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Olfactory function and alternation learning in eating disorders

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Abstract

Orbitofrontal dysfunction is a prominent feature of obsessive compulsive disorder (OCD). In the present study we assessed orbitofrontal functioning in eating disorders (EDs) which share many features with OCD. For this purpose we studied female adolescent inpatients with anorexia nervosa restricting type (n=40), anorexia nervosa binge/purge type (n=23), a normal weight group including patients with either bulimia nervosa or eating disorder not otherwise specified-purging type (n=33), and 20 non-ED control females. Patients were assessed at admission, and when achieving weight restoration and symptom stabilization at discharge, for depression, non-ED, and ED-related OC symptoms. Orbitofrontal functioning was assessed with an alternation learning task, and with a battery assessing olfactory threshold and discrimination. Control females were assessed once. ED patients of all subtypes performed better on olfactory threshold and discrimination, but not on alternation learning, in comparison to healthy controls. More favorable orbitofrontal functioning was associated with greater ED-related obsessionality. No changes were found in olfactory threshold and discrimination between acutely-ill and symptomatically-stabilized patients. The improvement shown in alternation learning from admission to discharge was suggested to reflect a learning effect rather than being an actual change. Our findings suggest that the better orbitofrontal functioning of ED patients in comparison to healthy controls may represent

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a core feature of the ED that is independent of malnutrition and deranged eating behaviors, but is associated with ED-related obsessionality.

1. Introduction

Eating disorders (EDs) are considered a major disease of the modern world, being among the most prevailing public health problems in female adolescents and young adults in recent decades. Traditionally regarded as socio-cultural disturbances related to issues of weight and shape (Weisman et al., 1992), there is currently a growing understanding that EDs are associated at least to some degree with altered brain functioning (Kerem and Katzman, 2003).

The relevance of brain dysfunction in EDs has its roots in the association found between starvation and both structural brain abnormalities (Golden et al., 1996) and neurocognitive derangements (Szmukler et al., 1992). Moreover, adequate functioning in several brain areas including the medial and orbitofrontal cortex, the hypothalamus, amygdala, limbic system, insula, and brain stem, and integrated interactions among these areas is considered essential for normal food-intake and normal eating behavior (Price, 1999).

Indeed, disturbances in different neurocognitive functions may be associated with pathological eating behaviors. These include impulse control (Brand et al., 2007), visuo-spatial abilities (Kingston et al., 1996), cognitive flexibility, set shifting, central coherence (Oberndorfer et al., 2011), problem solving, decision making (Szmukler et al., 1992; Kingston et al., 1996), and verbal and working memory (Green et al., 1996). These disturbances have been found in both anorexia nervosa (AN; Szmukler et al., 1992; Gillberg et al., 2007) and bulimia nervosa (BN; Brand et al., 2007) patients in comparison to healthy controls. Some of these disturbances, including in attention, concentration, visuo-spatial capabilities and problem-solving may improve with ED-related symptomatic improvement (Szmukler et al., 1992; Kingston et al., 1996; Gillberg et al., 2007), whereas disturbances in memory, as well as prolonged reaction time, cognitive over-control, and rigid set shifting may persist also in long-term asymptomatic patients (Green et al., 1996; Oberndorfer et al., 2011). The cognitive disturbances in EDs may be considered an at-risk pre-morbid propensity, and/or be the result of starvation, ED-related metabolic changes, structural and functional brain abnormalities, and/or comorbid psychiatric disturbances (Kerem and Katzman, 2003).

Structural brain imaging studies have found reduced gray and white matter in symptomatic AN and BN patients. Most (Wagner et al., 2006), although not all (Kingston et al., 1996), of these abnormalities return to normal with recovery. Functional task-activation brain imaging studies have mostly found diminished activity in AN and BN vs. control patients in brain regions involved in food intake such as the prefrontal (including medial and orbitofrontal), temporal (including the amygdala), parietal, occipital, insular, and/or cingulate regions in resting conditions (Delvenne et al., 1999; Oberndorfer et al., 2011), but greater activity in some of these regions when exposed to visual food-related challenges (Karhunen et al., 2000; Uher et al., 2004). Some of the disturbances in imaging studies may persist also in recovered ED patients (Uher et al., 2004; Oberndorfer et al., 2011). A few studies in AN patients have found an association between structural (Joos et al., 2010) and functional (Lask et al., 2005) brain alterations and cognitive deficits.

The aim of the present study is to investigate the relevance of cognitive dysfunction in EDs from a different angle, via their interrelationships with obsessive compulsive disorder. Thus, eating-related preoccupations and behaviors in ED patients are often highly obsessional (Rothenberg, 1986), and ED patients and their first degree relatives show elevated rates of OCD in comparison to healthy controls and their first-degree relatives (Lilenfeld et al., 1998).

Orbitofrontal dysfunction is considered a prominent feature of OCD (Hermesh et al., 1999). Our group (Gross-Isseroff et al., 1996; Hermesh et al., 1999) has previously studied OCD patients with two tasks assessing orbitofrontal functioning, alternation learning and odor quality discrimination. Alternation learning is a problem solving test in which the participant has to learn the rules deciding where an object is hidden. Adequate performance is based on the ability to update and maintain the rules related to the task, to ignore irrelevant information, and to inhibit wrong choices. Alternation tests have been developed for testing problem-solving behavior after orbitofrontal lesions in non-human primates (Mishkin et al., 1969). An adaptation of this test has been subsequently used to test orbitofrontal functioning in humans (Abbruzzese et al., 1995). OCD patients tend to perform poorly on this task in comparison to normal controls (Abbruzzese et al., 1995; Gross-Isseroff et al., 1996).

In the olfactory task, participants are required to identify odorants from non-odorant solvents (threshold), and to discriminate among different odorants. Physiological studies in non-human primates (Thorpe et al., 1983) and behavioral studies in human subjects (Zatorre et al., 1992) have found that the orbitofrontal cortex is involved in odor quality discrimination. The findings of studies using this task in OCD are inconclusive. Thus, whereas some studies have found impairment in OCD patients (Goldberg et al., 1991), others have failed to show differences in this task between OCD patients and healthy controls (Hermesh et al., 1999).

Reviewing the literature we have found only a few studies assessing olfactory functioning in EDs (to the best of our knowledge alternation learning has not been assessed previously in EDs). The findings of these studies are conflicting, likely reflecting differences in the tools and odorants used for the assessment of olfactory functioning, heterogeneity of the ED diagnosis, and relatively small sample sizes. Thus, some studies have found no differences in olfactory threshold and discrimination between ED patients and controls (Kopala et al., 1995; Rapps et al., 2010), whereas other have shown that only very low weight AN patients may differ in these tasks from controls (Fedoroff et al., 1995). Still other studies have found a reduction in olfactory discrimination, but not in olfactory threshold, in AN vs. control (Roessner et al., 2005;