NEUROPSYCHIATRIC DISORDERS

Othello syndrome—at the interface of neurology and psychiatry

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Othello syndrome, as demonstrated by Shakespeare's fictional character of that name, describes individuals with severe delusional jealousy. Retrospective analysis of data from patients with this syndrome suggests that it is frequently associated with neurological disorders, particularly those affecting the right frontal lobe. What are the implications of these findings?

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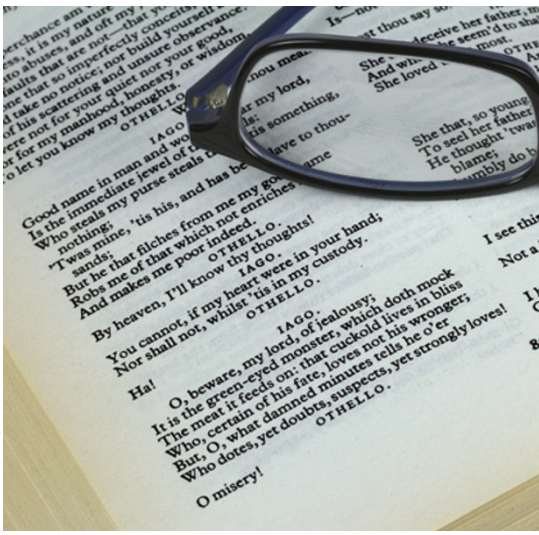
In a study published in the *European Journal of Neurology*, Graff-Radford *et al.* retrospectively reviewed the medical records of patients identified as having Othello syndrome—a condition associated with severe delusional jealousy—and investigated the clinical and imaging features in these individuals.[1] The authors have advanced current knowledge of delusional disorders by quantitatively examining neuroimaging features of this specific group of patients. The researchers used the Mayo Clinic medical records linkage and indexing system to retrospectively identify patients with possible Othello syndrome, probing the database using additional search terms including "delusions and infidelity" and "delusions of infidelity or jealousy". Their success highlights the importance of using detailed clinical databases for studying rare clinical phenomena—perhaps those who are not so meticulous should be jealous!

> "...cases of Othello syndrome and many cases of jealousy might not strictly meet DSM-IV criteria"

The term 'Othello syndrome' was coined by Todd and Dewhurst in 1954.[2] Their study included case histories of patients with predominantly psychiatric disorders, and a few patients with epilepsy, who had morbid delusions of infidelity. In his play of the same name, Shakespeare famously depicted Othello as being subject to intense feelings of jealousy that reached epic proportions. The Diagnostic and Statistical Manual, Fourth Edition, Text Revision (DSM-IV TR) includes a category titled 'Delusional Disorder—Jealous Type', which excludes coexistent psychiatric disorders, such as depression or other psychotic disorders, as well as secondary causes such as dementia or structural lesions; therefore, cases of Othello syndrome and many cases of jealousy might not strictly meet DSM-IV criteria.[3] Todd and Dewhurst suggested that morbid jealousy was a hereditary disorder, a view that is not prevalent today; however, genetic factors may be associated with delusions in some degenerative disorders, such as Alzheimer disease (AD).[4] Othello syndrome is a psychotic disorder that often occurs in the context of medical or neurological disorders, although its biological basis is not fully understood. Patients with this syndrome can be life-threatening to the person who is the object of jealousy, highlighting the importance of recognizing individuals with the condition.

Psychotic symptoms, including hallucinations (defined as false sensory perceptions) and delusions (defined as false beliefs), are not uniform in their biological bases. Models of delusional misidentification and duplication have been proposed, and these delusions are commonly associated with bifrontal and/or right hemispheric lesions. These models highlight the dual effects of loss of function due to damage of the right hemisphere and release of inhibition due to overactivity of the intact left hemisphere.[5,6] The functions of the right hemisphere include the ability to relate oneself to the internal and external world, self-monitoring, and the detection of anomalies; thus, the right hemisphere acts as an "inhibitor of mentation and behavior."[5,6] The left hemisphere creates an interpretation of the world, which could be fueled by 'false evidence' and cause an individual to jump to conclusions; thus, the left hemisphere acts as an "activator of mentation and behavior."[6]



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The heterogeneity of psychotic symptoms is highlighted by Nagahama *et al.*,[7] who used Tc-hexamethylpropyleneamine oxime single-photon emission CT scans to examine cerebral patterns of psychosis in patients who had dementia with Lewy bodies. Distinct patterns of cerebral hypoperfusion were found in left limbic regions and the bilateral frontal operculum of patients with delusional misidentifications, and in the bilateral angular gyri, right supramarginal gyrus, and left occipital lobe of patients with visual hallucinations. Patients with other delusions, such as delusions of theft or persecution, showed hyperperfusion of

both hemispheres, particularly in the right rostral medial frontal cortex.[7]

Of the 105 patients with putative Othello syndrome who were identified in the Mayo Clinic study, 73 had an associated neurological disorder.[1] The analysis showed that seven of the eight patients with brain lesions had structural abnormalities in the right frontal lobe, consistent with a study by Braun *et al.* that systematically examined structural lesions in patients with delusions and found most of them to have damage in the right hemisphere.[6] Graff-Radford and colleagues used voxel-based morphometry to compare volumetric MRI scans of 14 patients with Othello syndrome associated with a neurodegenerative disease (five patients with DLB, six patients with AD, and three patients with behavioral variant frontotemporal dementia), 14 patients matched for clinical neurodegenerative diagnoses without Othello syndrome, and 14 healthy control individuals. In patients with Othello syndrome, gray matter loss was greater in the dorsolateral frontal lobes, particularly in the superior frontal gyri, and the right posterior lateral temporal lobe, compared with the matched patients without Othello syndrome.[1] Changes in the right superior frontal lobe and posterior temporal lobe were common features across all patients with neurodegenerative disorders.

> “Of the 105 patients with putative Othello syndrome ... 73 had an associated neurological disorder”

Although many patients with Othello syndrome or delusional jealousy are described in the scientific literature as having an organic CNS disorder—a finding confirmed in this large case series[1]—this association may depend on the clinical setting. In a study of patients admitted to a major psychiatric hospital, the prevalence of delusional jealousy was 0.5% (72 of 14,309 admissions), and the majority of the patients with delusional jealousy had a primary psychotic disorder.[8] Some of the patients included in the 1955 study[2] might have had degenerative or structural disorders, but the techniques to identify these conditions were not available at the time. Todd and Dewhurst's paper[2] reminds us that Bleuler (whose seminal work has its centenary this year) had previously recognized delusions of infidelity in patients with schizophrenia.[9] Schizophrenia is associated with damage or modifications to the right frontal and temporal lobes of the brain, as illustrated in an MRI study in untreated patients with schizophrenia, which showed volume loss in these patients, along with functional network changes, that correlated with symptom severity.[10]

A total of 32 patients with Othello syndrome in the Mayo Clinic study had psychiatric disorders.[1] These were predominantly delusional disorders, although other syndromes, including depression, were present in some individuals. In specific patients, drugs, including dopamine agonists (in parkinsonian patients), methamphetamine, valproic acid, and polypharmacy, were associated with syndrome induction. The symptoms of Othello syndrome improved when drug doses were reduced or discontinued or when dopamine antagonists were used,[1] highlighting the possible role of neurochemical changes (particularly in the dopaminergic system) in these delusions. Coexistent delusions and hallucinations were frequent in all patients with Othello syndrome, occurring in approximately 30% and 40% of patients, respectively.[1]

The majority (62%) of patients with Othello syndrome in the study by Graff-Radford *et al.* were male,[1] consistent with the findings from a psychiatric study by Soyka and Shmidt.[8] Like “the Moorish captain” himself, Rodrigo and Iago (other male characters in the play) are also envious (of Othello), whereas the women in the play do not seem to be as prominently motivated by jealousy. Othello does not have a predisposing condition, such as diabetes or syphilis, although Iago suspects another diagnosis that could be associated with the syndrome: “My lord is fall'n into an epilepsy; this is his second fit; he had one yesterday.” Late in the play Othello “falls into a trance” after a tirade—does this fluctuating cognition suggest that Othello has dementia with Lewy bodies? We cannot determine from the script whether Othello meets the diagnostic criteria for dementia, but his occupation as a soldier would put him at risk of brain injury or trauma. The effect of alcoholism is another consideration in the cases of delusional jealousy that were described by Todd and Dewhurst,[2] yet while Othello's colleagues seem to be prone to drinking, he himself is not. In the discussion, Graff-Radford *et al.* remind us that a hypothesis linking the loss of frontal lobe function (particularly the right frontal lobe) to delusions suggests a role for this area of the brain in monitoring the interaction between ourselves and others. Othello clearly has impaired insight into the behaviors of his colleagues and his wife.

Paradoxically, it is not clear that Othello actually had Othello syndrome. Whether his symptoms were related to a psychiatric or degenerative disorder or to a structural lesion is unclear. Sadly, no autopsy was performed and we have no imaging findings—only our imagination. Mitigating factors in Othello's sad tale include the conspiracy of his circle of associates, which may have given Othello reason to be paranoid and delusional. When referring to jealousy, Shakespeare's character Emilia states “tis a monster, born upon itself, born on itself.” The study by Graff-Radford *et al.* may not reveal the cause of Othello's agonies, but we now know a little more about why this “green-eyed monster” affects our patients' minds.

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Competing interests
The author declares no competing interests.

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