Aggression as an independent entity even in psychosis – The role of cortisol

Sourav Das\textsuperscript{a)}, Soumik Sengupta\textsuperscript{b}, Kangkan Pathak\textsuperscript{b}, Divyashree Sah\textsuperscript{c}, Sumit Mehta\textsuperscript{b}, Priya Ranjan Avinash\textsuperscript{b}, Aparajeeta Baruah\textsuperscript{b}, Sailendra Kumar Deuri\textsuperscript{b}, Anil Sarmah\textsuperscript{d}, Vijay Gogoi\textsuperscript{b}, Kamal Narayan Kalita\textsuperscript{b}, Jyoti Hazarika\textsuperscript{e}

\textsuperscript{a} Somnos Sleep Clinic, Kolkata, WB, India
\textsuperscript{b} Dept. of Psychiatry, LGB Regional Institute of Mental Health, Tezpur, Assam, India
\textsuperscript{c} Dept. of Psychology, Kumaon University, Nainital, UK, India
\textsuperscript{d} Dept. of Pathology, LGB Regional Institute of Mental Health, Tezpur, Assam, India
\textsuperscript{e} Dept. of Microbiology, LGB Regional Institute of Mental Health, Tezpur, Assam, India

\section*{ABSTRACT}
Aggression is a common entity in psychiatric disorders, particularly psychotic disorders. Glucocorticoid hypofunction has been linked to abnormal forms of aggressive behavior in various studies in a ‘possibly causal’ role. We hypothesise that aggression, even among those having psychosis is associated with glucocorticoid alterations similar to those who are aggressive but not psychotic. To our knowledge, this is the first study attempting to look at the cortisol functioning in relation to both aggression and psychosis. The present study included 80 participants divided into four groups depending upon presence or absence of aggression and psychosis. Morning cortisol, afternoon cortisol and their variability were measured using ELISA. The groups were compared on measures of aggression, psychosis, morning cortisol, afternoon cortisol and their variability using standard statistical instruments. The present study found lower levels of morning cortisol, afternoon cortisol and cortisol variability among the aggressive group (vs. non aggressive group) and among the diseased group (vs. non diseased group). The differences were most marked for cortisol variability which was related to both aggression and psychosis independently. There were statistically significant correlation between cortisol variability and aggression, which was retained even after controlling for psychosis. There was no significant correlation of cortisol variability with psychosis severity (after controlling for aggression score) or with age, gender or duration of psychosis. We conclude that aggression, even among patients with psychosis, is an independent entity characterized by lower levels of morning cortisol and cortisol variability. The etio-pathology may lie in some altered neuro-immune parameters executed by cortisol and psychosis as trigger.

\section{1. Introduction}
Aggression is a common entity in psychiatric disorders, particularly psychotic disorders, often being the first or main symptom for which the patient is admitted or receives medical attention (Mohr and Pecenak, 2005). Various studies report the prevalence of aggression in psychosis patients in the range of 34–70\% (Spidel et al., 2010; Large and Niesssen, 2011; Huber et al., 2014). The usual victims are usually acquaintances and fellow patients only preceded by medical personnel (Mohr and Pecenak, 2005). As of now, there is no treatment approved for aggression in psychosis patients, and patients are managed with medications on a trial and error basis mostly (Mauri et al., 2011). Among the predictors of aggression are previous aggressive episodes, involuntary hospitalisation, drug abuse, higher psychopathology scores, paranoid thoughts, acute psychosis, presence of hostility/impulsivity, longer hospitalisation etc (Cornaggia et al., 2011). Cause of such aggression in patients with psychosis is a subject matter of many recent studies and different perspectives like emotional recognition deficit, metacognition deficit, cytokine alteration have been explored for the same (Malone et al., 2012; Bo et al., 2014; Das et al., 2016). Najjar and Pearlman concluded that neuroinflammation is associated with white matter pathology in people with psychosis, even at first episode of presentation, in a recent review article (Najjar and Pearlman, 2015). Glucocorticoid hypofunction has been linked to abnormal forms of aggressive behavior, characterized by reduced offensive threats, more preferential attacks towards vulnerable body parts of opponents in a ‘possibly causal’ role (Haller et al., 2001). Glucocorticoid is hypothesised to modulate monoamine secreting synapse via glucocorticoid
receptors in key areas of brain (Clark et al., 2007). Animal models show that such mediation leads to incorrect interpretation of social context, thereby resulting in aggressive behavior (Haller et al., 2013). Glucocorticoids, like Cortisol, have antiinflammatory properties, one way of manifestation of which is suppression of inflammatory cytokines (Fantuzzi and Ghezzi, 1993). Cytokines are hormone like, low-molecular-weight proteins, secreted by various cell types, which regulate the intensity and duration of immune response and mediate cell-to-cell communication. In this sense, it modulates the immune response via the so called ‘immune-adrenal axis’ (Mosmann and Sad et al., 1996).

Recently, cytokines have been implicated in aggressive behavior in healthy individuals as well as patients with psychosis (Provençal et al., 2013; Das et al., 2016). So it appears that there are structural and functional alterations of brain circuits in aggressive individuals which is precipitated by heredity and environmental stress. Exactly how glucocorticoid mediates such action is the subject of various investigations, though, it’s beyond doubt that there is complex, bidirectional communication within nervous, endocrine and immune systems (Blalock, 1989; Blalock, 1990).

We hypothesise that aggression, even among those having psychosis is associated with glucocorticoid alterations similar to those who are aggressive but not psychotic. Psychosis is associated with neuroinflammation, which somehow activates the pathway of aggression. Aggression is an independent entity, the resultant of a proinflammatory state, both in absence and presence of psychosis. We attempted to study the morning cortisol, afternoon cortisol and cortisol variability (difference between morning and afternoon saliva cortisol levels) in our study population which was divided into four subgroups, depending upon presence and absence of psychosis and aggression. This is a part of our earlier reported study on the role of inflammatory cytokines in aggression and psychosis (Das et al., 2016).

To our knowledge, this is the first study attempting to look at the cortisol functioning in relation to both aggression and psychosis.

2. Methods and materials

2.1. Site

The study was done in LGB Regional Institute of Mental Health, Tezpur, Assam, a tertiary care centre of excellence in psychiatry under the Ministry of Health and Family Welfare, Govt. of India. Being the ‘Regional institute’ of the entire North Eastern India, it has a large catchment area including seven North Eastern states of India and also West Bengal.

2.2. Participants

The study was done on 80 participants, in whom, 58 were patients having psychosis, whereas, 22 were healthy volunteers selected by advertising within the hospital campus (No payment was done in any form to the volunteers). Due clearance was taken from the institutional ethics committee before initiating the study and written informed consent were taken from each patient and their relatives.

2.3. Inclusion- exclusion criteria

During the period of three months, all the patients advised inpatient admission by the consultant psychiatrist of the day (n = 421) were approached. Only those who were admitted with a diagnosis of ‘Psychosis’ according to ICD 10 Diagnostic Criteria by the consultant psychiatrist (n = 328) and scored above 75 in PANSS (for establishing psychosis of ‘moderate severity’ or above) (Mortimer, 2007) were included for application of the inclusion exclusion criteria. Those within the age group of 18–60 years who gave written informed consent for the study were included. The exclusion criteria included those with primary/comorbid substance use disorder (other than tobacco use), mental retardation/autism/dementia/axis II diagnosis, regular 2nd generation antipsychotic or antidepressant use in last 3 months, electro convulsive therapy in last 3 months, depot antipsychotic inj. Use in last 6 m. or with physical examination suggestive of any infection or chronic disease or h/o infection/fever in last 3 months or any h/o chronic cardiac, pulmonary, hepatic, rheumatic, neurologic or kidney, h/o hormonal medications/immunosuppressant in last 3 month or with altered blood routine investigation parameters after admission. Finally, those who didn’t read or understand English were excluded. The exclusion criteria were made stringent so as to remove any condition that alters the inflammatory state of the body as far as practicable. Similar inclusion exclusion criteria were applied for the volunteers (except PANSS score). Lifetime History of Aggression Scale (LHAS) was applied to divide the patients as well as volunteers into aggressive and non-aggressive (trait aggression) based on cut off score of 12 (Coccaro and Berman, 1997). Since the catchment area of the study site included people from multiple states, having multiple local dialects and mother tongues, only those who were comfortable in English were included in the study and the original version of the LHAS was used. In most states of India, English is still used as the common language for communication between individuals of different native tongues. Using LHAS, the 58 patients were divided into 36 aggressive patients with psychosis (Aggressive diseased, AD) and 22 non aggressive patients with psychosis (Non Aggressive Diseased, NAD). Similarly, 22 volunteers were divided into 11 aggressives without psychosis (Aggressive Non Diseased, AND) and 11 non aggressives without psychosis (Non Aggressive Non Diseased, NAND).

2.4. Procedure

The saliva samples for measuring cortisol were collected on the next day following admission. The patients were requested not to eat or drink anything after getting up in the morning, including tobacco. On the next day following admission (Day 1), within 15 min after waking up (around 6 a.m.), each patient was requested to rinse his mouth thoroughly with plain water, without any toothpaste or sanitizer. Ten minutes after rinsing the mouth, 2 c.c. saliva sample was collected by Passive Drooling method using 2 in. polypropylene straws and the saliva was collected in a polypropylene vial which was stored at 4 degree centigrade from 2 to 3 h before centrifugation and deep freezer storage.

Out of 58 patients, 13 were uncooperative or refused to give saliva on Day 1. Their saliva was collected on a later date, but within Day 7. The afternoon sample was obtained only when the morning sample had already been collected.

After 8-10 h of Collection of the Morning Saliva sample (around 2–4 p.m.), the Afternoon Sample was collected in the same process as before. The patients were requested and monitored for not taking any food or liquid except plain water for 2 h prior to sample collection. For 4 patients, afternoon saliva could not be collected on Day 1, due to mistakenly taking food (2 patients) or non-cooperation (2 patients), though Morning samples were collected. Morning samples were discarded and repeated again for those 4 patients on the day of the afternoon sample collection. For those 4 patients, along with the 13 patients not giving saliva on Day 1, sample was collected at a later date, but all were collected within Day 7.

At the time of sample collection, the patients were free from medications except oral and/or injectable benzodiazepines given on PRN basis.

Saliva samples were collected from the volunteers following same protocol before analysis.

Before storage in the deep freezer [Deep Freezer, Revco Ultima Plus (model no- 5312, sl no.- 826509-7), from Thermo Scientific] at minus 40 degrees centigrade, the samples were centrifuged at 3000 rpm for 5 min for separating the mucin and other debris and only the supernatant was collected. Cortisol was assessed using Cortisol ELISA Kit
دریافت فوری متن کامل مقاله

امکان دانلود نسخه تمام متن مقالات انگلیسی
امکان دانلود نسخه ترجمه شده مقالات
پذیرش سفارش ترجمه تخصصی
امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
امکان دانلود رایگان ۲ صفحه اول هر مقاله
امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
دانلود فوری مقاله پس از پرداخت آنلاین
پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات