetry in depression and anxiety also been reported by others.

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The above mentioned studies thus, extend the hypothesis that both anxiety and depression may share similar hemispheric substrate (e.g., RH overactivation) or may have different hemispheric pathophysiology (e.g., RH overactivation in anxiety and RH under-activation in depression). In the former case the co-morbid presence of anxiety disorder is likely to add to the enhanced RH functioning in depression, and thus it is likely that the studies which have observed abnormally higher RH functioning in depression might have failed to control or assess the role of co-morbidity of anxiety disorder. This speculation is based on the observation that most of the studies reporting enhanced RH functioning have not explicitly mentioned that how co-morbidity of anxiety disorder was handled. In the latter case (i.e., opposing pattern of hemispheric asymmetry in anxiety and depression), it is likely that the co-morbid presence of anxiety may neutralize or reduce the generally observed enhanced RH functioning. Therefore, based on such observations the present study attempts to examine the role of co-occurring anxiety in the observed pattern of hemispheric asymmetry in depression by statistically controlling the effect of trait and free-floating anxiety and hypothesize that the pattern of hemispheric asymmetry in processing of emotional information observed in individuals with sub-clinical depression before controlling anxiety would differ from that observed after statistically controlling it.

Method

Sample

The study was conducted on twenty nine right handed sub-clinically depressed (identified on the basis of BDI; score of moderate to severe depression 19-29) university students and twenty nine age and gender matched non-depressed (BDI score less than 9). Further, participants who reported any history of present or past psychiatric illness, present or past history of neurological disorder and/or brain injury were not included in the present study.

Materials

Several tools and tasks (especially designed for the assessment of hemispheric asymmetry) were used. Following are the details of the tools and tasks used in the present study.

1. The Hand Preference Measure developed by Mandal and associates was used as a screening measure to identify right handed participants for the present study. This scale consists of 22 items that ask about the use of preferred hand in performing various types of unimanual activities. The average rating of 22 items for a given subject is calculated and a score of 6 and above indicates right-handedness.

2. The Beck Depression Inventory was also used as a screening measure to identify sub-clinically depressed and non-depressed participants. In BDI the testee rates the presence of the aforesaid symptoms using a series of four-point ordinal scales (ranging scale from 0 to 3). Individual category scores are summed to produce a total BDI scores. It assesses the cognitive, affective, and vegetative symptoms of depression. Higher score indicates greater level of depression.

3. The Self Evaluation Scale developed by Tripathi and Rastogi was used to assess the level of trait and free-floating anxiety of the participants, as anxiety was used as a co-variate. The trait anxiety subscale consists of twenty eight items, whereas the free-floating anxiety subscale has twenty four items. Both scales utilize a five point rating scale ranging from 1 (seldom) to 5 (always). There are several negatively keyed items on both scales which are scored in reversed order. The alpha coefficient of trait and free-floating anxiety scale was found to be 0.869 and 0.892 respectively.

Experimental Tools

The following experimental tasks for assessing hemispheric asymmetry in processing of emotional stimuli were designed using Super Lab Pro4. Here, it is important to mention that, chimeric face test was used under free-viewing measure, and rest two experimental tasks were used under split-field technique.

Chimeric face test

Chimeric Face Test similar to that proposed by Campbell was used in the present study to assess hemispheric asymmetry in processing of facial expressions of emotions. In this test half happy and half neutral face composites (chimeras) of the same poser is developed and its mirror reversed image is paired with it. The pairs are presented in top-bottom fashion. The emotional expression and its intensity remain same in each pair except that the happy hemi-face appears to the left of the respondent in one chimeric face and to the right in the other. Since, both chimera were of same expresser and of same emotional intensity, judging a specific chimeric face as more expressive reveals the effect of visual hemi-field. There are 32 pairs of chimeric faces in this test. The respondents were asked to indicate which of the two faces in a given pair appears to be happier to them. The responses were coded as leftward or rightward according to the side of the happy hemi-face.

Emotion discrimination task

The photographs of facial expressions of six universally recognized emotions (happy, sad, fear, anger, disgust and surprise) were used. The task was designed in split-field method using Super lab 4.0. On each trial, subjects were shown a unilateral presentation of photograph of facial expression of emotion (target emotion) followed by another photograph either with the same or different facial emotions (test emotion) on the center of the screen. The participants' task was to judge whether the target and test facial expressions of emotions were same or different. A central fixation dot with an arrow inside for 500 milliseconds was appeared and then a photograph of facial expression either to the LVF or RVF for 150 milliseconds was presented. The third event appeared immediately that presented a recognition slide containing facial expression of emotion (either emotion same to the target or different emotion) posed by a different expresser. The recognition slide was replaced by the fourth event- the response recording screen in which the response 'Same' and 'Different' appeared at the center of the screen along with the numeric response code 1 (for same) and 2 (for different). The final (fifth) event was presentation of blank white screen. Thus, the whole task consisted of a block of 48 trials [6 (emotions: happy, sad, anger, fear, disgust and surprise) X 2 (gender of posers: male and female) X 2 visual-field (left and right) X 2 response (same and different)].

Valence judgment task

In this task, a set of twelve positive and negative emotional words were used. On each trial either positive or negative emotional word was unilaterally presented, participants were asked to judge whether the word represents positive emotion or negative emotion. Following the similar experimental procedure of earlier task, a central fixation was presented with unilateral presentation of either a positive or negative emotional word. Immediately after this, the third event appeared (a recognition slide displaying two responses positive emotion and negative emotion with numbers 1 and 2 respectively). This slide appeared at the center of the screen until the participants verbally gave their response while pressing the response key (space bar). After the response of the participants, the third recognition slide was replaced by

the fourth event-the response recording screen which was identical to the recognition slide but was presented for the experimenter to record the correct response of the participants. The fifth event was similar to the earlier two tasks (a black white screen) which served the purpose of providing an inter-trial (break) screen and a mask to erase the iconic memory. Following this sequence and procedure a block of 48 trials [24 (stimuli-12 positive and 12 negative) X 2 visual-field (left and right)] were used.

Procedure

After screening of the sub-clinically depressed and non-depressed participants, measure of co-variate was administered along with the experimental task. First of all, CFT was administered individually. After that, participants performed on the experimental tasks one by one. Participants were given practice trials before they were exposed to actual experimental tasks. When the participants learned to perform on emotional discrimination and valence judgment, tasks, then the actual experimental tests was administered individually to each participant. The response of each participant was scored and saved in the computer through the same computer programme that was used to administer the experimental tests. The scoring for these tasks was calculated for each visual-field separately.

Results

To examine the role of trait anxiety (TA) in the observed hemispheric differences between depressed and non-depressed groups in the judgment of emotional intensity of happy-neutral chimeric faces a 2 (groups: depressed and non-depressed) X 2 (visual-fields: left and right) ANCOVA with repeated measure on the last factor was conducted, treating trait anxiety as a co-variate. The main effect of visual-field and the interaction of the Group X Visual-field (VF) remained statistically significant even after controlling for TA. A negligible difference in the level of significance and effect size of interaction of Group X VF was noted after controlling ($p=0.002$, $\eta_p^2=0.157$) TA, compared to before controlling it ($p=0.003$, $\eta_p^2=0.149$).

The fact that TA does not alter the observed pattern of hemispheric asymmetry becomes evident when the mean LVF and RVF preference scores of depressed and non-depressed are compared before and after. The overall, findings suggest that enhanced RH asymmetry observed among depressed individuals in processing of emotional intensity is not influenced by the level of co-existing TA.

To examine the role of free-floating (neurotic) anxiety (FFA) on the observed hemispheric differences between depressed and non-depressed groups in processing emotional intensity of happy-neutral chimeric faces, a similar two way ANCOVA was done using FFA as a co-variate (Figure 1a and 1b).

The main effect of VF remained unchanged even after controlling FFA, a change was noted in the significant interaction of Group X VF in terms of effect size and level of significance ($p=0.002$, $\eta_p^2=0.157$). The effect size of this interaction was 0.149 when the effect of FFA was not controlled but it reduced to 0.083 after controlling the co-variance of the FFA. This reduction in the effect size of the interaction of Group X VF after controlling for the effect of FFA suggests that co-morbid presence of neurotic anxiety in depression may alter the observed pattern of hemispheric asymmetry to some extent. The difference of the effect size of this interaction before and after controlling for the effect of FFA ($0.149-0.083=0.066$) indicates the amount of variance (around 6.6%) in the hemispheric asymmetry attributable to FFA. However, observation of the significant interaction after eliminating the effect of free-floating anxiety, only a mild reduction in the explained variance (6.6%) suggests that FFA has only a partial or very mild effect on the observed pattern of hemispheric asymmetry in depression in processing of emotional intensity.

The mean preference scores of depressed and non-depressed participants across the two VF in processing of emotional intensity of happy-neutral chimeric faces (before and after adjusting for the effect of free-floating anxiety) have been displayed in Figure 2a and b.

The comparison of Figure 2a and b reveals that the LVF advantage (reflected by a positive difference between LVF and RVF) observed in depressed group before controlling the effect of FFA was 9.932 (Figure 2a) and after controlling the effect of FFA (Figure 2b) it slightly reduced to 9.358 considered to be almost negligible (0.574).

To sum up, the findings of preceding analyses examining the role of trait and FFA on the pattern of hemispheric asymmetry in sub-clinically depressed individuals suggest that while TA does not alter the pattern of hemispheric asymmetry in depression, the FFA (neurotic) has only a mild and almost negligible influence on it.

Data obtained on the facial emotion discrimination task indicated that the main effect of VF as well as the interaction of Group X VF for this task not only remained statistically significant after controlling for the effect of TA but no change was noted in terms of effect size of the

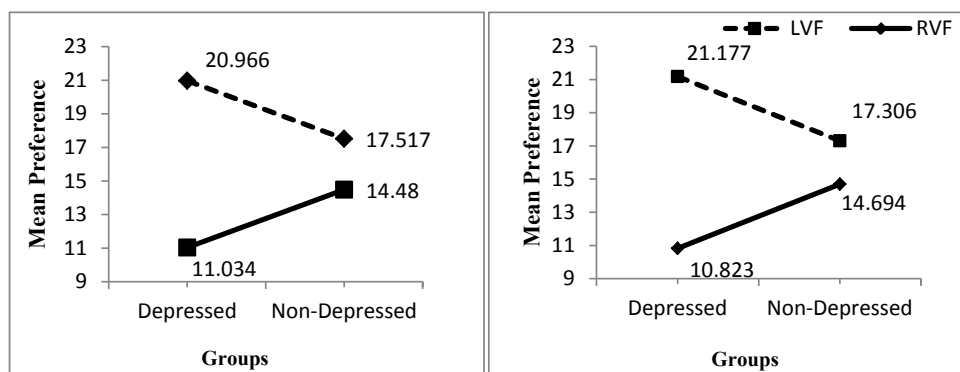


Figure 1a: Before Controlling TA

Figure 1b: After Controlling TA

Figure 1: The interaction of Group X Visual-field before and after controlling for the effect of trait anxiety.

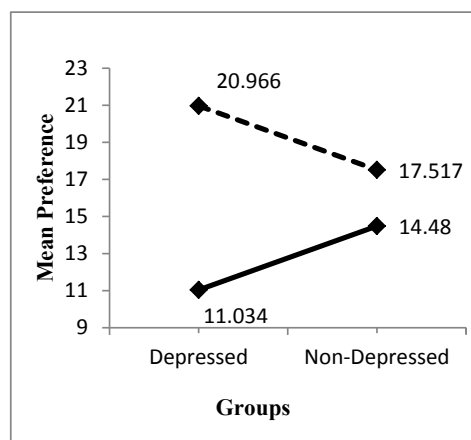


Figure 2a: Before Controlling For FFA

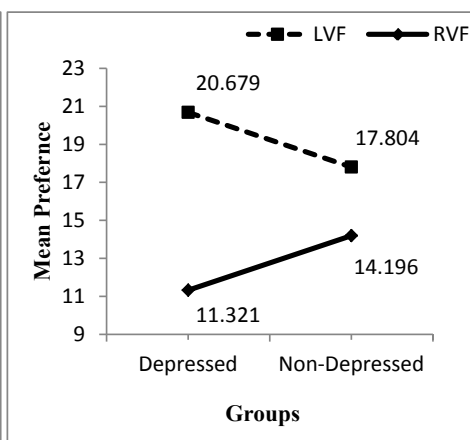


Figure 2b: After Controlling For FFA

Figure 2: The interaction effect of Group X Visual-field before and after controlling for the effect of free-floating anxiety.

main effect of VF [η_p^2 before (0.385) and after controlling (0.385) TA], as well as in the interaction of Group X Visual-field [η_p^2 before (0.130) and after controlling (0.138)].

This finding supports the previous observation that the observed enhanced right hemispheric asymmetry in depressed group is not influenced by the co-occurring TA. The observed stability in the level of significance and effect size of the interaction of Group X VF before and after controlling TA is supported by the observation of a similar pattern of mean difference in the LVF and RVF scores of depressed and non-depressed groups under the two conditions (see Figure 3a and b).

A similar 2 (groups: depressed and non-depressed) X 2 (visual-fields: left and right) ANCOVA with repeated measure on the last factor was conducted using FFA (mean centered score) as a co-variate for emotion discrimination task. Findings revealed that the main effect of VF and the interaction of the Group X VF which was statistically significant before controlling the FFA remained statistically significant. Moreover, very negligible change in the effect size of the main effect of VF was noted. The effect size of this interaction reduced by 0.02 (before controlling ($\eta_p^2=0.130$) after controlling ($\eta_p^2=0.111$)).

This negligible influence of FFA on observed pattern of hemispheric asymmetry in sub-clinically depressed group is evident from a similar pattern of mean perceptual accuracy difference between LVF and RVF for both conditions i.e., before (3.621) and after (3.693) controlling FFA (see Figure 4a and b).

Overall, the finding of the preceding analysis brings us to fore that the co-existing level of TA does not influence the nature of hemispheric asymmetry in sub-clinically depressed individuals either in processing of emotional informations of both tasks. Similar to this FFA (neurotic) also fail to show a substantial influence on the nature of hemispheric asymmetry observed in depressed group. Though, a mild effect of FFA was noted for emotional intensity judgment task, the comparison of the LVF (right hemispheric) advantage before and after controlling FFA revealed that this effect was negligible.

Sub-clinically depressed and non-depressed individuals were examined on the emotional words using a 2 (groups: depressed and non-depressed) X 2 (visual-fields: left and right) X 2 (valence: positive and negative emotional words) ANCOVA with repeated measure on the last two factors and the effect of TA and FFA was examined in

determining the hemispheric differences. Mean-centered scores of TA was treated as a co-variate in one analysis and the FFA (mean centered score) in the other. Findings revealed that none of the main as well as interaction effects were found to be statistically significant either before or after controlling the effect of TA except the interaction of Group X VF which was significant both before and after controlling TA. Further, the level of significance and effect size of the interaction of Group X VF also remained unchanged both before ($p=0.039$, $\eta_p^2=0.074$) and after ($p=0.047$, $\eta_p^2=0.070$) for the effect of trait anxiety.

This stability in the effect size of this interaction is evident from the comparison of difference in the mean perceptual accuracy scores between LVF and RVF before and after controlling the co-variance attributable to TA (see Figure 5a and b). The comparison of Figure 5a and b clearly suggests that the pattern of perceptual (hemispheric) asymmetry in processing of words (irrespective of its emotional valence) shown by depressed and non-depressed groups before controlling TA is almost comparable to that obtained after controlling for the effect of TA. This pattern of finding implies that the observed hemispheric anomaly in sub-clinically depressed individuals in processing of words (irrespective of valence) is not influenced by co-existing TA.

A three way repeated measure ANCOVA similar to the previous analysis was performed to examine the effect of the FFA on hemispheric differences between sub-clinically depressed and non-depressed groups in processing of emotional valence of words. Findings revealed that the interaction of Group X VF became non-significant after controlling it (before $p=0.05$ and after $p=0.064$). Further, a nominal change was also seen in terms of reduced effect size (before $\eta_p^2=0.074$ and after $\eta_p^2=0.061$). The findings though, suggest a statistically significant effect of FFA on the observed pattern of hemispheric asymmetry in depressed group (in processing of words irrespective of valence), it is theoretically not significant as the FFA accounted for only 1.3% of the total variance of this interaction. The findings suggest that similar to TA, the FFA also does not alter the pattern of hemispheric asymmetry in depression.

Findings suggest that FFA does not have any substantial influence on the observed pattern of hemispheric asymmetry in processing of words (irrespective of emotional valence) is evident in the change in the pattern of mean perceptual accuracy shown by depressed and non-depressed groups after controlling FFA (Figure 6a and b). The RVF

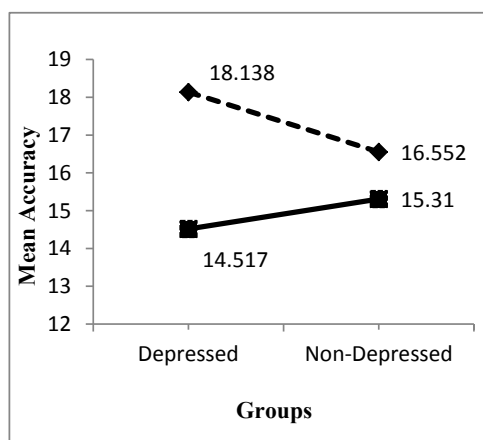


Figure 3a: Before Controlling TA

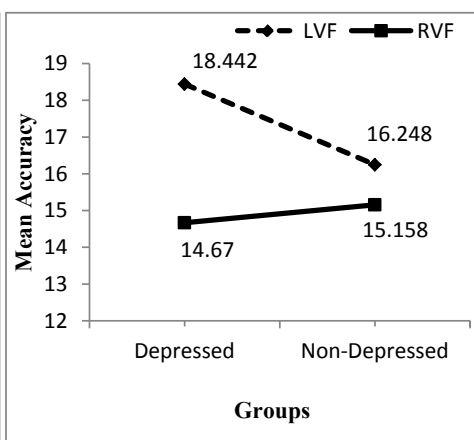


Figure 3b: After Controlling TA

Figure 3: The interaction of Group X Visual-field before and after controlling for the effect of trait anxiety.

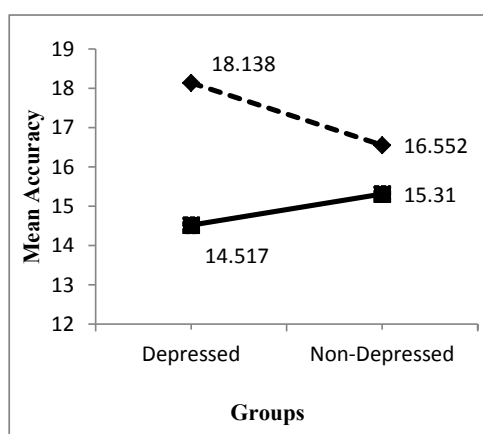


Figure 4a: Before Controlling FFA

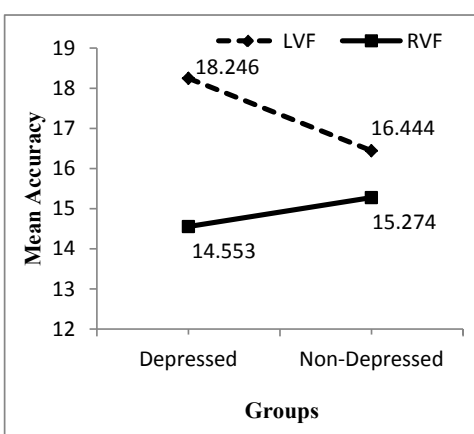


Figure 4b: After Controlling FFA

Figure 4: The interaction of Group X Visual-field before and after controlling for the effect of free-floating anxiety.

(LH) advantage observed in non-depressed group before controlling FFA ($RVF-VF=0.483$; Figure 6a) was only slightly lower than that obtained after controlling it ($RVF-LVF = 0.520$; Figure 6b).

Briefly, the obtained statistical evidences after controlling the effect of TA and FFA suggest that both forms of anxiety do not have much influence on the observed pattern of hemispheric asymmetry in depression. Though, a statistical significant influence of FFA was though, noted on the observed pattern of hemispheric asymmetry between depressed and non-depressed groups (in processing words), its impact is very nominal and practically insignificant.

Discussion

The present study aims to examine the effect of anxiety on the observed pattern of hemispheric asymmetry in depressed individuals. The observation of the study suggests that anxiety do not have any influence in determining the nature of asymmetry in depression. Though, the present analysis seems to be contradictory to the earlier observations that co-morbid presence of anxiety alters the pattern of hemispheric asymmetry in depression, the finding of the present study

revealed that the co-existing level of TA does not influence the pattern of observed hemispheric asymmetry (in processing of facial emotions) in sub-clinical depression. Further, FFA (neurotic) has only minimal (almost negligible) effect on the pattern of hemispheric asymmetry in depression for processing of facial expressions of emotions.

Therefore, the present observation of enhanced hemispheric asymmetry in depression remained unchanged (same) both before and after controlling the co-variance attributable to trait and free-floating anxiety extends the hypothesis that co-morbid presence of anxiety in depression is less likely to alter the nature of hemispheric asymmetry in depression. This observation, though a contrast with the earlier findings that have suggested that depression with anxiety is associated with either over-activation of the right hemisphere [12,16] or reduced right hemisphere activation [13,14]. Thus, the present observation, poses a difficulty in deducing the role of anxiety in hemispheric asymmetry in depression.

The close glance of the methodology used in previous studies [12,14,16] brings to fore that all of them have assessed cortical arousal asymmetry at resting state using EEG or brain imaging techniques.

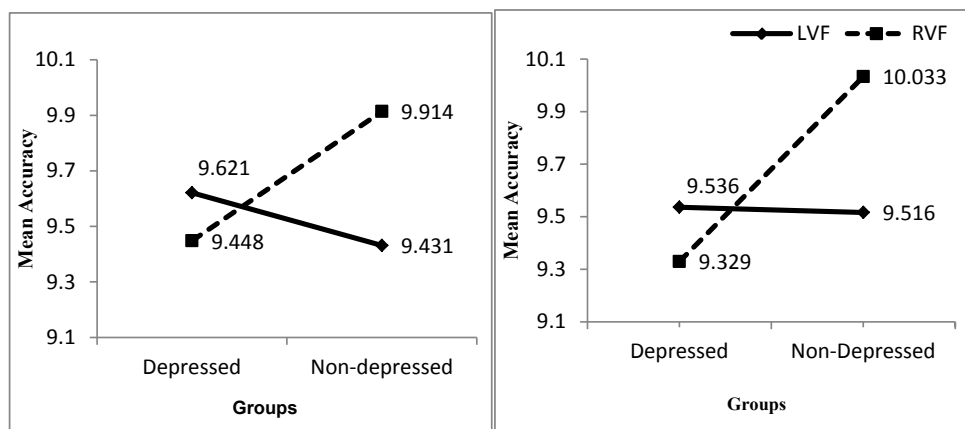
**Figure 5a:** Before Controlling TA**Figure 5b:** After Controlling TA

Figure 5: The interaction of Group X Visual-field before and after controlling the effect of trait anxiety.

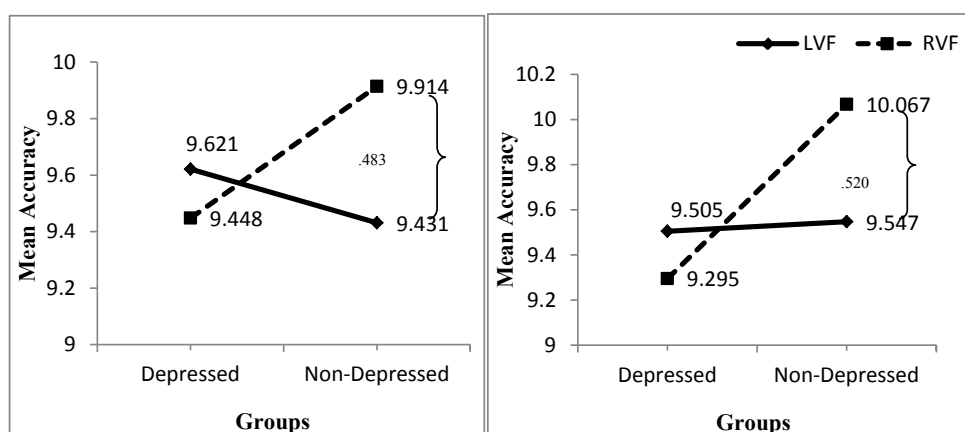
**Figure 6a:** Before Controlling FFA**Figure 6b:** After Controlling FFA

Figure 6: The interaction of Group X Visual-field before and after controlling for the effect of free-floating anxiety.

Moreover, those studies were performed on the cases of clinical depression with or without symptoms of anxiety disorder where, psychiatrically diagnosable anxiety disorders represented the co-morbidity. Hence, it appears that methodological differences would be one of the observed differences in findings.

The earlier studies have suggested that anxiety influences only the characteristic arousal asymmetry not the functional aspects in hemispheric asymmetry. The co-morbidity in anxiety in depression is more likely to influence the level of neuronal activity of cerebral hemisphere (arousal asymmetry) and less likely to influence the hemispheric organization of psychological functioning or processes. The finding thus, should not be interpreted as reflection of inconsistency in findings; rather such differences reflect the difference in the assessment of different aspects of hemispheric functioning.

To sum up, the aforesaid finding that variation in the level of co-occurring anxiety does not influence the enhanced right hemispheric performance for processing of emotional information in depressed individuals suggests the possibility that co-morbid presence of trait and free-floating anxiety does not alter the functional hemispheric

organization (emotional processes) in depression but an altered asymmetry in depression in earlier studies was due to 'characteristic right hemisphere arousal'. However, this theoretical speculation needs further empirical verification before its generalization inasmuch as the findings of the present study does not rule out other alternative explanations of the observed differences in the present finding and those reported by earlier researchers. For instance, it has been reported by several researchers that variations in the degree, severity, and type of co-occurring anxiety is an important factor related to differential pattern of brain activation in depression. Therefore, it is likely that failure to observe the influence of co-occurring anxiety on the observed pattern of hemispheric asymmetry in depression may be because of the lower degree or severity of the co-existing anxiety and not because of the differential influence of anxiety on different aspects (arousal versus specialization) of hemispheric asymmetry.

Thus, it can be concluded from the present observation that enhanced right hemispheric asymmetry in depression is not influenced by the co-morbid presence of anxiety. However, the findings have significant theoretical implication that if depressed individuals are also having symptoms of anxiety even then the observed pattern

of hemispheric anomaly in them (for processing of emotions) is not likely to alter which implies that hemispheric asymmetry in depression is selective and limited to certain psychological process of psychopathology.

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